SİİRT Bilimin Işığında ÜNİVERSİTESİ

9th INTERNATIONAL CONFERENCE ON MEDICAL & HEALTH SCIENCES

MAY 15-19, 2025 / DUBAI, UAE

CONFERENCE PROCEEDINGS BOOK

EDITORS

Assoc. Prof. Dr. H. Turan AKKOYUN

Spec. Dt. Elif BAŞTUĞ GÜVEN



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adopted by Mariam Rasulan

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(Abstracts & Full Texts)

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EVALUATION PROCESS and POLICIES

All applications have undergone double blind peer review process. In addition, each paper was accepted and the process of publishing in the book was carried out through editorial oversight. The published papers were presented and discussed at the meeting.

Full texts and abstracts published in accordance with the Symposium Policy have been prepared in accordance with ethical rules and APA standards. Authors of all papers are both ethically and legally responsible.

PARTICIPANTS COUNTRIES

Türkiye, Algeria, Azerbaijan, Bulgaria, Chennai, Germany, Georgia, India, Italy, Iran, Kosovo, Macedonia, Morocco, Nigeria, Pakistan, Romania, Ukraine

TOTAL ACCEPTED ARTICLES: 281

The Number of Accepted Papers from Türkiye: 129
The Number of Accepted Full Papers from Other Countries: 152
The Number of Total Papers: 281

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May 15 - 19, 2025

Dubai, UAE

SYMPOSIUM SCHEDULE



9th INTERNATIONAL CONFERENCE ON MEDICAL & HEALTH SCIENCES

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CONFERENCE PROGRAM

ONLINE & IN-PERSON PRESENTATIONS

ZOOM ID: 860 5266 6988 / PASSCODE: 151617

https://us02web.zoom.us/j/86052666988?pwd=slrkXlwXwpCdGYWHvp5w3OJrQYLWT9.1

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Face to Face / SWISSOTEL AL GHURAIR

18.05.2025	HALL-1 / SESSION-1

DUBAI LOCAL TIME: 10:00-12:00

HEAD OF SESSION: Prof. Dr. Nurhan DOĞAN

Authors	Affiliation	Presentation Title
Kübra Geçmez Cahan H. Turan Akkoyun Mahire Bayramoğlu Akkoyun Meltem Sağiroğlu	*Siirt University*	Caudamin involved in tumors and metabolic disorders: endotrophin
Kübra Geçmez Cahan Meltem Sağiroğlu H. Turan Akkoyun Mahire Bayramoğlu Akkoyun	*Siirt University*	Spexin as an adipokine and its functions
Zahide Yusra Yildiz Sema Gürgöze	*Siirt University*	New therapeutic targets myokines: myonectin
Sonay Değirmen Secem Özcelik Oğuz Özcelik Sermin Algül	*Van Yuzuncu Yıl University*	Assessing healthy body composition: a consensus on body mass index, fat mass percentage, and waist-to- hip ratio
Mesrure Ataş A. Ezgi Telli	*Selcuk University*	Biofilm formation in foodborne pathogens: mechanisms, associated genes and detection methods
Özcan Deveci Dünya Başol	*Infectious Diseases and Clinical Microbiology, Private Genesis Hospital*	Microbiological developments in bioterrorism
Dilan Dali Adnan Girti Taha Güven	*SBU Van Training and Research Hospital*	Angiokeratoma Circumscriptum: A Case Report
Nurhan Doğan Ismet Doğan	*Afyonkarahisar Health Sciences University*	Power analysis and sample size: theoretical foundations, types, and their role in research planning
Ayşe Şahin	*Kırsehir Ahi Evran University*	Determining social network fatigue levels of students at a public university based on their use of social platforms

(All speakers required to be connected to the session 10 min before the session starts)
Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

Face to Face / SWISSOTEL AL GHURAIR

18.05.2025 | HALL-2 / SESSION-1

DUBAI LOCAL TIME: 10:00-12:00

HEAD OF SESSION: Prof. Dr. Erdoğan ÖZTÜRK

Authors	Affiliation	Presentation Title
Tülay Gürsoy Gülen Önal Karakoyun	*Van Yuzuncu Yil University*	Grass plant (*Lolium* L.) as a bioindicator: Heavy metal content and toxicity
Sevgi Güneş Mehmet Üyüklü	*Siirt University*	The effect of cellular damage and suspension environment on blood fluıdity
Halide Temelci Rukiye Sumeyye Bakıcı Zulal Oner Serkan Oner Şeyma Toy	*İzmir Bakırcay University*	Morphometric analysis by computed tomography of the entry point and trajectory for safe screw fixation surgery of the C2 pedicuncle in the Turkish population according to age and gender
Selahattin Gönaylı Akın Temizer Sevinç Aydın Görkem Kırmızıkaya Tuba Okutan Ökkeş Yılmaz	*Fırat University*	Comparison of antioxidant activities of organic tomato (*Solanum lycopersicum* L.) and red pepper (*Capsicum annuum* L.) extracts against H2O2 toxicity
Serhat Koran	*Istanbul Medipol University*	The place of traditional medicine in preventive medicine
Seda Uğraş	*Mardin Artuklu University*	The metabolic transition points during incremental exercise test: Establishing moderate to heavy exercise intensity
Aziz Kılınç Feyza Açıkbaşağaoğlu Ali Emrah Bıyıklı	*Alanya Alaaddin Keykubat University*	Effect of some food components and diet patterns on Parkinson's disease
Şüheda İlhan Adile Can İlhan Seda Uğraş	*Mardin Artuklu University*	The effect of reformer Pilates during pregnancy on body awareness, balance, and vaginal delivery: A controlled clinical study
Feyza Açıkbaşağaoğlu Ezgi Toptaş Bıyıklı	*Alanya Alaaddin Keykubat University*	Current dietary approaches in irritable bowel syndrome

(All speakers required to be connected to the session 10 min before the session starts)
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Face to Face / SWISSOTEL AL GHURAIR

18.05.2025 HALL-3 / SESSION-1

DUBAI LOCAL TIME: 10:00-12:00

HEAD OF SESSION: Prof. Dr. Meltem SOYLU

Authors	Affiliation	Presentation Title
Şura Boyraz	*Yozgat Bozok University*	Capping in dentistry
Hava Bektas	*Van Yuzuncu Yil University*	Effects of radiofrequency radiation on oxidative stress and histopathological changes in liver tissue: An evaluation of current findings
Eda Şahin Cılız Meltem Soylu	*Alanya Alaaddin Keykubat University*	The relationship between macronutrient intake and diet glycemic load in cardiovascular patients
Ayşe Şeker Bahar Olmez	*Van Yuzuncu Yil University*	The modulatory role of the immune system in neuropathic pain: Cellular and molecular mechanisms
Ayşe Şeker Zehra Arslan	*Van Yuzuncu Yil University*	The interaction between metabolic syndrome and diabetic neuropathy: Mechanisms and therapeutic approaches
Meltem Soylu Eda Erkmen	*Alanya Alaaddin Keykubat University*	Dietary carcinogens
Selin GÜNEŞ Merve Bahçekapılı Sevgi GÜNEŞ Naci Ömer Alayunt	*Avrasya University*	The Impact of Nutrition on Neurodevelopmental and Psychosocial Health in Early Childhood
Merve Bahçekapılı Selin GÜNEŞ Sevgi GÜNEŞ Naci Ömer Alayunt	*Avrasya University*	The Impact of Sensory Play on the Immune System and Psychological Health in the Preschool Period
Turgut Dolanbay Naci Ömer Alayunt	*Siirt University*	Neurofilament light chain (NFL): An emerging biomarker for early detection of acute neurological injury in the emergency department
Naci Ömer Alayunt Turgut Dolanbay	*Siirt University*	Biochemical causes of phosphorylated tau increase: Critical clues for Alzheimer's

(All speakers required to be connected to the session 10 min before the session starts)
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ONLINE SESSION / 15.05.2025

HALL-1 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Enes Dalmanoğlu

Authors	Affiliation	Presentation title
Enes Dalmanoğlu	*Balikesir University*	Bibliometric analysis of publications on varicella zoster virus in the Web of Science database
Özge Özgenç Çınar Ahmet Ceylan	*Ankara University*	Evaluating the cytotoxic and proliferative effects of bee venom on prostate cancer cells: Insights from LNCaP cells
Elif Ece Akgün	*Ataturk University*	The protective effect of lycopene on liver disease
Elif Ece Akgün	*Ataturk University*	The chondrogenic effect of kartogenin on mesenchymal stem cells
Seda Nur Abatay Asiye Akyol	*Ankara Etlik City Hospital*	Acute kidney injury due to COVID-19 and nursing care
Işıl Duran Serap Altuntaş	*Bandırma Onyedi Eylul University*	Causes and consequences of nurse workforce migration
Fatma Atlı Çağrı Kandemir Turgay Taşkın	*Ege University*	Blowfly strike and the importance of sheep breeding
Fatma Atlı Turgay Taşkın Çağrı Kandemir	*Ege University*	In animal health, an approach to the health-prevention is better than cure strategy: The example of EU countries

(All speakers required to be connected to the session 10 min before the session starts)
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ONLINE SESSION / 15.05.2025

HALL-2 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Özlem DELIBAŞ

Authors	Affiliation	Presentation title
Özlem Delibaş Serpil Ünver Saraydın	*Sivas Cumhuriyet University*	The histological examination of adipose tissue in PCOS mice
Kıymet Aygün Atiye Karakul Duygu Sönmez Düzkaya	*Tarsus University*	Evidence-based practices in newborns: Baby massage
Kıymet Aygün Atiye Karakul Duygu Sönmez Düzkaya	*Tarsus University*	Evidence-based practices in newborn: Skin care practices
Halil Ayhan Sema Gürgöze	*Ministry of Agriculture*	Effects of age and sex on hematological parameters in thoroughbred and arabian horses
Ayşe Nur Balaban	*Saglik Bilimleri University*	Atypical clinical findings in benign paroxysmal positional vertigo: Two case reports.
Sermin Algül Sonay Değirmen Ecem Özçelik Oğuz Özçelik	*Van Yuzuncu Yil University*	Healthy body composition: Consensus among the body mass index, fat mass percent, and waist-to-hip ratio
Şükran Ceyhan	*Kahramankazan State Hospital*	Presenteeism in health workers: An invisible risk
Melek Akıncı Çağatay Oltulu Elvan Bakar	*Trakya University*	Protective role of galangin against methotrexate-induced damage in AML12 cells

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ONLINE SESSION / 15.05.2025

HALL-3 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Ahmet AKÇAY

Authors	Affiliation	Presentation title
Yasemin Özdemir Şahan Emine Gülşah Torun	*Malatya Training and Research Hospital*	Evaluation of children referred to a pediatric cardiology outpatient clinic at a tertiary center for pre-participation sports examination
Nesrin Aştı Pervin Tunç	*Demiroglu Bilim University*	A pragmatic approach to the worth and value of the human and health care professional
Gamze Erkılınç	*Bakircay University*	Retrospective analysis of molluscum contagiosum results in skin excision biopsies
Arife Nisa Ak Aylin Seylam Küşümler	*Istanbul Okan University*	The role of the ketogenic diet in drug-resistant epilepsy
Erkan Özkan Caner Öztürk Neşe Hayat Aksoy	*Aksaray University*	Effects of PDE5 inhibitors on cGMP, PKG, and protein metabolism in spermatogenesis
Şevval Öz Üstün Aslı Kurtgöz	*Amasya University*	Determination of nursing students' knowledge levels regarding medical device-related pressure injuries
Ahmet Akçay	*Bezmialem Vakıf Universitesi*	Novel preoperative CT-derived parameters to enhance SEMS outcomes in obstructive colorectal cancer
Esra Bilici	*Usak University*	Recombinant DNA

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ONLINE SESSION / 15.05.2025

HALL-4 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Yousra Anwar

Authors	Affiliation	Presentation title
Tengiz Kantaria Temur Kantaria David Makharadze Nino Zavradashvili Nodar Sulashvili Ramaz Katsarava Lali Patsia Igor Seniuk David Aphkhazava	*The University of Georgia*	Core aspects of enhancing the capabilities and versatility of degradable triazole 'click' polymer libraries for broad biomedical applications: Progress, obstacles, strategies for future development and innovative practical solutions
Nodar Sulashvili Nana Gorgaslidze	*The University of Georgia*	Investigating the deep environmental impact of medication waste, their effects on natural systems: Public health threats, intricate relationships, risk analysis, holistic solutions, and the need for advanced hazard assessment
Nodar Sulashvili Nana Gorgaslidze Tamar Tsintsadze Marika Sulashvili Lali Patsia	*The University of Georgia*	The academic discourse on pharmacy professionals' career outlooks: Insights and assessments of critical factors shaping occupational growth for pharmacists in Georgia, overall
Lali Patsia Ketevan Lartsuliani Nodar Sulashvili Nana Gorgaslidze Marika Sulashvili	*The University of Georgia*	The key issue features of wearable-device-identified rapid heart rhythm – Innovative tech advancements supporting medical care (A case report)
Brahim Ennasraoui Amane Jada Abdelaziz Ait Addi	*Ibn Zohr University*	Nanocomposites of gCN/BiOCl/Ag2MoO4 are designed for superior sunlight sensitivity, enhancing the photocatalytic breakdown of OG dye
Ikram Saliha Benayahıa Wefa Boughrara Amina Lakmeche Fatma Belhoucıne Amel Alıoua Berrebbah	*University of Science and Technology of Oran Mohamed Boudiaf*	Risk factors and impact of taxane toxicity in lung cancer treatment
Yousra Anwar	*David Tvildiani Medical University*	Advancing surgical precision: A novel approach using personalized 3D printing in complex spinal osteotomy for ankylosing spondylitis-related kyphoscoliosis
Sadaf Rehman Sadia Saleem Sayyeda Taskeen Zahra	*University of Management & Technology*	Unpacking the complexities of dating violence: A moderated-mediation analysis of optimism, self-confidence, honesty, and emotional distress in young adults. Acknowledgement and credits:

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ONLINE SESSION / 15.05.2025

HALL-5 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Lətafət Beybutova Ələsgər qızı

Authors	Affiliation	Presentation title
Lətafət Beybutova Ələsgər qızı	*Elmi Arasdirmalar*	The nations which belong to Shahdagh group of languages
Soukaina El Bourachdi Amal Lahkimi	*Sidi Mohamed Ben Abdellah University*	Development of a novel low-cost adsorbent chitosan@EDTA@Cellulose composite to effectively remove methyl orange dye from wastewater: Experimental and theoretical investigation
Namazova Kamala Hasanov Fuad Mustafayev İsa Muradov Nizami Abbasova Mahrux Askerova Gunel Musayeva Narmina Mamedova Gunel	*Scientific Center of Surgery Named After Academician*	The importance of some biomarkers in the diagnosis of H1N1 viral pneumonia complicated by ARDS
Mammadov Aliniyaz Alieva Aygun Namazova Kamala Aliyeva Gunay Gunel Mamedova Behbudov Vugar	*Scientific Center of Surgery Named After Academician*	Evaluation of the function of the Vater's mouth in choledochoduodenal anastomoses with VEGDS
Taskeen Fatima Mehran Majeed Mahna Fatima Raheela Muqadus Areeba Arif Nabiha Iqbal Mah-ru-nisa Atif	*Hajvery University*	Correlation study on etiological factors of heart disease in diabetic patients in Lahore, Pakistan
Taskeen Fatıma Mahna Fatıma Areeba Arıf Mehran Majeed Raheela Muqadus	*Hajvery University*	Formulation and evaluation of OTF of cetirizine for rapid systemic action
Walter Chickenstein	*University of Helsinki*	Quantum chickens and their social behavior dynamics in parallel universes
Yassine El Allouche Sofia Elmarjany Abdellah Elaıssouq Hicham Zaıtan Fouad Khalıl	*Sidi Mohamed Ben Abdellah University*	Evaluating 3,5-disubstituted indole derivatives as Pim1 kinase inhibitors: In silico design and analysis of novel therapeutics for hematological cancer management

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ONLINE SESSION / 15.05.2025

HALL-6 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Gurleen Kaur

Authors	Affiliation	Presentation title
Sofia Eel Marjany Yassine El Allouche Abdellah Elaıssouq Hicham Zaıtan Fouad Khalıl	*Sidi Mohamed Ben Abdellah University*	Exploring Advanced Computational Approaches for Identification of Anti-prostate Cancer Compounds: 2D-QSAR, ADMET prediction, molecular Docking analysis
Lulzime Ballazhi Edita Alili-Idrizi Merita Dauti Sihana Ahmeti-Lika Gjylai Alia Drita Havziu-Yzeiri	*University of Tetovo*	Understanding disease-drug interactions: Implications for treatment and patient safety
Gurleen Kaur	*Llm Student Iilm Law University Gurgaon India*	Legal and ethical issues in organ transplantation: The Indian perspective
Gurleen Kaur	*Llm Student Iilm Law University Gurgaon India*	Bridging the gap: Public and private healthcare insurance in India's path to universal health coverage
Gheorghe Gıurgıu Manole Cojocaru	*Titu Maiorescu University*	What we know about psoriasis so far?
Tukaz Mammadova	*Scientific Research Institute of Pediatrics named after K.Y. Farajova*	Mathematical modeling of sepsis diagnosis
Rachda Rıffı Wefa Boughrara Wassila Ilıas Amina Chentouf	*Ecole Supérieure en Sciences Biologiques d'Oran (ESSBO)*	ABCB1 c.3435 C > T (rs1045642) as a biomarker for carbamazepine efficacy in Algerian patients with epilepsy
Dabla Fahd El Yamani Amal	*Moammed V University in Rabat*	The evolution of dental zirconia: From conventional to hyper-translucent

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ONLINE SESSION / 15.05.2025

HALL-1 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Seda TAŞDEMIR

Authors	Affiliation	Presentation title
Seda Taşdemir	*Inonu University*	The gut–blood pressure connection: Microbiota's role in hypertension and drug response
Seda Taşdemir	*Inonu University*	Vascular protective mechanisms of SGLT-2 inhibitors: Beyond glucose lowering
Derya Balcan Haluk Tanrıverdi Suzan Ergn	*Istanbul Nisantası University*	Zero waste project approach for a safe environment
Derya Sahın Ozturkcan Nadire Unver Dogan Serefnur Ozturk Mustafa Koplay Ahmet Kagan Karabulut Zeliha Fazliogullari	*Yuksek Ihtisas University*	Evaluation of thalamus, hippocampus, and cerebellum volumes and three-dimensional visualization in multiple sclerosis patients
Derya Balcan Haluk Tanrıverdi Suzan Ergun	*Istanbul Nisantası University*	Examination of the effect of personnel practices on costs in medical waste management
Meryem Elif ÖZTÜRK Yeşim Arslan Gizem Bilgin Nazife Merve Çiftci Hatice Kübra Haktanır Evin Kara	*Karamanoglu Mehmetbey University*	The relationship between breakfast habits of school-age children and mothers' nutritional knowledge and attitudes
Arda Özdemir	*Siirt Research and Education Hospital*	Hypothermic injuries in plastic surgery
Aynur Müdüroğlu Kırmızıbekmez	*Istanbul Nisantası University*	The inhibitory effects of Aronia melanocarpa on NO, iNOS, and COX-2 in LPS-stimulated BV-2 cells

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ONLINE SESSION / 15.05.2025

HALL-2 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Benay TÜFEKÇI

Authors	Affiliation	Presentation title
Aliye Arkan	*Yıldız Technical University*	Production and characterization of a wound dressing based on polyvinyl alcohol (PVA) and chitosan (CS) incorporated with Pteridium aquilinum (PA) fern extract
Hilal Doğan	*Health Sciences University*	Analysis of radiation dose levels for patient caregivers in PET/CT units
Tuğba Türkkan Ahmet Burhan Çakıcı	*Gümüshane University*	Stigma associated with addiction: Psychological consequences and intervention recommendations
Gamze Uzun Serkan Bentli	*Malatya Turgut Özal University*	Effects of eating disorders diagnosed during pregnancy and pre-pregnancy on maternal and baby health
Ezgi Kara Serkan Bentli	*Malatya Turgut Özal University*	Mediterranean diet and sustainability
Mehmet Hanifi Yalçın Mahmut Şamil Şamlı Cafer Tayyar Ateş	*Necmettin Erbakan University*	Weight-based properties of ostrich egg
Benay Tüfekçi	*Istanbul Nisantası University*	Investigation of the relationship between genetic polymorphisms and Parkinson's disease: A case-control study
Erkan Bilgin	*Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital*	Experience with totally implantable venous access ports in patients with hematological malignancies

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ONLINE SESSION / 15.05.2025

HALL-3 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Neşe İşcan Ayyıldız

Authors	Affiliation	Presentation title
Halime Bozkurt Büşra Altınel	*Selcuk University*	Health literacy and women's health
Nupelda Akbal Tülay Yıldırım Üşenmez	*Dicle University*	Sleep quality and affecting factors in mental illnesses
Muhammed Tekinhatun	*Dicle University*	Isolated coronary sinus atresia with direct drainage of cardiac veins into the left atrium: A rare anatomical variant identified by cardiac CT
Cansu Yılmaz Güler Balcı Alparslan	*Balıkesir Atatürk City Hospital Intensive Care Unit*	Spontaneous subcutaneous emphysema in a COPD patient: A clinical nursing case report
Ümmühan Kandemir Derya Osmaniye Cevşen Yazıcı Özgür Devrim Can Ümide Demir Özkay	*Bilecik Şeyh Edebali University*	Antidepressant effects of some phenylpropionic acid derivatives in chronic unpredictable mild stress-induced rat model of depression
Neşe İşcan Ayyıldız	*Trabzon University*	Alexithymia in epilepsy
Neşe İşcan Ayyıldız	*Trabzon University*	Breast CA risk levels and cancer screening behaviors in women living in rural areas of Turkey: A descriptive and correlational study
Aylin Demiryürek Cemil Yıldız Rabia Tuğba Tekin	*Ankara Yıldırım Beyazıt University*	Efficacy of craniosacral therapy in patients with gonarthrosis

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ONLINE SESSION / 15.05.2025

HALL-4 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Irina-Ana Drobot

Authors	Affiliation	Presentation title
Barbora Dauderytė Daumantas Kondratavičius Milda Pucėtaitė	*Lithuanian University of Health Sciences*	CT-based diagnostic insights in a rare case of laryngeal tuberculosis
Deona Taraj Denada Selfo Majlinda Rakipaj Neada Cakerri	*University of Vlorë*	Immunization in doubt: Addressing the roots of vaccine hesitancy
Irina-Ana Drobot	*Technical University of Civil Engineering Bucharest*	Will artificial intelligence replace psychotherapists?
Etibaria Belghalıa Farid Elbamtari Motasim Jawi Abdelkrim Guendouzi Abdelouahid SBAI M'barek Choukrad Tahar Lakhlıfı Mohammed Bouachrıne	*University Moulay Ismail*	Pyrazole-benzimidazole derivatives targeting MCF-7 breast cancer cells as potential anti-proliferative agents: 3D QSAR and in-silico investigations via molecular docking and molecular dynamics simulations
Busari M. B. Hamzah R. U. Yusuf R. S. Yahaya, A. S. Oladejo N. A.	*Federal University of Technology Minna*	Comparative qualitative phytochemical contents and antimicrobial activities of methanol extract of Calotropis procera flower and latex
Aloui Mourad Menana Elhalaoui	*Sidi Mohamed Ben Abdellah University*	Rational design of potent and selective survivin inhibitors based on MX-106 hydroxyquinoline derivatives: A 2D-QSAR, molecular docking, dynamics, and ADMET study

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ONLINE SESSION / 15.05.2025

HALL-5 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Ayesha Batool

Authors	Affiliation	Presentation title
Agaba Halidu Oladımejı Olusegun Michael	*University of Abuja*	The African Union on sociopolitical stability in Africa: Achievements and challenges, 2002-2022
Said AIT Messaad Nourdine El Harrar Miloud Chakıt	*Higher Institute of Nursing Professions and Health Techniques*	Epidemiological investigation of intestinal parasites in children hospitalized at Moulay Abdellah Hospital Sale (Morocco)
Ayesha Batool	*University of Agriculture*	Investigating the drivers of global health inequities: A multidisciplinary study of access, policy, and social determinants
Monika LOPUSZANSKA-DAWID Bartosz MOLIK Katarzyna MILDE Paweł TOMASZEWSKI	*Józef Piłsudski University*	Family determinants of children's participation in the Polish national project: "PE with UPE: Active return to school and active today for health in the future
Zdravka Harizanova Ferihan Popova Atanas Baltadjiev Zlatizara Todorova Vyara Zaykova Elena Bozhikova	*Medical University - Plovdiv*	Dimensions of lower teeth in Bulgarian population
Ram Prataap Yadav Sunil Kumar Srivastav	*DDU Gorakhpur University*	Ameliorative effect of Jamun (Syzygium cumini) seed and orange (Citrus sinensis) peel extracts against lead-induced alteration in liver biomarkers of rats
Sushovan Khatua Debashis De	*Maulana Abul Kalam Azad University of Technology*	Blockchain-based sustainable transportation framework in IOVT
K.R.Padma K.R.Don	*Women's University*	From cup to cure: Silver nanoparticles synthesized from butterfly pea and ginger herbal tea for diabetes and obesity management

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ONLINE SESSION / 15.05.2025

HALL-6 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Subhashish Dey

Authors	Affiliation	Presentation title
Gunasekar G	*Tamil Nadu Agricultural University*	Biochemical basis for insecticide resistance
Subhashish Dey	*Gudlavalleru Engineering College*	Experimental production and comparison of biogas using co-digestion of organic waste
Surajit Sarkar Amitabha das	*Jadavpur University Kolkata*	FPGA-based data handling for deep-space applications under power and computing constraints
Mostapha Abourrich Rachida Elbarghmi Nadira Mourabit Samia Boussa Hossain El Ouarghi	*Laboratory of Applied Sciences*	Water, sanitation, and hygiene in health care facilities in the province of Al-Hoceima (Morocco): Status and prospects
Tasawar Iqbal Sidra Altaf	*University of Agriculture*	Green tea as a therapeutic agent: Exploring its anti-inflammatory and immunomodulatory roles in rheumatoid arthritis management
Saheed A. Adekola Musa A. Muhibi Mathew F. Olaniyan	*University of Abuja*	MicroRNA 21 and prostate in Nigeria, a review study
Anam Shoukat Afshan Naseem	*University of Management and Technology*	Effectiveness of concept mapping in enhancing science achievement of grade 8 students
Lorenzo Adamo Francesco Evolo Sofia Leporale Arianna Antonelli Niccolò Carrai Giuseppe Ferri Luca Testarelli Massimo Galli Gabriele Miccoli Rebecca Sylvie Palumbo Ludovica Lucente Rodolfo Reda	*Sapienza University of Rome*	Radiographic, clinical, and biochemical comparison of Cr-Co-ceramic implant-supported single crowns using screw or cement retention: A cohort study

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ONLINE SESSION / 15.05.2025

HALL-1 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Dr. Tuğçe ANTEPLIOĞLU

Authors	Affiliation	Presentation title
Merve Dokumacıoğlu Tülay Turgut Genç Gökhan Görgişen	*Çanakkale Onsekiz Mart University*	Insulin receptor substrate 1 (IRS1) and insulin receptor substrate 2 (IRS2) proteins with bioinformatics analyses in gastric cancer: What is explainable?
Saniye Merve Cengiz Tuğba Yılmaz	*Mersin University*	Treatment of a non-syndromic oligodontic case with a multidisciplinary orthodontic approach
Tuğçe Anteplioğlu	*Kırıkkale University*	Role of IGF2 in fibrotic responses to hepatic cystic echinococcosis in cattle
Işık Çelik Tuğba İduğ Hikmet Gülben Güç	*Istanbul University*	Evaluation of in vitro biological activity and quality-safety of food supplements containing Tribulus terrestris
Omer Eesmez Merve Yıldız Esmez Gulnihal Deniz	*Orthopedics, Fethi Sekin City Hospital*	Triple pathology: A rare case of intersection of aplastic anemia, chronic hepatitis B, and oral lichen planus
Cansu Öztürk Leyla Khorshtd Ülkü Güneş	*Ege University*	Retrospective investigation of complications encountered in the use of a drug called antithymocyte globulin (ATG) used in stem cell transplantation in pediatric patients
Melek Yüksel Leyla Khorshtd	*Ege University*	Effect of education given to nurses on prevention of medical device-related pressure injury on their knowledge level
Ahu Gizem Akkuş Berrak Varhan Hande Çağlıyan Erdoğan Yasemin Buran Çırak	*Istinye University*	The role of inspiratory muscle training supported by manual therapy in improving posture and functional mobility in neuromuscular diseases

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ONLINE SESSION / 15.05.2025

HALL-2 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Dr. Hasan Mansur Durgun

Authors	Affiliation	Presentation title
Sumeyye Yildirim Nevin Karakus Gokhan Aykun	*Tokat Gaziosmanpasa University*	Investigation of miR125a expression level in chronic obstructive lung disease
Nevin Karakus Sumeyye Yildirim	*Tokat Gaziosmanpasa University*	Investigation of miR22 in chronic obstructive pulmonary disease
Hasan Mansur Durgun	*Dicle University*	Case report: Diagnosis of aortic aneurysm in a patient admitting with left side pain
Hasan Mansur Durgun	*Dicle University*	A case of leptospirosis with fulminant course in the emergency department: Case report
Bişar Amaç Mesut Engin	*Harran University*	Effect of cardiopulmonary bypass on thyroid hormone levels

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ONLINE SESSION / 15.05.2025

HALL-3 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Dr. Fatma Karagözoğlu

Authors	Affiliation	Presentation title
Muhammed İbrahim	*Mosul Training and Research Hospital*	Advances in the treatment of cleft lip and palate using low-frequency vibration devices
Muhammed İbrahim	*Mosul Training and Research Hospital*	Locally use of dexamethasone injection in the treatment of aphthous ulcers
Fatma Karagözoğlu	*Dokuz Eylul University*	Effects of olive pomace on biochemical parameters, performance, carcass, and internal organs in poultry nutrition
Abdulsamed Enes Akın Özal Keleş	*Biruni University*	The effect of foot posture on dynamic and static balance in young individuals
Merve Öztürk Çağlayan Nuran Tosun	*Hasan Kalyoncu University*	Vocational school health programs students examination of occupational anxiety levels
Gülbeyaz Baran Durmaz Gülsüm Yıldırım	*Dicle University*	Illness experience of parents of children with special needs: Guilt - shame
Emine Karacan Bengisu Tüfekçi	*Gaziantep Islam Science and Technology University*	Digital identity and access problems of disabled individuals after disasters: A study on crypto technologies and blockchain-based solutions
Gulsah Yıldız Deniz	*Atatürk University*	Effects of Punica granatum flowers EXTRACT ON HEMATOLOGICAL PARAMETERS OF RATS EXPOSED TO CADMIUM CHLORIDE TOXICITY
Emine Karacan Ahmet Şahin	*Gaziantep Islam Science and Technology University*	The new face of climate change on health: A period of increasing antibiotic resistance

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ONLINE SESSION / 15.05.2025

HALL-4 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Franz Hessel

Authors	Affiliation	Presentation title
Nicholas Prosperi Andrea Morgante Andrea Luzi Lorenzo Adamo Marta Cianfriglia Elisa Maccari Alessandro Auletta Chiara Bramucci Rosemary Abbagnale Dario Di Nardo Luca Testarelli Rodolfo Reda	*University of Rome La Sapienza*	Clinical outcomes of full-arch implant-supported fixed prostheses in the edentulous maxilla: Implant survival and prosthetic complications
Andrea Luzi Alessandro Auletta Arianna Antonelli Francesco Evolo Nicholas Prosperi Gualtiero Gherardi Valeria Martini Alessio Zanza Sofia Leporale Marta Cianfriglia Luca Testarelli Rodolfo Reda	*Sapienza University of Rome*	Evaluation of clinical and biochemical outcomes in two variants of screw-retained single implant crowns
Chıke-Okolı Felıcıa Chıbuogwu Halıma Shehu	*Federal University of Technology*	Repositioning the teaching of spoken English in the 21st century secondary schools in Minna metropolis, Nigeria
Chahid Slımanı Abdellah Bahtat	*Sidi Mohamed Ben Abdellah University*	The impact of innovative healthcare technologies on medical liability
Franz Hessel,	*SRH University*	Personalized medicine on the rise – Opportunity or risk for worldwide healthcare systems?
Hablass A Hessel F	*SRH University*	Applications, challenges, and limitations of AI use in healthcare: An analysis of AI responses for drug information
Mohd Arsh Khan Zeba Ali Mumtaj Saimah Khan	*Integral University*	Advanced strategies for the removal of pharmaceuticals from wastewater
Muhammad Awais T. Salahuddin Farrukh Riaz Sana Sakinder Moeen Taj	*Mirpur University of Science and Technology*	Numerical simulation for the thermal and solutal system of unsteady naturally convective flow of Casson fluid near a vertical oscillating surface

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ONLINE SESSION / 15.05.2025

HALL-5 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Mirazim Zaidov

Authors	Affiliation	Presentation title
Vivekanand Kattimani Ratna Kumari Anantha	*SIBAR Institute of Dental Sciences*	Eggshell membrane: Past, present, and future in medical applications
Leila Sojoodi	*University of Tabriz*	In vitro study of piperine's effects on structural, functional, and kinetic properties of bovine liver catalase enzyme
Sidra Altaf Muhammad Ahsan Naeem Humaira Muzaffar	*University of Agriculture Faisalabad*	Targeting key enzymes in glucose metabolism: An in silico approach using phytochemicals from medicinal plants of Pakistan
Zehra Hashim Nida Syed	*University of Karachi*	Potential biomarkers and therapeutic targets for TNBC
Mirazim Zaidov	*Swiss Montreux Business School*	Syndromes that cause cleft lip and cleft palate
A.Ashwini M.K Vijayalakshmi E. Hamsini Eisha V, Selva Kumar S. Sheron Kevin V .Venkateshwaran	*Bharath University of Higher Education and Research*	Acalypha indica: Phytochemical constituents, traditional uses, and pharmacological properties: A review
AR Sami A Baqi AM Sami AR Carmichael	*University Hospital of Derby and Burton NHS Foundation Trust*	The role of artificial intelligence in managing diabetic retinopathy in low-and middle-income countries
M. Cianfriglia S. Leporale R. Moramarco V. Martini C. Marocco C. Bramucci F. Sestito R. Reda L. Testarelli T. Testori G. Perrotti	*Sapienza University of Rome*	Evaluation of vertical dimensions in orthognathic surgery using 3D cephalometry and TFA superimposition

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ONLINE SESSION / 15.05.2025

HALL-6 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Najlae Adadı

Authors	Affiliation	Presentation title
Rares Voroneanu	*University of Medicine and Pharmacy*	A brief analysis of the contribution of European physicians to the development of medical science
Souvik Halder Samiran Chattapadhyay Kartick Chandra Mondal	*Jadavpur University*	Attention-guided multimodal fusion with fuzzy inference for early depression detection
Pooja Rasal Kalyani Khajure Gaurav Kasar	*JES's SND College of Pharmacy*	Formulation and evaluation of antioxidant-rich herbal liquid toner
Rajko Igić Živojin S Jonjev	*Medical and Health Sciences*	The authors should share citations of a paper (iC), to eliminate inconsistencies in citation metrics
Najlae Adadı	*Institut Supérieur des Professions Infirmières et Techniques de Santé*	First application of next-generation sequencing in patients with hypertrophic cardiomyopathy in Morocco and report of a novel frameshift mutation of MYBPC3 gene
Amira M. Abd-Elmonem Emam H. El-Negamy Mahmoud A. Mahran Asmaa T. Ramadan	*Cairo University*	Clinical and radiological outcomes of corrective exercises and neuromuscular electrical stimulation in children with flexible flatfeet: A randomized controlled trial
Amira M. Abd-Elmonem Sara Samir Saad-Eldien Walaa Abd El-nabie	*Cairo University*	Effect of oral sensorimotor stimulation on oropharyngeal dysphagia in children with spastic cerebral palsy: A randomized controlled trial
Amira M. Abd-elmonem Hazem A. Ali Sara S. Saad-eldien Walaa A. Abd El-nabie	*Cairo University*	Efficacy of plyometric exercises on upper extremity function, selective motor control, and hand grip strength in children with unilateral cerebral palsy: A randomized controlled study

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ONLINE SESSION / 16.05.2025

HALL-1 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Tuba ÜNVER

Authors	Affiliation	Presentation title
Ahmet Yolaçan Püren Taş Eskimez Yaren Yılmaz Cihan Küden	*Çukurova University*	Regenerative endodontic treatment: Biological foundations, clinical protocols, and future perspectives
Şüheda Keleş Bahriye Horasanlı	*KTO Karatay University*	Balance evaluation in a pediatric patient with Marfan syndrome: Case study
Reyhan Metin Ayhan Emel Ege	*KTO Karatay University*	Evidence-based practices related to breast milk and breastfeeding
Reyhan Metin Ayhan Emel Ege	*KTO Karatay University*	The birth process of a patient with a history of unplanned advanced pregnancy using the Travelbee model of human-to-human relationships: Case report
Tuba Unver Zehra Torun	*Inonu University*	Antifungal properties of *Eruca vesicaria* flower essential oil against non-*albicans Candida* species using resazurin-based dilution method
Hatice Beyza Güney Alime Selçuk Tosun	*Selcuk University*	Examination of potential health risks of social media use in children and adolescents
Emine Dönmez Alime Selçuk Tosun	*Selcuk University*	Evaluation of intervention programs on health-related quality of life and glycemic control in individuals with type 2 diabetes
Püren Taş Eskimez Yaren Yılmaz Ahmet Yolaçan Cihan Küden	*Çukurova University*	Conventional and potential natural therapeutic dressing materials in endodontics: Current approaches

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ONLINE SESSION / 16.05.2025

HALL-2 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Dr. Muhammed Zahid ATLI

Authors	Affiliation	Presentation title
İrem Küçükakkaş Alime Selçuk Tosun	*Selcuk University*	An examination of nursing interventions in promoting cardiovascular health behaviors among adolescents
Muhammed Zahid Atlı	*Siirt University*	Kidney morphology in tortoise (*Testudo graeca*, Linnaeus, 1758)
Hakan Değerli Hasan Giray Ankara	*Bilecik Seyh Edebali University*	Digital health literacy and the digital transformation of healthcare institutions: A conceptual review
Çiğdem Eryılmaz Canlı Özlem Beşik Topçu	*Yüksek Ihtisas University*	Turkish language development in a French-Turkish bilingual child with fragile X syndrome: Intervention-based case report
Bahar Gezer Tuğba Kul Köprülü	*University of Health Sciences*	Evaluation of antiproliferative and apoptotic effects of aloe vera in glioblastoma multiforme
Arzu Bulut Gökhan Aba Sümeyye Kaya	*Bandırma Onyedi Eylül University*	Big data-based epidemiological surveillance applications
Sümeyye Kaya Arzu Bulut Gökhan Aba	*Bandırma Onyedi Eylül University*	Inservice training practices in prehospital emergency medical services: A literature-based evaluation
Rıdvan Muhammed Adın Sevim Acaröz Yeliz Salcı	*Ordu University*	Ankle-foot orthoses in patients with multiple sclerosis: An investigation of physiotherapists' clinical perspectives, experiences, and expectations

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ONLINE SESSION / 16.05.2025

HALL-3 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Matanat Burjali Aliyeva

Authors	Affiliation	Presentation title
Billel Larbaoui Rafik Menad	*University of Bejaia*	Single-click molecular docking-based virtual screening via SwiftDock
Neada Cakërri Denada Selfo Majlinda Rakipaj Deona Taraj	*University of Vlorë*	Factors contributing to medication errors during administration by nursing staff
Aliyeva E.A. Mamedov A.A. Shirinov Z.T. Kazymov I.L. Idrisov F.S.	*Scientific and Surgical Center Named After Academician M.A. Topchibashev*	Analysis of features of iatrogenic damage of extrarenal bile ducts during cholecystectomy
Matanat Burjali Aliyeva	*Azerbaijan Medical University*	Etiological structure of genitourinary tract infections caused by conditionally pathogenic microorganisms in women
Shahnise Elif Ibayeva	*Azerbaijan Medical University*	Features of the etiopathogenesis of upper respiratory tract infections caused by conditionally pathogenic microorganisms
Leyla Gahraman Aliyeva	*Azerbaijan Medical University*	Comparative analysis of the prognostic significance of tumor markers HE-4 and CA-125 in benign and malignant ovarian tumors
Vusala Mirsahib Bayramova	*Azerbaijan Medical University*	Clinical features of endo-periodontal lesions of supporting teeth during prosthetics
Javid Nadir Jahangirli	*Odlar Yurdu University*	The importance of microbiological parameters of individuals with harmful habits in forensic medicine

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ONLINE SESSION / 16.05.2025

HALL-4 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: S Sheron Kevin

Authors	Affiliation	Presentation title
M. Cianfriglia S. Leporale R. Moramarco V. Martini C. Marocco C. Bramucci F. Sestito R. Reda L. Testarelli T. Testori G. Perrotti	*Sapienza University of Rome*	Soft tissue imaging without radiation: An alternative to CBCT volumetric rendering
El.Majdi S. Zerraf M.E. Belghiti Said Belaaouada	*Hassan II University of Casablanca*	Synthesis, crystal structure, and computational techniques (DFT, HSA, ELF) studies of melaminium dihydrogen pyrophosphate ($C_3N_6H_7)_2$ ($H_2P_2O_7$)
Suket Rawat Franz Hessel Vaibhavi Dargude Vivek Gaurav	*SRH University of Applied Sciences*	Stakeholders' perceptions and feasibility of collaborative psychological approach in the treatment of dental phobia: A survey on the Indian population
Baba Ahmed Sihem Abı-Ayad fadya Chouıkhı Chaimaa Nour el houda	*Abou Bakr Belkaid University*	Knowledge, use, and perception of artificial intelligence by pharmacy students of Tlemcen, Algeria
S Sheron Kevin M K Vijayalakshmi V Selvakumar S Venkateshwaran A Ashwini E Hamshini Esha R Srinivasan	*Bharath Institute of Higher Education and Research*	Lawsonia inermis therapeutic potential: A thorough review
V Selvakumar M K Vijayalakshmi S Sheron Kevin S Venkateshwaran A Ashwini E Hamshini Esha R Srinivasan	*Bharath Institute of Higher Education and Research*	Wound healing activity in poly herbal
O. A. Odebiyi W.O.Salahu J.K.Oladejo O.O.Olabisi O.A.Oladapo E.A.Adetoyi	*Ladoke Akintola University of Technology*	Mathematical modeling of HIV/AIDS considering the effect of treatment non-adherence
Jingru Hu Yujuan Qin Xiufeng Tian Yu Sha Dongyang Wang	*The Third People's Hospital of Henan Province*	Longitudinal qualitative study on the care needs journey map of primary caregivers of patients undergoing total knee arthroplasty (TKA)

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ONLINE SESSION / 16.05.2025

HALL-5 / SESSION-1	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 11:^{00} – 13:^{00}	TÜRKİYE LOCAL TIME: 10:^{00} – 12:^{00}

HEAD OF SESSION: Saloni Sharma

Authors	Affiliation	Presentation title
Yang shuhua Wang dongyang Mao qin Li meng Yao guanglin	*The Third People's Hospital Of Henan Province*	Impact of psychological resilience intervention on negative emotions and nursing compliance in CAUTI patients: An evidence-based practice study using the Delphi method
Valentina Marınescu Ramona Marınache	*University of Bucharest*	Medicine in Dacia
Valentina Marınescu Ramona Marınache	*University of Bucharest*	Social reconstruction of a biological fact
Madiha Anwar Muhammad Usman Ali Naqi Hassan Manzoor	*Government College University*	Role of different surfactants (TX-100 and Tween-80) in enhancing the solubility of antibiotic drugs (levofloxacin) for better drug delivery system
Saloni Sharma Suhani Sharma	*Deemed to be University*	Phytopharmaceuticals in chronic disease management
Kaouthar Elbırguı Ali Zourıf Oussama Rafik Nadia Iounes Samir Ibenmoussa	*Hassan II-University*	Phytochemical profiling via FTIR and evaluation of antihemolytic properties of *Adenocarpus decorticans* Boiss. extracts
E. Elavarasi Yuvaraj AR J. Jayadurka R. Srinivasan	*Bharath Institute of Higher Education and Research*	Non-communicable diseases risk factors and their trends in the medical system
S.Kalaivanan Yuvaraj AR J. Jayadurka R.S. Deekshith R. Srinivasan	*Bharath Institute of Higher Education and Research*	Anticancer potential of *Plumbago zeylanica* as herbal medicinal treatment

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ONLINE SESSION / 16.05.2025

HALL-1 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Sümeyye Özarslan

Authors	Affiliation	Presentation title
Buket Karatop Elif Demirel Yasemin Kırmanlı Nihat Okuşluk	*Istanbul University*	Determination of human resources recruitment criteria in health sector: An approach based on multi-criteria decision making methods and artificial intelligence
İhsan Nalkıran Hatice Sevim Nalkıran	*Recep Tayyip Erdogan University*	In silico analysis of potential interactions between apremilast and anti-apoptotic proteins: A molecular docking study on BCL-2, BCL-XL, and survivin
Sümeyye Özarslan	*Inonu University*	The effectiveness of simulation-supported pediatric nursing education on nursing students: A systematic review
Sümeyye Özarslan	*Inonu University*	Simulation applications in the development of professional competencies of nurses working in pediatric clinics
Emine Göktaş Çağlar Doğuer Hatice Baygut Birol Topçu Aykut Demirkıran Cihan Aydın	*Tekirdag Namık Kemal University*	The relationship between polyphenol consumption level and lipid parameters in individuals diagnosed with cardiovascular disease
Elif Bayrakçı Eroğlu	*Gaziantep İslam Bilim ve Teknoloji University*	Sustainable development goals and midwifery services
Buket Karatop Ersin Kocabay Hatice Rışvan Beyza Damla Güzel	*İstanbul University - Cerrahpasa*	Sustainability and human resources management in the context of the United Nations sustainable development goals
Hatice Sevim Nalkıran Esen Kulac Polat	*Recep Tayyip Erdogan University*	Evaluation of sertraline-induced cytotoxicity in C6 glioma cells: A preliminary in vitro study

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ONLINE SESSION / 16.05.2025

HALL-2 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Dr. Hilal Arslan

Authors	Affiliation	Presentation title
Berna Erdal Bahar Yılmaz	*Tekirdag Namik Kemal University*	Antifungal effect of cell-free supernatants of *Lactobacillus delbrueckii* subsp. *bulgaricus* on *Candida* spp.
Hilal Arslan	*University of Health Sciences*	Association between fine particulate matter and dermatitis in Erzincan, Türkiye
Murat Genç Uğur Özentürk	*Ataturk University*	Colostrum management strategies in cattle farms
Uğur Özentürk Murat Genç	*Atatürk University*	Relationship between stress and behavior in dairy cattle farming
Turan Yaman Mehmet Çubukcu	*Van Yuzuncu Yil University*	Histopathological, immunohistochemical, and biochemical effects of bee bread (perga) administration in experimental diabetes
Nevin Karakus Tugay Sandalcı Mustafa Kocak Asker Zeki Ozsoy	*Tokat Gaziosmanpasa University*	The possible immunosuppressive effect of miR375 and miR223 in pregnancy and in cancer
Nevin Karakus Kaan Eray Uzun Irem Yildiz Asker Zeki Ozsoy	*Tokat Gaziosmanpasa University*	The similar proliferative effect of miR451a and miR141 in pregnancy and cancer
Volkan Sabur	*Private Erciyes Hospital*	Does the dimension of the prostate have any influence on urinary incontinence subsequent to holmium laser enucleation of the prostate (HOLEP)?

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ONLINE SESSION / 16.05.2025

HALL-3 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Javid Nadir Jahangirli

Authors	Affiliation	Presentation title
K.E.Jafarova S.A.Atakishizade M.H.Bagirova	*Azerbaijan Medical University*	Modern aspects of studying the issue of diagnostics of intestinal infections among children
R.Q. Naghiyeva A.F. Mehdiyeva A.H. Jafarova	*Azerbaijan Medical University*	The role of socio-economic factors in shaping nutrition patterns in Azerbaijan
Ulviya Rasim Shahmaliyeva	*Research Institute of Obstetrics and Gynecology*	Analysis of the impact of optimized treatment on the volume of myomatous nodes in uterine myoma
R.Vindhyalakshmı K.Rajaganapath	*Bharath Institute of Higher Education and Research*	Recombinant DNA technology in pharmaceutical research: Design, development, and applications of biopharmaceuticals for disease treatment and prevention
Saloni Sharma Suhani Sharma	*Manav Rachna International Institute of Research Studies*	Innovations in neurosurgery: Exploring the latest advancements and techniques in brain and nerve surgery
Javid Nadir Jahangirli	*Odlar Yurdu University*	The importance of microbiological parameters of individuals with harmful habits in forensic medicine
Fidan Enver Shikhaliyeva	*Azerbaijan Medical University*	Study of dental status in patients with perimucositis and periimplantitis
Fuzuli Framan Khalilov	*Odlar Yurdu University*	Changes in the microbiological picture of the body in women with breast cancer

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ONLINE SESSION / 16.05.2025

HALL-4 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Jobin Jose

Authors	Affiliation	Presentation title
Giuseppe Ferri Andrea Morgante Gualtiero Gherardi Niccolò Carrai Rebecca Palumbo Roberta Moramarco Luca Testarelli Anamaria Beatrice Burete Dario Di Nardo Alessio Zanza Elisa Maccari Rodolfo Reda	*Sapienza University of Rome*	Evaluation of the marginal adaptation and fracture resistance of digitally fabricated endo-crowns made from two different materials: An in vitro study
Carrai N Gherardi G Maccari E Ferri G Morgante A Auletta A Testarelli L Di Nardo D	*University of Rome La Sapienza*	Preliminary evaluation of the adaptability of post-and-core structures produced via SLS compared to lost-wax casting
Obasi Blessing Ihemelandu Favour C. Uroko	*University Of Nigeria,*	An appraisal of the reference range for bleeding time amongst Christians in Nigeria
Syed Anam Shaheen Abbas Shah Muhammad Shoaib Muhammad Yasin Naz Shazia Shukrullah	*University of Agriculture*	Synthesis and study of kinetics of $CoFe_2O_4$ @SiO_2-chitosan adsorbents for removal of cadmium and lead from water
Jobin Jose Reeshma Shetty	*Deemed to be University*	Formulation and evaluation of micelle nanogel–based drug delivery system for lutein in age-related macular degeneration
Islam Zuzaku Skender Demaku Arbnora Alıu Donika Sylejmanı	*University of Pristina*	The ecological risk of contamination with toxic metals in the soils, waste, and ash, around the "Trepça" complex, the "Kosovo" thermal power plants and the new ferronickel complex
Fedwa Beghdadı El-Hadj Drıche	*Hassiba Benbouali University of Chlef*	Actinobacteria as a promising method of biological control against pathogenic bacteria and fungi
Fedwa Beghdadı El-Hadj Drıche	*Hassiba Benbouali University of Chlef*	The inhibition of some phytopathogenic bacteria by actinobacteria isolated from Algerian Saharan soils

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ONLINE SESSION / 16.05.2025

HALL-5 / SESSION-2	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 13:30 – 15:30	TÜRKİYE LOCAL TIME: 12:30 – 14:30

HEAD OF SESSION: Syed Mohsan Raza Shah

Authors	Affiliation	Presentation title
Muhammad Safdar Syed Mohsan Raza Shah	*University of Education,*	Unveiling adaptive components for environmental heterogeneity in *Ipomoea carnea* Jacq.
Skender Demaku Arbnorë Alıu Arditë Karaxha	*University of Prishtina*	Nitrate ion (NO_3^-) levels in fruits and vegetables in the cities of Prishtina and Graçanica were measured using the "Green Test ECO 5 F -ANMEZ" equipment
Rossı Manal Benboubker Moussa Belchkar Salim Hmamı Fouzia Oumokhtar Bouchra	*University of Sidi Mohamed Ben Abdellah*	Evaluating aseptic interventions and catheter management strategies to prevent catheter-associated infections in neonates
Said Babou Miloud Chakit Abdelhalem Mesfioui Moulay Laarbi Ouahidi Youssef Sqalli-Houssaini	*Ibn Tofail University*	Neuroprotective effects of *Rosmarinus officinalis* ethanolic extract on cognitive-affective functions and hippocampus oxidative stress in Wistar rats exposed to cadmium
Said Babou Miloud Chakit Abdelhalem Mesfioui Youssef Sqalli Houssaini	*Ibn Tofail University*	Dose-dependent effects of cadmium on anxiety-like and depressive-like behaviors and oxidative stress in the prefrontal cortex of female rats
Habil. Cristina Raluca Gh. Popescu	*University of Bucharest*	Fostering an interdisciplinary and innovative approach to medical sciences, health sciences, and biology: United Nations' Sustainable Development Goals Initiative and European Partnership ERA4Health
Amal Bassam Rajaa Bassam Younes Rachdi Marouane El Alouani Mohammed Hafid Hamid Saufi Said Belaaouad	*Hassan II University of Casablanca*	The application of synthesized geopolymer waste red clay-based for the removal of anionic dye from industrial wastewater
Imane Ahnouz Rajaa Sebıhı	*Mohammed V University in Rabat*	Signal processing techniques for neutron-gamma discrimination in scintillators

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ONLINE SESSION / 16.05.2025

HALL-1 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Abdul-Rahman Balogun

Authors	Affiliation	Presentation title
Abdul-Rahman Balogun Muhammed-Shittu	*British School in Baku*	Endowment concept as the supply of medical care: an exploratory study on sustainability of health insurance at higher institutions
Halima Hajhı Mohamed Ouabane Fatima En-nahli Tahar Lakhlifi Mohammed Bouachrine Mohammed Aziz Ajana	*Moulay Ismail University*	Computational and bioinformatics investigation of novel GABA A ligands with anticonvulsant activity
Gulnar Atakishiyeva Shafiga İbrahimova Sevinç Muhtarova Shukufa Eyvazova Naila Veysova Namiq Shikhaliyev	*Baku State University*	Evaluation of blood–brain barrier permeability and CNS drug potential of hydrazone ester derivatives
Rossı Manal Benboubker Moussa Belchkar Salim Hmamı Fouzia Oumokhtar Bouchra	*University of Sidi Mohamed Ben Abdellah*	Bacterial colonization and infection risks in neonatal care: focus on peripheral venous catheter management
I.T. Rasul R.A. Rzayeva N.R. Baghırova M.R. Abbasova I.B.Alizada G.I.Bakhshaliyeva	*Azerbaijan Medical University*	Characteristics of heart rate variability depending on blood pressure level
Mammadzada Aytan Yagub Huseynova Shola Mohub Gasimova Aida Shokat Ahmadzada Ulviyya Israfil Niftaliyeva Saadat Faxreddin Guliyeva Asmatkhanim Alibala	*Azerbaijan Medical University*	Endothelin-1 dysregulation and its association with endothelial dysfunction: a cross-sectional physiological analysis
Leyla Akberlı Hacar Ismayılova	*Azerbaijan Medical University*	Infections around the prosthesis
Leyla Akberlı Hacar Ismayılova	*Azerbaijan Medical University*	Complications associated with removable dentures due to improper use and poor oral hygiene

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ONLINE SESSION / 16.05.2025

HALL-2 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Parvin Mahir Abbasaliyeva

Authors	Affiliation	Presentation title
Matanat Murguzova Ismayil Gafarov Khayala Mammadova	*Azerbaijan Medical University*	Biophysical properties of the cell membrane and drug transport
Tahira Askarova Nazanin Hasanzade Khayala Mammadova	*Azerbaijan Medical University*	Molecular basis and diagnosis of inherited diseases
Yousra Anwar	*David Tvildiani Medical University*	Platelet-rich plasma therapy- enhanced ovarian rejuvenation: a promising approach towards ovarian insufficiency and fertility preservation
Aynur Polukhova Sevinj Nasirova Nurana Huseynova	*Scientific Recearch Institute of Pediatrics named after K.Y.Farajeva*	Rubinstein-taybi syndrome in a child with floating harbor syndrome
Nargiz Huseynova Nigar Agayeva	*Azərbaycan Tibb Universiteti*	Effect of vitamin d deficiency on cytokine secretion in bacterial vaginosis and aerobic vaginitis
Volodymyr Sulyma Olena Sulima	*Dnipro State Medical University*	The drug budesonide (budenofalk®) in the treatment of patients with an immunological component in Crohn's disease and Bechterew's disease
Parvin Mahir Abbasaliyeva	*Azerbaijan Medical University*	Analysis of the effect of immunofan on inflammation markers in patients with liver echinococcosis

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ONLINE SESSION / 16.05.2025

HALL-3 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Iram Liaqat

Authors	Affiliation	Presentation title
Muhammad Asad Shanza Khanum	*University of Education Lahore*	Ameliorative effects of Solanum nigrum methanolic leaf extract on sub-lethal toxicity of carbon nanotubes in the brain, gills, and heart of Cirrhinus mrigala
Saira Malik Syed Mohsan Raza Shah Uniza Fatima bukhari Tasawar Fatima bukhari Iqra	*University of Education*	Leaf structural and functional modification of Ipomoea carnea Jacq. an invasive plant species, under diverse salinity gradient
Arooj Anwar Fozia Anjum Samreen Gul Khan	*Government College University*	Murraya koengii: an alternative to treat burn infection
Valery V. Belakhov	*Technion – Israel Institute of Technology*	Hydrophosphoryl derivatives of perimycin: preparation, pharmacological properties and antifungal activity
Gulnar Atakishiyeva Shafiga İbrahimova Nurana Gurbanova Sevinc Mukhtarova Gunel Mahmudova Irada Shikhaliyeva Namiq Shikhaliyev	*Baku State University*	Structural dependence of antimicrobial activity in dichlorodiazadiene derivatives
Iram Liaqat	*Government College University*	Honey efficacy as antimicrobial agent against multispecies bacterial biofilms
Iram Liaqat	*Government College University*	Quorum sensing inhibition by algal compounds against marine biofilms
Mirzayev M.I. Hasanov R.P Akbarov E. Farzaliyeva S Alekbarov A.A.	*Azerbaijan Medical University*	The effect of reperfusion on liver tissue structure after medium-term ischemia

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ONLINE SESSION / 16.05.2025

HALL-4 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Faizan Afzal

Authors	Affiliation	Presentation title
K.pooja M.K Vijayalakshmi	*Bharath Institute of Higher Education and Research*	Administrative science in the field of pharmacy
Arraji Maryem Iderdar Younes Mourajid Yassmine Boumendil Karima Mohamed Chahboune	*Hassan First University of Settat,*	Translation, cultural adaptation and validation of the General Medication Adherence Scale (GMAS) in Moroccan patients with type-2 diabetes
Priya Chaudhuri Mainan Ray	*Amity University Kolkata,*	Critically analyzing global legal response to the effect of thawing of permafrost on human health
Taskeen Fatima Mahna Fatima	*Hajvery University*	An overview of CAD; etiological factors & surgical managements
Kalsoom Nazir Hira Firdous Shahnila Tariq	*University of Management and Technology Lahore,*	Overprotection, self-doubt and Cinderella syndrome in female university students
R. Vıdhyalakshmı C. Rejıtha	*Bharath Institute Of Higher Education And Research*	Neuroinflammation as a key mechanism in neurological diseases
Faizan Afzal	*Hajvery University Lahore*	The role of high fast food, sugary beverage, and sugar intake in the development of chronic kidney disease: a clinical and literature-based analysis
Gulnar Atakishiyev Ayten Qajar Nigar Ahmedova Sevinc Mukhtarova Gunel Mahmudova Gulnara Babayeva Akademic Abel Maharramov	*Baku State University*	In silico prediction of bactericidal potential using antibac-pred for dichlorodiazadiene derivatives
Gulnar Atakishiyeva Sevinc Mukhtarova Sima Musayeva Ilhama Hamdullayeva Irada Shikhaliyeva Gulnara Babayeva	*Baku State University*	In silico prediction of cyp450 inhibition profiles and metabolic stability of hydrazone ester derivatives

(All speakers required to be connected to the session 10 min before the session starts)
Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

ONLINE SESSION / 16.05.2025

HALL-5 / SESSION-3	ZOOM ID: 860 5266 6988 / PASSCODE: 151617
UAE LOCAL TIME: 16:^{00} – 18:^{00}	TÜRKİYE LOCAL TIME: 15:^{00} – 17:^{00}

HEAD OF SESSION: Assoc. Prof. Dr. Devran COŞKUN

Authors	Affiliation	Presentation title
Şahin Gülcan Elif Toku Alperen Çoşkun Özlem Alptekin	*Cukurova University*	Evaluation of the effect of methimazole on urease activity with different kinetic equations
Alperen Çoşkun Elif Toku Şahin Gülcan Özlem Alptekin	*Cukurova University*	Immobilization of lipase on modified ZrO_2 and investigation of its hydrolytic activity
Songül Ötkün	*Siirt University*	Molecular detection of *Coxiella burnetii* in vaginal swab samples from nomadic sheep that aborted in Siirt province
Fatma Akin Devran Coşkun Orhan Çorum	*Siirt University*	Use of pentoxifyline in veterinary medicine
Fatma Akin Devran Coşkun Orhan Çorum	*Siirt University*	Antidepressant use in dogs
Orhan Çorum Kamil Üney Pedro Marin Duygu Durna Çorum Devran Coşkun Elena Badillo Muammar Elmas	*Siirt University*	Pharmacokinetics of tolfenamic acid after intravenous and oral administration of increasing doses to ducks
Rabia Gülbakti Yılmaz Koçak Fahri Aşkan	*Van Education and Research Hospital*	Rational use of antibiotics in children
Erdal POLAT Mehmet Özkan TİMURKAN Hakan AYDIN Ayfer Fındık PAKROOH	*Siirt University*	Important arboviral infections of sheep and goats (Bluetongue, Akabane, Schmallenberg and Rift Valley Fever)
Mohamed Belkhaoud Younes Yassine Lamri Driss Guerss Fatima-Ezzahraa	*Ibn Tofail University*	Sports physiology for performance optimization
Tuhina Sinha	*Amity University*	Climate change litigation: transnational legal mobilization and the evolution of global climate governance
Yunus Emre Beyhan Şeyma Işık	*Van Yüzüncü Yıl University*	The importance of mirnas in cystic echinococcosis

(All speakers required to be connected to the session 10 min before the session starts)
Moderator is responsible for ensuring the smooth running of the presentation, managing the group discussion and dynamics.

SYMPOSIUM PHOTOS






IKSAD DUBAI


GRASS PLANT (LOLIUM L.) AS A BIOINDICATOR: HEAVY
METAL CONTENT AND TOXICITY






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CERTIFICATE


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ABSTRACTS

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IMPORTANT ARBOVIRAL INFECTIONS OF SHEEP AND GOATS

(Bluetongue, Akabane, Schmallenberg and Rift Valley Fever)

ABSTRACT

Arboviruses (arthropod-borne viruses) are significant viral pathogens transmitted by arthropod vectors such as *Culicoides* spp., mosquitoes, and ticks, with substantial implications for animal health. Infections caused by these viruses in small ruminants result in severe economic losses, primarily due to abortions, stillbirths, and congenital abnormalities. Among the most relevant arboviruses affecting sheep and goats are Bluetongue virus (BTV), Akabane virus (AKAV), Schmallenberg virus (SBV), and Rift Valley fever virus (RVFV). Despite belonging to distinct taxonomic families, these pathogens exhibit similar transmission dynamics and pathogenesis patterns.

BTV is a non-enveloped, double-stranded RNA virus classified under the *Orbivirus* genus of the *Sedoreoviridae* family. It is transmitted by *Culicoides* biting midges and causes severe clinical disease in sheep, while infections in cattle are generally subclinical. To date, over 30 serotypes have been identified worldwide. Seroepidemiological studies across multiple regions in Turkey confirm the endemic circulation of the virus.

AKAV, a segmented negative-sense RNA virus of the *Orthobunyavirus* genus within the *Peribunyaviridae* family, is also spread by *Culicoides* spp. It is primarily responsible for reproductive losses in ruminants, especially through congenital anomalies such as the arthrogryposis-hydranencephaly (AH) complex when infection occurs during gestation. Serological data from Turkey report approximately 45% antibody positivity in cattle, with lower rates in sheep and goats.

SBV, another *Orthobunyavirus* within the Simbu serogroup, was first identified in Europe in 2011. It causes malformations similar to AKAV. In Turkey, limited data indicate around 40% seroprevalence in cattle, with much lower levels in small ruminants.

RVFV, a zoonotic *Phlebovirus* from the *Phenuiviridae* family, is transmitted by mosquitoes and can lead to abortion and hemorrhagic disease in animals, as well as life-threatening infections in humans. Although no clinical RVF cases have been reported in Turkey, seropositivity has been detected in water buffaloes and humans.

In conclusion, the implementation of active surveillance and integrated control programs is essential to sustain livestock productivity and mitigate emerging zoonotic risks in Turkey.

Keywords: Arbovirus, Bluetongue virus (BTV), Akabane virus (AKAV), Schmallenberg virus (SBV), Rift Valley Fever virus (RVFV), Small ruminants, Vector-borne infection

KOYUN VE KEÇİLERİN ÖNEMLİ ARBOVİRAL ENFEKSİYONLARI (Mavidil, Akabane, Schmallenberg ve Rift Vadisi Humması)

ÖZET

Arbovirüsler (arthropod-borne viruses), *Culicoides* spp, sivrisinekler ve keneler gibi eklem bacaklı vektörlerle taşınan ve hayvan sağlığı açısından büyük öneme sahip viral etkenlerdir. Küçük ruminantlarda görülen arboviral enfeksiyonlar, ciddi ekonomik kayıplara yol açmakta; abortlara, ölü doğum ve konjenital anomalilerle karakterize klinik tablolar oluşturmaktadır. Bu kapsamda, koyun ve keçilerde görülen temel arbovirüsler; *Bluetongue (Mavidil) virus* (BTV), *Akabane virus* (AKAV), *Schmallenberg virus* (SBV) ve *Rift Vadisi Humması* (RVFV) olarak öne çıkmaktadır. Bu patojenler farklı taksonomik gruplara ait olmasına rağmen bulaşma yolları ve patogenez mekanizmaları açısından benzerlik göstermektedir.

BTV, *Sedoreoviridae* ailesinin *Orbivirus* cinsinde; zarfsız, çift sarmallı RNA genomuna sahip, *Culicoides* türü sokucu sineklerle bulaşır. Özellikle koyunlarda belirgin klinik belirtilere neden olan BTV, sığırlarda çoğunlukla subklinik seyretmektedir. Dünya genelinde 30'dan fazla serotipi tanımlanmış olup, Türkiye'de çeşitli bölgelerde yapılan seroepidemiyolojik çalışmalar, virüsün endemik olarak sirküle olduğunu göstermektedir.

AKAV, *Peribunyaviridae* ailesinin *Orthobunyavirus* cinsinde, zarflı ve segmentli negatif-sarmallı RNA genomuna sahip bir virüstür. *Culicoides* türleriyle bulaşan ve gebelik döneminde enfekte olan ruminantlarda, özellikle artrogriposis-hidranensefali (AH) kompleksine yol açan konjenital malformasyonlara sebep olmaktadır. Türkiye'de yapılan çalışmalar, sığırlarda yaklaşık %45 oranında AKAV antikor pozitifliği saptarken koyun ve keçilerde bu oran daha düşüktür.

SBV, Simbu serogrubu içerisinde yer alan ve 2011 yılında Avrupa'da tanımlanan bir *Orthobunyavirus* olup, klinik olarak AKAV enfeksiyonuna benzer tablolar oluşturmaktadır. Türkiye'deki sınırlı veriler, sığırlarda %40 civarında seroprevalans bildirirken, küçük ruminantlarda düşük pozitiflik oranları dikkat çekmektedir.

Zoonotik potansiyele sahip olan RVFV ise, *Phenuiviridae* ailesinin *Phlebovirus* cinsi içerisinde yer alan zoonoz karakterde viral bir etkendir. Sivrisineklerle bulaşan RVFV, hayvanlarda abort ve hemorajik sendromlara sebep olurken, insanlarda ise ciddi sistemik ve ölümcül seyirli enfeksiyonlara neden olmaktadır. Türkiye'de bildirilen klinik RVF vakası bulunmamakla birlikte, su mandalarında ve insan popülasyonunda seropozitiflik bildirilmiştir.

Sonuç olarak; Türkiye'de sürdürülebilir hayvancılığın korunması ve zoonotik tehditlerin önlenmesi açısından bu enfeksiyonlara yönelik aktif sürveyans çalışmalarının yapılması, koruma-kontrol programlarının uygulanmasının gerekli olduğu düşünülmektedir.

Anahtar kelimeler: *Arbovirüs, Bluetongue virüsü (BTV), Akabane virüsü (AKAV) Schmallenberg virüsü (SBV), Rift Vadisi Humması virüsü (RVFV), Küçük ruminantlar, Vektör kaynaklı enfeksiyon*

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SPEXIN AS AN ADIPOKINE AND ITS FUNCTIONS

ABSTRACT

Spexin (SPX), also known as neuropeptide Q (NPQ), is a bioactive peptide consisting of a short chain of 14 amino acids and shares a common ancestral origin with galanin (GAL) and kisspeptin. First identified in 2007 through bioinformatic approaches aimed at discovering novel peptide hormones, SPX represents a next-generation neuropeptide with a highly conserved amino acid sequence across mammalian and non-mammalian species. This evolutionary conservation is believed to contribute to its widespread distribution in various tissues and organs. SPX expression has been reported in multiple organ systems, including the hypothalamus, gastrointestinal tract, lungs, pancreas, adrenal glands, adipose tissue, and kidneys. Functionally, SPX exerts its biological effects primarily through its interaction with galanin receptor subtypes GALR2 and GALR3, to which it bears structural similarity. Through these receptors, SPX plays a role in the regulation of several physiological processes such as metabolism, energy homeostasis, appetite control, glucose regulation, nociception, mood modulation, and endocrine function. Its broad tissue distribution and multifaceted physiological effects suggest that SPX may represent a promising candidate for therapeutic applications. Accumulating evidence indicates that SPX reduces food intake and body weight, enhances gastrointestinal motility, negatively correlates with leptin levels in obesity, shows decreased expression in type 2 diabetes mellitus, and exhibits antidepressive properties. These findings underscore its potential importance in metabolic regulation and neuroendocrine signaling. The aim of this review is to evaluate the molecular characteristics,

receptor interactions, and physiological roles of SPX in light of the current literature. Moreover, considering the growing body of research suggesting that SPX may function not only as a neuropeptide but also as a potential biomarker and therapeutic agent, special emphasis will be placed on its relevance in the context of energy balance, metabolic disorders, and neuroendocrine dysfunctions. However, due to the relatively limited data available on its physiological mechanisms, further comprehensive clinical and experimental studies are necessary. Advancing research in this field may offer innovative approaches to the prevention and treatment of metabolic and neurological diseases.

Keywords: Spexin, neuropeptide Q, galanin receptors, metabolic diseases

BİR ADİPOKİN OLARAK SPEKSİN VE İŞLEVLERİ

ÖZET

Speksin (SPX) diğer tanımıyla nöropeptit Q (NPQ), biyoaktif peptitler olarak da bilinen galanin (GAL) ve kisspeptin ile ortak bir ata kökene sahip 14 amino asit dizisinden oluşan kısa bir peptit zinciridir. İlk olarak 2007 yılında tanımlanan SPX, peptit hormonlarını tanımlayıcı biyoinformatik teknikler kullanılarak keşfedilen yeni nesil bir nöropeptittir. Amino asit dizisinin memeli ve memeli olmayan türler arasında oldukça korunmuş olması, bu peptitin çok sayıda doku ve organda geniş dağılım göstermesine katkı sağlamaktadır. Hipotalamus, gastrointestinal sistem, akciğer, pankreas, adrenal bezler, yağ dokusu ve böbrek gibi birçok organda eksprese edildiği bildirilmektedir. Yapısal olarak benzerlik gösteren SPX'in aktive ettiği bilinen başlıca reseptörleri galanin reseptör 2 (GALR2) ve galanin reseptör 3 (GALR3)'tür. Söz konusu reseptörler aracılığıyla metabolizma, enerji homeostazisi, iştah, diyabet, ağrı, depresyon, endokrin düzenleme gibi fizyolojik fonksiyonlarda roller üstlenmektedir. Geniş doku dağılımı ve çok yönlü etkilere sahip olması SPX'in potansiyel bir terapötik ajan olabileceğine işaret etmektedir. SPX'in gıda alımını ve vücut ağırlığını azalttığı, gastrointestinal motiliteyi desteklediği, obezitede leptin ile negatif korelasyon gösterdiği, tip 2 diabetes mellitusta düzeylerinin azaldığı ve ek olarak antidepresif etkilerinin olduğu bildirilmektedir. Bu derlemenin amacı güncel literatür bilgisi ile SPX'in moleküler yapısını, reseptör etkileşimlerini ve fizyolojik fonksiyonlarını değerlendirmektir. Ek olarak SPX'in sadece bir nöropeptit değil aynı zamanda tanı ve tedavi açısından umut vadeden bir biyomolekül olabileceği fikri temel alınarak, enerji homeostasisi, metabolik hastalıklar ve nöroendokrin bozukluklar çerçevesinde olası rollerine dikkat çekmek hedeflenmiştir. Ancak SPX'in fizyolojik fonksiyonlarına dair mevcut verilerin sınırlı olması sebebiyle mekanizmalarının tam olarak aydınlatılabilmesi için daha fazla klinik ve deneysel çalışmaya ihtiyaç duyulmaktadır. Bu doğrultuda SPX üzerine yapılacak ileri araştırmaların, bazı metabolik hastalıklar ve nörolojik bozuklukların yönetiminde yenilikçi yaklaşımlar geliştirilmesine katkı sağlayacağı düşünülmektedir.

Anahtar Kelimeler: Speksin, nöropeptit Q, galanin reseptörleri, metabolik hastalıklar

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NEW THERAPEUTIC TARGETS MYOKINES: MYONECTIN

ABSTRACT

Skeletal muscle is the largest organ in the human body and plays a vital role in maintaining whole body metabolic homeostasis. Not only a motor organ, skeletal muscle also functions as an important endocrine organ. It was recently identified that skeletal muscle, the main site of movement, secretes metabolites called “myokines” - proteins, peptides and amino acids - that have an effect on other parts of the body. Numerous studies have subsequently revealed the abundant systemic effects of these myokines and have shown that the endocrine aspect of skeletal muscle needs further attention. Myokines play an important role in the mutual communication between skeletal muscles, myocardium and distant organs such as brain, vasculature, bone, liver, pancreas, white adipose tissue, intestine and skin. In particular, myokines have been found to be important regulators of oxidative stress and inflammation. Myokines, whose plasma levels increase significantly after exercise, provide valuable information in the prevention of sarcopenia and many metabolic diseases including obesity, diabetes and fatty liver disease. Examples of these myokines include myostatin, β-aminoisobutyric acid, interleukin-15, interleukin-6, meteorin-like and myonectin. Myonectin is a recently discovered mycophenolate belonging to the C1q/TNF-related protein family (C1QTNF isoform 5), which is predominantly released by skeletal muscle. Studies have shown that myonectin expression is stimulated by two main factors: exercise and nutrients. In general, myonectin is an important mediator of inter-organ cross-talk and its secretion by skeletal muscle functions as a compensatory mechanism to improve glucose tolerance and increase fatty acid oxidation. It is envisaged that myonectin may be used as a new pharmacological agent in the treatment of metabolic diseases, especially obesity and diabetes, with new studies to be conducted in the future. In this review, we aim to summarize the research on myokines and especially myonectin, which have recently been reported as some specific biomarkers, to present new perspectives on the myokine mechanism, to examine the potential of myonectin as a therapeutic target and to contribute to future studies.

Keywords: Skeletal muscle, myokines, myonectin

YENİ TEDAVİ HEDEFLERİ MİYOKİNLER: MİYONEKTİN

ÖZET

İskelet kası insan vücudundaki en büyük organdır ve tüm vücut metabolik homeostazının korunmasında hayati rol oynar. Yalnızca motor bir organ olmayan iskelet kası aynı zamanda önemli bir endokrin organ olarak işlev görür. Yakın zamanda hareketin ana bölgesi olan iskelet kasından "miyokinler" adı verilen ve vücudun diğer bölümleri üzerine etkili olan proteinler, peptidler ve amino asitler gibi metabolitlerin salgılandığı tespit edilmiştir. Daha sonra yapılan çok sayıda çalışmayla, bu miyokinlerin bol miktarda sistemik etkileri ortaya çıkarılmış ve iskelet kasının endokrin yönünün daha fazla dikkate alınması gerektiği gösterilmiştir. Miyokinler iskelet kasları, miyokard ve beyin, damar sistemi, kemik, karaciğer, pankreas, beyaz yağ dokusu, bağırsak ve cilt gibi uzak organlar arasındaki karşılıklı iletişimde önemli bir rol oynamaktadır. Özellikle oksitadif stres ve inflamasyonla mücadelede miyokinlerin önemli düzenleyiciler olduğu tespit edilmiştir. Egzersiz sonrasında plazma düzeyleri önemli ölçüde yükselen miyokinler; sarkopeniyi önleme, obezite, diyabet ve karaciğer yağlanması dahil birçok metabolik hastalığın önüne geçilmesinde değerli bilgiler sunmaktadır. Bu miyokinler grubunda miyostatin, β-aminoizobütirik asit, interlökin-15, interlökin-6, meteorin benzeri ve miyonektin gibi örnekler bulunmaktadır. Miyonektin, yakın zamanda keşfedilen ve ağırlıklı olarak iskelet kası tarafından salınan C1q/TNF ile ilişkili protein ailesine (C1QTNF izoformu 5) ait bir mikofenolattır. Yapılan çalışmalarla miyonektin ekspresyonunun egzersiz ve besinler olmak üzere iki ana faktör tarafından uyarıldığı belirlenmiştir. Genel olarak, miyonektin organlar arası çapraz iletişimde önemli bir aracıdır ve iskelet kası tarafından salgılanması ile, glikoz toleransını iyileştirmek ve yağ asidi oksidasyonunu artırmak için telafi edici bir mekanizma olarak işlev görür. Gelecekte yapılacak yeni çalışmalarla başta obezite ve diyabet olmak üzere metabolik hastalıkların tedavisinde yeni bir farmakolojik ajan olarak miyonektinin kullanılabileceği öngörülmektedir. Bu derlememizde de son zamanlarda bazı özel biyobelirteçler olarak bildirilen miyokinler ve özellikle miyonektin ile alakalı araştırmaları özetlemeyi, miyokin mekanizmasına ilişkin yeni bakış açıları sunmayı, miyonektinin tedavi hedefi olarak potansiyelini incelemeyi ve ayrıca bundan sonra yapılacak çalışmalara katkı sunmayı hedeflemekteyiz.

Anahtar Kelimeler: İskelet kası, miyokinler, miyonektin

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HEALTHY BODY COMPOSITION: CONSENSUS AMONG THE BODY MASS INDEX, FAT MASS PERCENT, AND WAIST-TO-HIP RATIO

ABSTRACT

Aim: Human body composition is measured with various methods based on direct fat or anthropometric measurements in order to evaluate the state of health condition in normal, fit people, patients, obese, and elderly individuals. The frequently preferred body composition analysis methods are bioelectrical impedance analysis (BIA) based on direct fat measurement, body mass index (BMI) based on anthropometric measurement, and waist-to-hip ratio (WHR) an indicator of regional fat distribution. This study evaluated the agreement between body mass index (BMI), bioelectrical impedance analysis (BIA), and waist circumference measurements in young men and women. We aimed to determine the validity and limitations of each method in assessing body health by examining the relationship between the values considered normal for healthy body composition and abdominal fat accumulation obtained by these three different measurement methods.

Materials and Methods: A total of 480 healthy young females (19.6±1.4 years, 164.2±6.0 cm and 60.19±12.79 kg) participated, and body composition measurements were performed using BIA, BMI, and WHR. Pearson correlation analysis and Paired t-tests were used to evaluate the data for statistical analysis.

Results: The values accepted in the normal range were observed in 336 participants (70%) for BMI, 249 participants (51.8%) for FM percent, and 407 participants (84.8%) for WHR ($p<0.001$). On the other hand, interestingly, there was consensus in normal range values only in 176 individuals (36.6%) by all three methods ($p<0.001$).

Conclusions: Consequently, the significant differences in the values accepted as normal ranges between the three techniques and, importantly, the consensus in (36.6%) extremely low numbers among the three methods should be considered before making a critical decision concerning the normality or abnormality of the individual's health status. The gender difference and cut-off point regarding ethical origin may be an essential factor for measurement efficacy, and it is crucial to accept as the normal from multiple measurement methods rather than one technique.

Keywords: Body Composition, Bioelectrical Impedance Analysis (BIA), Body Mass Index (BMI), Waist-to-Hip Ratio (WHR), Abdominal Fat, Anthropometric Measurements

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MICROBIOLOGICAL DEVELOPMENTS IN BIOTERRORISM

Abstract

The 9/11 attacks on New York and Washington, DC,underscored the urgent need for comprehensive research on biological warfare (BW) and other agents in the globalfightagainst terrorism. During the Cold War, the former USSR secretly developed, tested, and stockpiled vast quantities of biological weapons,establishing the world's largest and most sophisticated biological warfare program. The knowledge gained in these laboratories and production facilities was undoubtedly shared with other regimes and terrorist organizations. These agents pose a serious threat to both military personnel and civilians in the event of a bioterrorist attack. BW pathogens are expected to enhance genome sequencing forthe development of better vaccines, diagnostic methods, and treatments, paving the way for a deeper understanding of fundamental biological processes.Novel technological devices have made it possible to sequence entire genomes rapidly and efficiently. Microbiologists established a coordinated national approach before the 2001 anthrax bioterrorism attack. However, the network system and its development were also significantly impacted by the anthrax bioterrorism. Recognizing the potential for such an attack prior to the 2001 anthrax incident, the CDC, FBI, and the Association of Public Health Laboratories (APHL) created the Laboratory Response Network (LRN) in 1999. The goal of the LRN is to establish a fully equipped national and international integrated laboratory network capable of responding swiftly to acts of chemical or bioterrorism, emerging infectious diseases, and other public health threats and emergencies. The LRN is commonly illustrated as a pyramid, with sentinel laboratories at its base.These microbiology laboratories are where the primary diagnosis of an infectious agent usually occurs. Another concept involves biosurveillance, which is a broad term referring to a comprehensive approach to bioterrorism and biological events. Due to the technological requirements and costs, biological weapons are considered high-risk, as they are relatively easy and inexpensive to produce. Therefore, it is crucial to stay informed about developments in microbiological bioterrorism.

Keywords: Bioterrorism, Microbiological, Developments

BİYOTERÖRİZMDE MİKROBİYOLOJİK GELİŞMELER

Özet

11 Eylül 2001 tarihinde New York ve Washington DC'de gerçekleşen saldırılar, dünya çapında terörizmle mücadele girişimine yardımcı olmak amacıyla biyolojik savaş (BS) ve diğer etkenler hakkında kapsamlı araştırmalara ihtiyaç duyulduğunu göstermiştir. Soğuk Savaş döneminde eski adı ile SSCB, dünyanın en büyük ve en gelişmiş biyolojik savaş programını inşa etme etmek için gizlice muazzam miktarda biyolojik silah geliştirerek test etti ve stokladı. Bu laboratuvarlarda ve üretim tesislerinde geliştirilen bilgi, şüphesiz diğer rejimlere ve terör örgütlerine de yayıldı. Tüm bu etkenler, biyoterörist saldırı durumunda hem askerî personel hem de siviller için ciddi bir tehdit oluşturmaktadır. BS patojenleri için beklenti, genom dizisinin daha iyi aşıların, tanı testlerinin ve tedavilerin geliştirilmesine yardımcı olmasıdır. Böylece temel biyolojik süreçlerin kapsamlı bir şekilde anlaşılmasına giden yolun açılmasıdır. Son teknolojik ekipmanlar ile tüm genomların hızlı ve etkili bir şekilde dizilenmesine olanak sağlanmıştır. Mikrobiyoloji uzmanları, 2001 yılındaki şarbon biyoterörizm saldırısından önce koordineli bir ulusal yaklaşım geliştirmişlerdir. Ancak ağ sistemi ve gelişimi de şarbon biyoterörizminden önemli ölçüde etkilenmiştir. 2001'deki şarbon saldırısından önce böyle bir saldırının potansiyelini fark eden CDC, FBI ve Halk Sağlığı Laboratuvarları Derneği (APHL), 1999 yılında Laboratuvar Müdahale Ağı'nı (LRN) geliştirmiştir. LRN'nin amacı, kimyasal veya biyoterörizm eylemlerine, ortaya çıkan bulaşıcı hastalıklara ve diğer halk sağlığı tehditlerine ve acil durumlara hızlı bir şekilde yanıt verebilecek şekilde tam donanımlı ulusal ve uluslararası entegre bir laboratuvar ağı oluşturmaktır. LRN genellikle bir piramit şeklinde gösterilir. Piramidin tabanında nöbetçi laboratuvarlar bulunur. Bunlar, bulaşıcı bir etkenin primer tanısının genellikle gerçekleştiği mikrobiyoloji laboratuvarlarıdır. Diğer bir kavram biyosürveyans kavramıdır. Biyosürveyans biyoterörizm ve biyolojik olaylara yönelik daha kapsamlı bir yaklaşım için genel bir ifadedir. Teknoloji gereksinimleri ve maliyetinden dolayı biyolojik silahların üretimi nispeten kolay ve ucuz olduğundan, bu silahlar yüksek riskli kabul edilir. Bu yüzden biyoterörizm ile ilgili mikrobiyolojik gelişmelerin bilinmesi önemlidir.

Anahtar Kelimeler: Biyoterörizm, Mikrobiyolojik, Gelişmeler

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GRASS PLANT (LOLIUM *L.*) AS A BIOINDICATOR: HEAVY METAL CONTENT AND TOXICITY

ABSTRACT

Heavy metals; they are elements that have metallic properties, have a relatively high density, and can have toxic effects even at low concentrations. In this research study, grass plants (Lolium L.) grown in two different locations were taken, their species and taxon were determined, and some heavy metal amounts (As, Cd, Co, Cr, Cu, P, Pb, S, Zn) were measured in fresh and dry form. The samples were fragmented (burned) by the microwave method and measurements were determined with the ICP-OES (Inductively Coupled Plasma Optical Emission Spectrometry) spectrometer. The analysis results were compared among themselves and with the standards set by the World Health Organization and determinations were made. Results have been obtained regarding environmental pollution due to industrial, transportation and humanitarian activities carried out in the locations. Heavy metal contents of plant samples include; differences have been detected due to growing in different soil conditions and the variability of microelement levels in the soil. The contribution of natural water contamination of the location to heavy metal toxicity was determined. Unlike natural wastes, heavy metals are harmful and dangerous because they do not degrade.

Keywords: Grass Plant, Location, Heavy Metal, Environmental Pollution

BİYOİNDİKATÖR OLARAK ÇİMEN BİTKİSİ (LOLİUM *L.*): AĞIR METAL İÇERİĞİ VE TOKSİSİTE

ÖZET

Ağır metaller; metalik özellik gösteren, göreceli olarak yüksek yoğunluğa sahip, düşük derişimlerde bile toksik etki gösterebilen elementlerdir. Bu araştırma çalışmasında, iki ayrı lokasyonda yetişmiş çimen bitkisi (*Lolium L.)* alınmış, tür ve taksonu belirlenmiş, yaş ve kuru halinde bazı ağır metal miktarları (As, Cd, Co, Cr, Cu, P, Pb, S, Zn) ölçülmüştür. Örnekler mikrodalga yöntemi ile parçalanmış (yakılmış) ve ICP-OES (Inductively Coupled Plasma Optical Emission Spectrometry) spektrometre ile ölçümler belirlenmiştir. Analiz sonuçları kendi aralarında ve Dünya Sağlık Örgütünün belirlediği standartlar ile kıyaslanmış ve tespitlerde bulunulmuştur. Lokasyonlarında gerçekleştirilen endüstriyel, ulaşım ve insani faaliyetlere bağlı olarak çevresel kirlilik ile ilgili olarak sonuçlar elde edilmiştir. Bitki numunelerinin ağır metal içerikleri arasında; farklı toprak koşullarında yetişmesi ve toprakların mikroelement seviyelerinin değişkenliğinden kaynaklanan farklılıklar tespit edilmiştir. Lokasyona ait doğal su kontaminasyonunun ağır metal toksisitesine katkısı belirlenmiştir. Doğal kaynaklı atıkların aksine ağır metaller degrage olmadıkları için zararlı ve tehlikelidirler.

Anahtar Kelimeler: Çim bitkisi, Lokasyon, Ağır Metal, Çevresel Kirlilik

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MORPHOMETRIC ANALYSIS BY COMPUTED TOMOGRAPHY OF THE ENTRY POINT AND TRAJECTORY FOR SAFE SCREW FIXATION SURGERY OF THE C2 PEDIUNCLE IN THE TURKISH POPULATION ACCORDING TO AGE AND GENDER

ABSTRACT

Aim: The aim of this study was to evaluate the morphometry and morphology of the C2 vertebra for screw fixation surgery, to establish metric standards for the safe entry site and trajectory of the pedicle screw, to determine the feasibility of screw placement to reduce injury to the vertebral artery and medulla spinalis, and to establish metric standards for our population with the data obtained in this study.

Material and Method: Computed tomography images of 323 individuals, 163 females and 160 males aged 20-59 years, were used in the study. In the retrospective study, pedicle length (PL), pedicle thickness (PT), pedicle height (PH), pedicular angle (PA), pedicle-lamina angle (PLA), sagittal angle (SA) and ideal entry length (EL) parameters were evaluated on the right (R) and left (L) sides. The measured parameters were analysed in a total of 4 groups divided into age deciles.

Results: As a result of our study, it was found that PL, PH, EL parameters were higher in males between genders on both sides ($p<0.05$). It was found that RPL and RPA parameters were smaller than LPL and LPA, while RPLA parameter was larger than LPLA ($p<0.05$). In males, RPA, RSA and LSA parameters were greater in group 1 than in group 4 ($p<0.05$). In females, RPH and LPH parameters were found to be the largest in group 1 ($p<0.05$).

Conclusion: As a result of the study, C2 morphometry was found to be larger in males. Larger results in the 20-29 age group suggested the possibility of osteoporosis with advancing age. Significant morphometric differences were obtained between age groups, and we believe that C2 morphometry needs radiological imaging procedures for cervical screw fixation surgery.

Keywords: C2, Axis, Pedicle, Pedicular angle, Screw fixation surgery,

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THE PLACE OF TRADITIONAL MEDICINE IN PREVENTIVE MEDICINE

ABSTRACT

Objective: To investigate the place of acupuncture treatment in immunization (vaccination).

Material and Method: Studies on acupuncture treatment conducted on immunization and the immune system were reviewed through PubMed.

Findings: Immunization/vaccination is a preventive treatment method widely practiced across the world. A healthy immune system is an inevitable condition for proper immunization. Acupuncture treatment is one of the most frequently practiced traditional and complementary medicine applications worldwide. There are many studies on the immunomodulatory effect of acupuncture treatment. When we examine these studies, the effect of acupuncture treatment on the immune system is related to the effects of endogenous opioids β-endorphin, methionine enkephalin, and leucine enkephalin on the immune system. Therefore, leukocytes can synthesize β-endorphin from promolecules. (3,6,7) Additionally, endogenous opioid receptors have been found on B-lymphocytes, T-lymphocytes, natural killer cells, granulocytes, monocytes, platelets, and the complement terminal complex. It is known that endorphin and enkephalin increase the activity of natural killer cells, the production of cytotoxic T lymphocytes, the chemotaxis of monocytes, and the production of IF-γ, IL-1, IL-2, IL-4, and IL-6. (3,6,7) It is known that alpha, beta, and gamma endorphins have different immune functions. Alpha endorphins such as methionine enkephalin and leucine enkephalin are effective in antibody production. The immunomodulatory effect of acupuncture treatment is associated with the endogenous opioids that increase in plasma following acupuncture application. (1-3, 5, 13-15)

Conclusion: Acupuncture treatment has an immunomodulatory effect, and its application before and after immunization in cases where the immune system is negatively affected may enhance vaccine efficacy. Moreover, acupuncture treatment is known to be a safely applicable method in conditions such as cancer, HIV, chronic renal and liver failure, which adversely affect the immune system.

Keywords: Immunization, preventive medicine, vaccination, immune system, acupuncture, traditional and complementary medicine.

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THE METABOLIC TRANSITION POINTS DURING INCREMENTAL EXERCISE TEST: ESTABLISHING MODERATE TO HEAVY EXERCISE INTENSITY

ABSTRACT

Purpose: This study aimed to evaluate MET values at the LT, RCP and maximal exercise intensity and to explore their relationships with the percentage of VO_2max.

The exercise intensity is a critical determinant in modulating the body's physiological stress response and optimizing the health benefits of regular physical activity. A widely adopted and practical method for prescribing exercise intensity to achieve targeted health benefits is using Metabolic Equivalent (MET) levels, which categorize exercise intensity as light for activities below 3 METs, moderate between 3 and 5.9 METs, heavy between 6 and 9 METs, and severe for activities exceeding 9 METs. The individual's exercise intensity spectrum from rest to maximal oxygen uptake (VO_2max) can be precisely segmented using two key physiological thresholds: the lactate threshold (LT) and the respiratory compensation point (RCP), indicating intensity domains, as moderate, heavy and severe.

Material and Methods: Ten healthy sedentary males (age: 20.7±2.0 yrs) underwent an incremental exercise test with a cycle ergometer. The LT and RCP were estimated using respiratory and gas exchange parameters.

Results: LT occurred at 60.9±6.6 percent of VO_2max (varied from 53% to 71%) and RCP occurred at 71.1±7.8 percent of VO_2max (varied from 60% to 82%). MET values at the LT, RCP and at maximal exercise were found to be 6.9±1.3 (varied from 5.3 vs 9.1), 8.0±1.4 (varied from 5.9 to 10.4) and 11.6±1.42 (varied from 9.9 to 14.3), respectively.

Conclusion: The criteria for determining exercise intensity based on LT and RCP varied percentage of VO_2max across individuals. The corresponding MET values defining moderate, heavy and vigorous intensities also showed significant inter-individual variability. Consequently, when determining exercise intensity, LT and RCP offer more precise and individualized benchmarks than percentage of VO_2max and MET values, enhancing both the accuracy and effectiveness of exercise prescription.

Keywords: lactate threshold, respiratory compensation point, MET, incremental exercise test

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THE EFFECT OF REFORMER PILATES DURING PREGNANCY ON BODY AWARENESS, BALANCE, AND VAGINAL DELIVERY: A CONTROLLED CLINICAL STUDY

ABSTRACT

Purpose: The aim of this study was to investigate the effects of Reformer Pilates exercises during pregnancy on body awareness, balance skills, and type of delivery.

Material and method: A total of 63 healthy pregnant women participated in this controlled clinical study. Participants were equally divided into two groups (n=31). The study group received Reformer Pilates training twice a week from the 12th week of pregnancy until delivery. The control group was provided with a basic home-based exercise program. Body awareness was assessed using the Body Awareness Questionnaire; balance was assessed with the Timed Up and Go (TUG) test. The type of delivery (vaginal/cesarean) and duration of delivery were recorded postpartum. For multiparous participants, delivery duration was compared to previous births.

Results: The delivery duration in the Reformer Pilates group was significantly shorter compared to the control group ($p<0.05$). Additionally, among multiparous women, this delivery was shorter compared to previous ones. The vaginal delivery rate in the Pilates group was notably higher than in the control group (approximately 81%). Significant improvements in body awareness and balance test scores were observed in the Pilates group ($p<0.01$).

Conclusion: Regular Reformer Pilates practice during pregnancy improves body awareness and balance, reduces delivery duration, and increases the likelihood of vaginal delivery. These findings suggest that Reformer Pilates can be considered a safe and effective exercise approach in prenatal care.

Keywords: Pregnancy, Reformer Pilates, vaginal delivery, balance, body awareness

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CAPPING IN DENTISTRY

ABSTRACT

Capping involves the application of a biocompatible agent onto exposed pulp tissue to preserve the vitality, function, and pulp-dentin complex, and to promote the formation of a new dentin bridge or dentin-like structure. Capping treatment is applied in two different ways: direct and indirect.Several factors influence the success of capping treatment. These factors can be summarized as the patient's age, gender, symptoms of the tooth requiring capping, the cause of pulp exposure, the size and location of pulp exposure, the capping material used, and the restoration applied. In vital pulp treatments, which are simple and effective procedures, the use of a material suitable for the case is one of the most critical factors for treatment success.One of the most critical factors for successful pulp capping is the use of a material that is compatible with the tissue and capable of maintaining the vitality and function of the pulp.

Over time, various materials have been studied and recommended for pulp capping. The materials used for capping can be classified under the following categories: calcium hydroxide-containing materials, tricalcium silicate-containing materials, resin-containing materials, and other potential capping materials. When these materials are compared, various advantages and disadvantages are observed. Capping materials are indispensable for preserving pulp health in dentistry. Therefore, research continues to eliminate the disadvantages of existing capping materials, increase the success rate of capping applications, and achieve the ideal capping material. In this context, modifications are being made to existing materials, and new potential materials are being explored. Thanks to research and technological developments, the effectiveness and durability of these materials are improving.

Keywords: Dentistry, Pulp, Capping

DİŞ HEKİMLİĞİNDE KUAFAJ

ÖZET

Kuafaj; pulpanın canlılığını, fonksiyonlarını ve pulpa-dentin kompleksini korumak, yeni bir dentin köprüsü veya dentin benzeri yapı oluşumunu teşvik etmek amacıyla ekspoze pulpa dokusu üzerine doku dostu bir ajanın uygulanmasını içermektedir. Kuafaj tedavisi direkt ve indirekt olmak üzere iki farklı şekilde uygulanır. Kuafaj tedavisinin başarısını etkileyen pek çok faktör mevcuttur. Bu faktörler; hastanın yaşı, cinsiyeti, kuafaj uygulanacak dişin semptomları, pulpa ekspozunun nedeni, pulpa ekspozisyonun boyutu ve lokalizasyonu, kullanılan kuafaj materyali ve uygulanan restorasyon olarak özetlenebilir. Basit ve etkili uygulamalar olan vital pulpa tedavilerinde vakaya uygun materyal kullanımı, tedavi başarısında en önemli hususlardan biridir. Pulpa kuafajının başarılı olması için en önemli kritik faktörlerden biri; pulpa canlılığını ve fonksiyonunu koruyacak, doku ile uyumlu bir materyalin kullanılmasıdır. Günümüze kadar pulpa kuafajı için pek çok materyal incelenmiş ve tavsiye edilmiştir. Kuafaj amacıyla kullanılan materyaller; kalsiyum hidroksit içerikli materyaller, trikalsiyum silikat içerikli materyaller, rezin içerikli materyaller ve diğer potansiyel kuafaj materyalleri başlıkları altında sınıflandırılabilir. Mevcut materyaller birbirleriyle kıyaslandığında, çeşitli avantaj ve dezavantajlarının bulunduğu görülmektedir. Kuafaj materyalleri, diş hekimliğinde pulpa sağlığının korunması için vazgeçilmezdir. Bu nedenle mevcut kuafaj materyallerinin dezavantajlarını ortadan kaldırmak, kuafaj uygulamalarında başarı oranını arttırabilmek ve ideal kuafaj materyaline ulaşabilmek için araştırmalar devam etmektedir. Bu doğrultuda mevcut materyallerde modifikasyonlar yapılmakta ve yeni potansiyel materyaller araştırılmaktadır. Araştırmalar ve teknolojik gelişmeler sayesinde bu materyallerin etkinliği ve dayanıklılığı artmaktadır.

Anahtar Kelimeler: Diş Hekimliği, Pulpa, Kuafaj

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THE MODULATORY ROLE OF THE IMMUNE SYSTEM IN NEUROPATHIC PAIN: CELLULAR AND MOLECULAR MECHANISMS

ABSTRACT

Objective

Neuropathic pain is a complex form of chronic pain resulting from damage or dysfunction in the peripheral or central nervous system, often occurring without any nociceptive stimulus. The aim of this study is to evaluate the role of immune system components in the modulation and resolution of neuropathic pain, with an emphasis on the underlying cellular and molecular mechanisms.

Material and Method

This literature-based review examines recent experimental studies investigating the interactions between immune cells and neural structures in animal models of neuropathic pain. Key focus areas include the roles of innate and adaptive immunity, the meninges, gut microbiota, and specialized pro-resolving mediators (SPMs) derived from polyunsaturated fatty acids.

Results

Innate immune cells such as neutrophils, macrophages, microglia, and NK cells, as well as adaptive immune cells including regulatory T (Treg) and B cells, contribute significantly to the modulation of neuropathic pain via cytokine release, opioid peptide secretion, and anti-inflammatory pathways. Studies show that gut microbiota can influence pain perception by altering immune cell activity and inflammatory responses. Moreover, SPMs such as resolvins, protectins, maresins, and lipoxins have demonstrated promising antinociceptive effects in preclinical models by promoting tissue resolution and modulating neuroinflammation.

Conclusion

Recent findings highlight that the immune system plays an active and multifaceted role in the attenuation of neuropathic pain. Understanding these immunomodulatory mechanisms may provide novel therapeutic targets for the management of chronic pain conditions.

Keywords: Neuropathic pain, immune system, macrophages, Treg cells, specialized pro-resolving mediators

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THE INTERACTION BETWEEN METABOLIC SYNDROME AND DIABETIC NEUROPATHY: MECHANISMS AND THERAPEUTIC APPROACHES

ABSTRACT

Objective

Metabolic syndrome is a complex clinical condition characterized by the coexistence of hyperglycemia, dyslipidemia, obesity, and hypertension. Diabetic neuropathy, one of its frequent complications, is a progressive neurodegenerative disorder caused by peripheral nerve damage. This review aims to evaluate the impact of metabolic syndrome components on diabetic neuropathy and to elucidate the underlying pathophysiological mechanisms.

Material and Method

Based on recent literature, the structural and functional changes in the peripheral nervous system induced by hyperglycemia, dyslipidemia, and oxidative stress were examined. In addition, immunohistochemical markers and both pharmacological and lifestyle-based therapeutic approaches were reviewed.

Results

Hyperglycemia promotes axonal degeneration via energy deficiency and ROS production, while dyslipidemia enhances inflammatory responses that compromise neural integrity. Oxidative stress contributes to mitochondrial dysfunction, playing a pivotal role in disease progression. Immunohistochemical evaluation of epidermal nerve fibers may facilitate early diagnosis. Therapeutic agents such as vitamin derivatives, aldose reductase inhibitors, and antioxidants show promise in alleviating symptoms.

Conclusion

The influence of metabolic syndrome on neuropathy is multifactorial, and targeting a single metabolic pathway is often insufficient. Thus, personalized treatment strategies involving multidisciplinary and combined approaches are gaining importance.

Keywords: Metabolic syndrome, diabetic neuropathy, oxidative stress, dyslipidemia, hyperglycemia

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BIBLIOMETRIC ANALYSIS OF PUBLICATIONS ON VARICELLA ZOSTER VIRUS IN THE WEB OF SCIENCE DATABASE

ABSTRACT

Introduction: Varicella zoster virus (VZV) is a double-stranded, enveloped DNA virus in the Herpesviridae family. VZV remains latent in the dorsal root ganglia following primary infection with varicella; reactivation results in recurrent infection with herpes zoster (shingles). Since the introduction of the varicella vaccine in 1995, the incidence of varicella has decreased by 98% in all age groups. Bibliometric analysis can be defined as a quantitative analysis of academic studies published in a certain field and in a certain period determined by the researcher, and an analysis method in which these studies are associated with units such as author, country, journal and organization.

Objective: This study aims to provide a theoretical basis for future studies on Varicella zoster virus by focusing on research on Varicella zoster virus in the world and bibliometrically analyzing indexed publications in the Web of Science database.

Material, Methods and Results: The study covers the time period from January 1, 2005 to December 31, 2024 and focuses on research articles. The keyword “varicella zoster” was used to retrieve relevant publications. The analysis included areas such as publication trends over time, journals with the highest number of publications, leading institutions and authors. The keyword search yielded 9,768 records. 7,016 journal articles, as well as review articles (1,369), meeting abstracts (560), letters (389), editorial materials (359), book chapters (237). It is seen that the most publications were made in 2023 with 629 studies. Table 1 provides a summary view of the search strategy. It is seen that 8,344 of the studies are indexed in Science Citation Index Expanded (SCI-EXPANDED), 1,190 in Emerging Source Citation Index (ESCI), 484 in Conference Proceedings Citation Index- Science (CPCI-S) and 240 in Book Citation Index-Science (BKCI-S). An analysis by country and number of publications shows that the highest number of publications was made in the USA with 3,184, followed by Germany with 768 publications and the UK with 720 publications. The number of publications and citations by years are shown in Graph 1.

Conclusion: The bibliometric analysis conducted in this study is intended to provide a theoretical basis for future studies on Varicella zoster virus.

Keywords: Varicella zoster, Herpes zoster, varicella vaccine, bibliometric analysis

VARİCELLA ZOSTER VİRÜSÜ ÜZERİNE WEB OF SCİENCE VERİ TABANINDAKİ YAYINLARIN BİBLİYOMETRİK ANALİZİ

ÖZET

Giriş: Varicella zoster virüs (VZV), Herpesviridae ailesinde yer alan çift iplikli, zarflı bir DNA virüsüdür. VZV, primer enfeksiyonu olan suçiçeğinin sonrasında dorsal kök gangliyonlarında latent olarak kalır; reaktivasyonu sonucunda rekürren enfeksiyonu olan herpes zoster (zona) ortaya çıkar.1995 yılında suçiçeği aşısının piyasaya sürülmesinden bu yana suçiçeği insidansı tüm yaş gruplarında %98 oranında azalmıştır. Bibliyometrik analiz belirli bir alanda ve araştırıcı tarafından belirlenen, belirli bir dönemde yayımlanmış olan akademik çalışmaların, nicel analizi ile birlikte bu çalışmaların; yazar, ülke, dergi ve organizasyon gibi birimlerle ilişkilendirildiği bir analiz yöntemi olarak tanımlanabilir.

Amaç: Bu çalışma, Dünya'da Varicella zoster virüsü üzerine yapılan araştırmalara odaklanarak, Web of Science veri tabanındaki indekslenmiş yayınları bibliyometrik analiz ederek ileriki yıllarda Varicella zoster virüsü ile ilişkin yapılacak çalışmalara teorik temel sağlaması hedeflenmektedir.

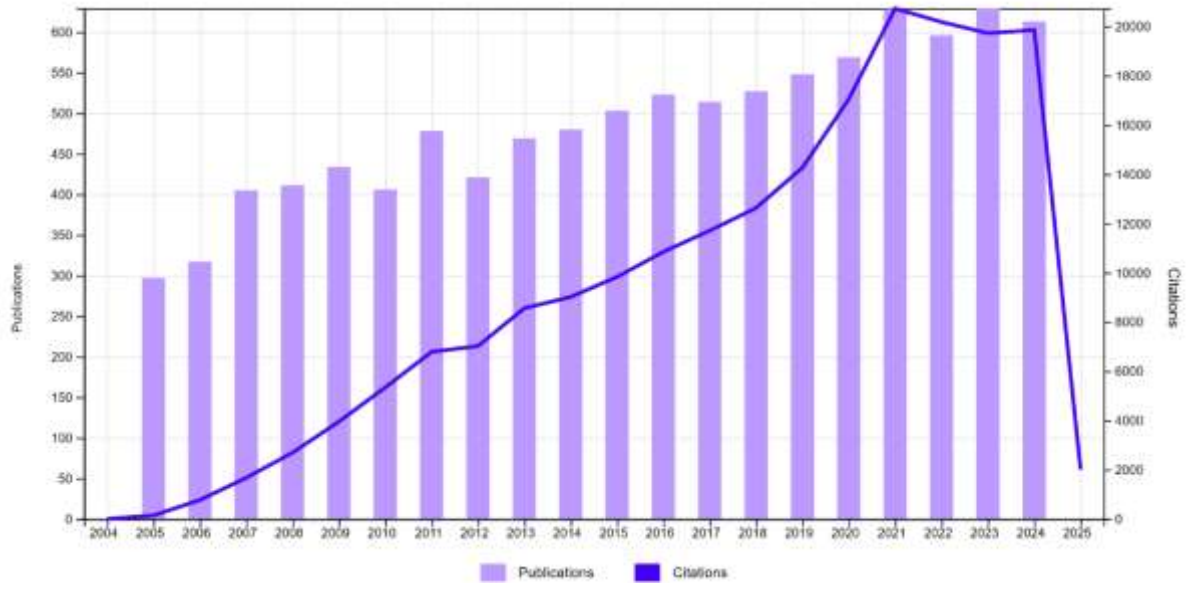
Materyal, Yöntem ve Bulgular: Çalışma, 1 Ocak 2005- 31 Aralık 2024 arasındaki zaman aralığını kapsamaktadır ve araştırma makalelerine odaklanmaktadır. "Varicella zoster" anahtar kelimesi, ilgili yayınları almak için kullanılmıştır. Analiz, zaman içindeki yayın eğilimleri, en yüksek yayın sayısına sahip dergiler, önde gelen kurumlar ve yazarlar, gibi alanları içermiştir. Anahtar kelimelerle yapılan aramayla 9.768 kayıt elde edilmiştir. 7.016 dergi makalesinin yanı sıra; inceleme makaleleri (1.369), toplantı özetleri (560), mektuplar (389), editoryal materyaller (359), kitap bölümleri (237)' den oluşmaktadır. En fazla yayının 629 çalışma ile 2023 yılında yapıldığı görülmektedir. Tablo 1'de arama stratejisine ilişkin özet görünümü verilmiştir. Çalışmaların 8.344 adedinin Science Citation Index Expanded (SCI-EXPANDED), 1.190 adedinin Emerging Source Citation Index (ESCI), 484 adedinin Conference Proceedings Citation Index – Science (CPCI-S) ve 240 adedinin Book Citation Index-Science (BKCI-S)'de indekslendiği görülmektedir. Ülkeler ve yayın sayılarına göre bir analiz yapıldığında ise en fazla çalışmanın 3.184 ile ABD'de yapıldığı, bunu sırası ile 768 çalışma ile Almanya'nın ve 720 çalışma ile İngiltere'nin izlediği görülmektedir. Yıllara göre yayın ve atıf sayısı şekil 1'de gösterilmiştir.

Sonuç: Bu çalışmada yapılan bibliyometrik analizin, ileriki yıllarda Varicella zoster virüsü ile ilişkin yapılacak çalışmalara teorik temel sağlaması hedeflenmektedir.

Anahtar kelimeler: Varicella zoster, Herpes zoster, suçiçeği aşısı, bibliyometrik analiz

Tablo 1. Arama Çerçevesi

Parametre	**Seçim**
Seçim Yaklaşımı	Bibliyometrik Analiz
Kullanılan Veritabanı	Web of Science (WoS)
Analiz için Kullanılan Araç	VosViewer 1.6.20
Arama Sorgusu (Bütün Alanlar)	Varicella zoster
Belgenin Niteliği	Makale, Toplantı özeti, Mektup, Editoryal materyal, Kitap Bölümü, Bildiri
Zaman Aralığı	2005-2024
Dil	İngilizce, Almanca, Fransızca, İspanyolca, Türkçe
Konu Alanı	Tümü
Analiz Edilmek Üzere Seçilen Toplam Belge Sayısı	9.768



Şekil 1. Yıllara göre yayın ve atıf sayısı

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EVIDENCE-BASED PRACTICES IN NEWBORNS; BABY MASSAGE

ABSTRACT

Massage is a treatment method known since ancient times, which is applied to the body with methods such as touching, patting and stroking with hands. The basic techniques of massage include efflorescence (stroking), petrisage (kneading), friction (rubbing), taputman (tapping) and vibration (vibration). It is a very useful method for infants and children with both physical and clinical effects and biochemical effects. It increases physical, sensory, motor, mental and social well-being in infants. The sense of touch in the baby is one of the earliest developing senses and body contact strengthens the sense of feeling safe for the newborn. Appropriate stimulation of the baby's sense of touch contributes positively to its psycho-social and biological development. For this reason, nurses should guide parents in infant massage by teaching the correct techniques and making practical demonstrations. They also have an important role in emphasising the benefits of massage on the baby and providing a safe care process with evidence-based information. Nurses support physical and emotional development by adapting the massage according to the individual needs of the baby.

Keywords: Newborn,baby massage,nursing care

YENİDOĞANLARDA KANIT TEMELLİ UYGULAMALAR; BEBEK MASAJI

ÖZET

Masaj, vücuda ellerle dokunma, sıvazlama ve okşama gibi yöntemlerle uygulanan, çok eski çağlardan beri bilinen bir tedavi metodudur. Masajın temel teknikleri arasında efloraj (sıvazlama), petrisaj (yoğurma), friksiyon (ovma), taputman (vurma) ve vibrasyon (titreşim) yer alır. Hem fiziksel ve klinik etkileri hem de biyokimyasal etkileriyle bebek ve çocuklar için oldukça yararlı bir yöntemdir. Bebeklerde fiziksel, duyusal, motor, zihinsel ve sosyal iyilik halinin artmasını sağlar. Bebekte dokunma duyusu en erken gelişen duyulardan biridir ve vücut teması, yenidoğan için güvende hissetme duygusunu güçlendirir. Bebeğin dokunma duyusunun uygun şekilde uyarılması, onun psiko-sosyal ve biyolojik gelişimine olumlu katkılar sağlar. Bu nedenle bebek masajında hemşireler, ebeveynlere doğru teknikleri öğreterek ve uygulamalı gösterimler yaparak rehberlik etmelidir. Ayrıca, masajın bebek üzerindeki faydalarını vurgulayıp kanıt temelli bilgilerle güvenli bir bakım sürecinin sağlanmasında önemli görevleri vardır. Hemşireler, bebeğin bireysel ihtiyaçlarına göre masajı uyarlayarak fiziksel ve duygusal gelişimi desteklerler.

Anahtar Kelimeler: Yenidoğan, bebek masajı, hemşirelik bakımı

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EVIDENCE-BASED PRACTICES IN NEWBORN; SKIN CARE PRACTICES

ABSTRACT

The skin, the largest organ of human beings, protects the body against physical, biological and chemical factors. The skin has many tasks. It also plays an important role in mother-baby bonding, especially by providing skin-to-skin contact in the newborn period. Skin care constitutes an important part of newborn care. The newborn is protected by the skin against external factors while passing from intrauterine life to extrauterine life. Skin barrier plays an important role in thermoregulation, fluid-electrolyte balance, environmental factors and protection against trauma. While term babies have an adequate skin barrier, this barrier is not fully developed in preterm babies. Therefore, care practices should be carried out more sensitively. After birth, this barrier needs special care to maintain its health. Correct skin care practices have an important place in protecting the integrity of the skin, acid mantle, skin flora, immunity and preventing infections. Nurses have important responsibilities in skin care. In this process, nurses should follow current information and use evidence-based practices while applying skin care of infants.

Keywords: Newborn,skin care, nursing care

YENİDOĞAN BEBEKLERDE KANIT TEMELLİ UYGULAMALAR; CİLT BAKIM UYGULAMALARI

ÖZET

İnsanoğlunun en büyük organı olan cilt, vücudu fiziksel, biyolojik ve kimyasal etkenlere karşı bir korur. Cildin çok fazla görevi vardır. Yenidoğan döneminde özellikle ten tene temas sağlanarak anne-bebek bağlanmasında da önemli rol oynar. Cilt bakımı yenidoğan bakımının önemli bir kısmını oluşturur. Yenidoğan intrauterin yaşamdan ekstrauterin yaşama geçerken dış etkenlere karşı cildi tarafından korunur. Cilt bariyeri termoregülasyon, sıvı-elektrolit dengesi, çevresel faktörler, travmaya karşı bebeği korumada önemli rol oynar. Term bebeklerde yeterli bir cilt bariyeri bulunurken preterm bebeklerde bu bariyer tam olarak gelişmemiştir. Bu nedenle bakım uygulamaları daha hassas bir şekilde gerçekleştirilmelidir. Doğum sonrasında da bu bariyerin sağlığını devam ettirebilmesi için özel bakıma ihtiyaç duyar. Doğru cilt bakımı uygulamaları; cildin bütünlüğünü, asit mantosunu, cilt florasını, bağışıklığı korumada ve enfeksiyonların önlenmesinde önemli yer tutar. Cilt bakımında hemşirenin önemli sorumlulukları vardır. Bu süreçte hemşireler güncel bilgileri takip ederek bebeklerin cilt bakımlarını uygularken kanıta dayalı uygulamalarını kullanmalıdır.

Anahtar Kelimeler: Yenidoğan,cilt bakımı,hemşirelik bakımı

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EFFECTS OF AGE AND SEX ON HEMATOLOGICAL PARAMETERS IN THOROUGHBRED AND ARABIAN HORSES

SAFKAN İNGİLİZ VE ARAP ATLARINDA HEMATOLOJİK PARAMETRELER ÜZERİNE YAŞ VE CİNSİYETİN ETKİLERİ

ÖZET

Bu çalışma, Arap ve safkan İngiliz atlarında temel hematolojik parametrelerin belirlenmesinin yanı sıra, cinsiyet ve yaş gibi biyolojik değişkenlerin söz konusu parametreler üzerindeki potansiyel etkilerini değerlendirmek amacıyla yürütüldü. Araştırma kapsamında, klinik olarak sağlıklı, 3 ve 4 yaş grubunda yer alan toplam 116 safkan yarış atı incelendi. Bu çalışmada hayvanlar, 46 İngiliz atı (23 dişi, 23 erkek) ve 70 Arap atı (32 dişi, 38 erkek) olmak üzere iki gruba ayrıldı.

Değerlendirilen hematolojik parametreler arasında hemoglobin (HGB), ortalama eritrosit hacmi (MCV), eritrosit sayısı (RBC), hematokrit (HCT), ortalama eritrosit hemoglobini (MCH), ortalama eritrosit hemoglobin konsantrasyonu (MCHC), lökosit sayısı (WBC), kırmızı hücre dağılım genişliği (RDW), nötrofil yüzdesi ve sayısı (%NEU, NEU), lenfosit yüzdesi ve sayısı (%LYM, LYM), monosit yüzdesi ve sayısı (%MONO, MONO), eozinofil yüzdesi ve sayısı (%EOS, EOS), bazofil yüzdesi ve sayısı (%BASO, BASO) ile trombosit sayısı (PLT) yer aldı.

Çalışmada, ırklar arasında yapılan karşılaştırmalarda sadece MCV, %NEU, NEU, %LYM ve %EOS düzeylerinde, cinsiyete göre yapılan karşılaştırmalarda ise, İngiliz atlarında LYM, %LYM ve %NEU düzeyleri ile Arap atlarında MCH ve MCV düzeylerindeki farklılık istatistiki açıdan anlamlı bulundu. İngiliz atlarında %LYM ve LYM düzeyleri hem yaş hem de cinsiyet faktörlerinden etkilenirken, Arap atlarında yaş ve cinsiyet değişkenlerinin değerlendirilen hematolojik parametreler açısından anlamlı bir farklılık oluşturmadığı saptandı.

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ATYPICAL CLINICAL FINDINGS IN BENIGN PAROXYSMAL POSITIONAL VERTIGO: TWO CASE REPORTS

BENİGN PAROKSİSMAL POZİSYONEL VERTİGO'DA ATİPİK KLİNİK BULGULAR: İKİ OLGU SUNUMU

ÖZET

Amaç: Benign Paroksismal Pozisyonel Vertigo (BPPV), periferik vestibüler sistemin en yaygın hastalıklarından biridir. Ancak bazı olgular atipik nistagmus paternleri gösterebilir. Bu çalışmada, atipik BPPV bulguları sergileyen iki olgu sunulmaktadır.

Materyal ve Yöntem: Çalışmaya vertigo şikayetiyle başvuran iki hasta dahil edilmiştir. Hastalar, spontan nistagmus, pozisyonel testler (Dix-Hallpike/DH ve supine roll testleri/SRT) ile değerlendirildi. Bulgulara göre uygun repozisyon manevraları uygulanarak tedavi süreçleri takip edildi.

Bulgular:

Vaka 1: 63 yaşında kadın hasta, 2 gün önce aniden başlayan ve geçmeyen baş dönmesi şikayetiyle kliniğimize başvurdu. Spontan nistagmus izlenmedi. SRT'de baş sağdayken 35.6°/s sağa vuran horizontal nistagmus 60 saniye devam etti, ardından yön değiştirerek sola vuran 3.2°/s horizontal nistagmus gözlendi. Baş soldayken başlangıçta 10 saniye sağa vuran, ardından 131°/s sola vuran horizontal nistagmus 60 saniye devam etti ve yön değiştirerek sağa vuran 18°/s horizontal nistagmus ve tekrar sola vuran nistagmus izlendi. Dört kez yön değiştiren nistagmus gözlendi. Hastaya barbekü manevrası uygulandı, ancak iki gün sonra düzelme gözlenmediği için Gufoni manevrası uygulandı. Kontrol muayenesinde, SRT'de apogeotropik nistagmus gözlenen hastaya tekrar barbekü manevrası uygulandı. Bir hafta sonraki kontrolde semptomlarının tamamen geçtiği belirlendi.

Vaka 2: 62 yaşında kadın hasta, 7-8 yıl önce yemek yerken başlayan baş dönmesinin o günden beri her yatağa yattığında tekrarlandığını belirtti. DH'de sağa yatışta sağa yukarı torsiyonel nistagmus ve vertigo izlendi, 32. saniyeden sonra downbeat nistagmus gözlendi. Sola yatışta sola yukarı torsiyonel nistagmus izlendi ve 22. saniyeden sonra downbeat nistagmus izlendi. Sağ taraf daha şiddetli olduğu için sağ Epley manevrası uygulandı. Kontrolünde Sol epley manevrası uygulandı. DH'de downbeat nistagmus devam ettiğinden, iki defa Deep Hanging manevrası uygulandı. Ancak, nistagmus tamamen kaybolmadı.

Sonuç: BPPV'nin atipik nistagmus paternleri sergileyebileceği ve bazı hastaların standart repozisyon manevralarına direnç gösterebileceği unutulmamalıdır. Özellikle horizontal kanal ve kupulolitiyazis bulguları gösteren olguların tedavisinde farklı manevraların kombinasyonu gerekebilir. Downbeat nistagmus saptanan hastalarda ise posterior semisirküler kanal tutulumu veya santral patolojiler açısından dikkatli olunmalıdır.

Anahtar Kelimeler: Benign Paroksismal Pozisyonel Vertigo, Olgu, Atipik

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PRESENTEEISM IN HEALTH WORKERS: AN INVISIBLE RISK

ABSTRACT

Objective: This article aims to examine the prevalence, underlying causes and workplace implications of presenteeism (employees continuing to work despite health problems) among healthcare workers. It aims to contribute to sectoral management strategies by assessing the invisible risks of presenteeism on employees' physical and mental health, patient safety and overall productivity of healthcare organisations.

Material and Method: The study was conducted by document analysis method, one of the qualitative research methods. The national and international literature on the health sector was reviewed; the documents examined in this context were selected from sources that focus specifically on the issue of presenteeism and provide data on the working conditions of health workers. The data were analysed and the causes, consequences and prevalence of presenteeism were classified. During the analysis process, the information obtained from the documents was compared with the literature and interpreted.

Findings: According to the literature, presenteeism is quite common among healthcare workers. Especially nurses and female employees exhibit this behaviour more frequently. Intense workload, economic pressures and job security concerns are among the main causes of presenteeism. While presenteeism leads to a significant decrease in work performance, it also causes an increase in errors in patient care quality. Long working hours and insufficient rest periods contribute to exacerbate this problem.

Conclusion: Presenteism is a phenomenon that carries serious risks at both individual and organisational levels in the healthcare sector. This situation, which threatens employee health and patient safety, also negatively affects the effectiveness of health services. Balancing the workload, implementing flexible working models and expanding psychological support programmes may be effective in reducing the negative effects of presenteeism. Healthcare organisations should develop comprehensive strategies and implement employee-oriented policies to manage this risk based on the findings from the literature.

Keywords: Presenteeism, Healthcare Workers, Workload, Health Service Quality

SAĞLIK ÇALIŞANLARINDA PRESENTEİZM: GÖRÜNMEYEN BİR RİSK

ÖZET

Amaç: Bu makale, sağlık çalışanlarında presenteizmin (çalışanların sağlık sorunlarına rağmen işe devam etmesi) yaygınlığını, altında yatan nedenleri ve iş yeri üzerindeki etkilerini incelemeyi amaçlamaktadır. Presenteizmin, çalışanların fiziksel ve zihinsel sağlığı, hasta güvenliği ve sağlık kuruluşlarının genel verimliliği üzerindeki görünmeyen risklerini değerlendirerek, sektörel yönetim stratejilerine katkı sağlamayı hedeflemektedir.

Materyal ve Yöntem: Çalışma, nitel araştırma yöntemlerinden doküman inceleme yöntemiyle yürütülmüştür. Sağlık sektörüne ilişkin ulusal ve uluslararası literatür taranmaya çalışılmış; bu kapsamda incelenen dokümanlar özellikle presenteizm konusuna odaklanan ve sağlık çalışanlarının çalışma koşullarıyla ilişkili veriler sunan kaynaklardan seçilmiştir. Veriler, değerlendirilerek; presenteizmin nedenleri, sonuçları ve yaygınlığı sınıflandırılmıştır. Analiz sürecinde, dokümanlardan elde edilen bilgiler literatürle karşılaştırılarak yorumlanmıştır.

Bulgular: Literatüre göre, sağlık çalışanları arasında presenteizm oldukça yaygın bir durumdur. Özellikle hemşireler ve kadın çalışanlar, bu davranışı daha sık sergilemektedir. Yoğun iş yükü, ekonomik baskılar ve iş güvencesi kaygıları, presenteizmin temel nedenleri arasında öne çıkmaktadır. Presenteizm, iş performansında belirgin bir düşüşe yol açarken, hasta bakım kalitesinde hataların artmasına da neden olmaktadır. Uzun çalışma saatleri ve yetersiz dinlenme süreleri, bu sorunun daha da derinleşmesine katkıda bulunmaktadır.

Sonuç: Presenteizm, sağlık sektöründe hem bireysel hem de kurumsal düzeyde ciddi riskler barındıran bir olgudur. Çalışan sağlığını ve hasta güvenliğini tehdit eden bu durum, aynı zamanda sağlık hizmetlerinin etkinliğini de olumsuz etkilemektedir. İş yükünün dengelenmesi, esnek çalışma modellerinin uygulanması ve psikolojik destek programlarının yaygınlaştırılması, presenteizmin olumsuz etkilerini azaltmada etkili olabilir. Sağlık kuruluşları, literatürden elde edilen bulgulara dayalı olarak bu riski yönetmek için kapsamlı stratejiler geliştirmeli ve çalışan odaklı politikalar uygulamalıdır.

Anahtar Kelimeler: Presenteizm, Sağlık Çalışanları, İş Yükü, Sağlık Hizmet Kalitesi

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PROTECTIVE ROLE OF GALANGIN AGAINST METHOTREXATE-INDUCED DAMAGE IN AML12 CELLS

ABSTRACT

Aim: This study aimed to evaluate the potential of galangin (GAL) in mitigating the cytotoxic and apoptotic effects of methotrexate (MTX), a commonly used antimetabolite in cancer therapy, on the alpha mouse liver 12 hepatocyte cell line (AML12).

Materials and Methods: Our study was designed with four groups in the AML12 cell line: control, MTX, GAL, and MTX+GAL. Substance concentrations to be applied to the cell lines were determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. Superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) enzyme expression levels were measured by Real-Time Polymerase Chain Reaction (RT-qPCR) to determine oxidative stress. Cytotoxicity was evaluated using IC50 doses determined by the MTT assay after 24-hour exposure. The mRNA expression levels of genes related to the antioxidant mechanism (SOD, CAT, GSH), cellular stress (Topoisomerase 1, Topoisomerase 2, P53), and apoptosis (BAX, B-cell lymphoma-2, apoptotic protease activating factor-1, second mitochondria-derived activator of caspase/direct IAP-binding protein with low pI, caspase-3, caspase-9) were analyzed by RT-qPCR.

Results: MTT assay results demonstrated that MTX alone induced cytotoxic effects on the AML12 cell line. However, a reduction in these cytotoxic effects was observed in the MTX+GAL combination group. RT-qPCR analyses revealed the activation of the antioxidant defense signaling pathway in all experimental groups. Interestingly, the antioxidant response was attenuated in the MTX+GAL group. Furthermore, the activation of the apoptotic signaling pathway was not prevented by the combination treatment.

Conclusion: This study suggests that treatment with GAL in combination with MTX may reduce the cytotoxic effects of MTX on the AML12 cell line. Although the antioxidant defense mechanism was activated in all groups, this response was lower in the combination group. The combination treatment did not suppress the apoptotic signaling pathway, and further studies are warranted to elucidate whether apoptosis actually occurs.

Keywords: MTX, GAL, AML12 cell line, cytotoxicity, apoptosis

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EVALUATION OF CHILDREN REFERRED TO A PEDIATRIC CARDIOLOGY OUTPATIENT CLINIC AT A TERTIARY CENTER FOR PRE-PARTICIPATION SPORTS EXAMINATION

ABSTRACT

Objective: In recent years, with the increasing participation of children and adolescents in sports activities, the importance of pre-participation health screenings has also grown. In this context, the evaluation of the cardiovascular system is of critical importance to prevent sudden cardiac events. This study aimed to present our findings from pre-participation cardiac assessments in children and adolescents in light of the existing literature.

Material and Methods: Children and adolescents who applied to our center between August 2023 and August 2024 for sports clearance were retrospectively evaluated. Demographic data, personal and family history, electrocardiography (ECG), echocardiography (ECHO) findings, and further investigations were reviewed from pediatric cardiology clinic records.

Results: Of 311 cases, 182 (58.5%) were male. The mean age was 12.5±2 years. At admission, 295 patients (94.9%) were asymptomatic. The most common symptom was exertional chest pain (n=6, 1.9%). Eight had endocrine/neurological disease, and 11 had a family history of cardiac disease. ECG was normal in 305 patients (98.1%); minor abnormalities were seen in 6 (1.9%), most commonly ventricular extrasystoles (n=4, 1.3%). ECHO was normal in 266 patients (85.5%) and showed minor findings in 45 (14.5%). The most frequent ECHO findings were minimal mitral regurgitation (n=19, 6.1%), mitral valve prolapse (n=9, 2.9%), atrial septal defect (n=4, 1.3%), and mitral cleft (n=4, 1.3%). Advanced tests such as Holter monitoring, exercise testing, and imaging were performed in selected cases based on symptoms or risk factors. No contraindications to sports participation were identified, and all patients were approved for activity.

Results: Our study found no significant cardiac abnormalities that would prevent children and adolescents from participating in sports following a pre-participation cardiac evaluation. Most patients can be safely assessed at the primary or secondary care level through detailed history-taking, physical examinations, and basic tests. Referrals to pediatric cardiology should be reserved for individuals with a concerning medical history, notable physical findings, or abnormal ECG results.

Keywords: Child; pediatric cardiology; pre-participation evaluation

SPOR ÖNCESİ KATILIM MUAYENESİ İÇİN ÜÇÜNCÜ BASAMAK MERKEZDE ÇOCUK KARDİYOLOJİ POLİKLİNİĞİNE YÖNLENDİRİLEN ÇOCUKLARIN DEĞERLENDİRİLMESİ

ÖZET

Amaç: Son yıllarda çocuk ve adölesanların spora katılımının artmasıyla, spor öncesi sağlık taramalarının önemi giderek artmaktadır. Bu süreçte kardiyovasküler sistemin değerlendirilmesi, ani kardiyak olayların önlenmesi açısından kritik öneme sahiptir. Bu çalışmada, çocuk ve adölesanlarda spora katılım öncesi yapılan kardiyak değerlendirme sonuçlarımızın literatür eşliğinde sunulması amaçlanmıştır.

Materyal ve Yöntem: Ağustos 2023–Ağustos 2024 tarihleri arasında spora katılım amacıyla merkezimize başvuran çocuk ve adölesanların demografik verileri, kişisel ve aile öyküleri, elektrokardiyografi (EKG), ekokardiyografi (EKO) bulguları ve yapılan ileri incelemeler retrospektif olarak değerlendirildi..

Bulgular: Toplam 311 olgunun 182'si (%58,5) erkekti; yaş ortalaması 12,5±2 yıl idi. Başvuru sırasında 295 olguda (%94,9) semptom yoktu. En sık semptom eforla göğüs ağrısı olup 6 olguda (%1,9) görüldü. Sekiz olguda endokrin/nörolojik hastalık, 11'inde kardiyak hastalık açısından riskli aile öyküsü vardı. EKG bulguları 305 olguda (%98,1) normaldi; 6 olguda (%1,9) minör anomali saptandı. En sık EKG bulgusu ventriküler erken atım idi (n=4, %1,3). EKO sonuçlarına göre 266 olguda (%85,5) normal, 45 olguda (%14,5) minör patoloji mevcuttu. En yaygın EKO bulguları minimal mitral yetersizlik (n=19, %6,1), mitral valv prolapsusu (n=9, %2,9), atriyal septal defekt (n=4, %1,3) ve mitral kleft (n=4, %1,3) idi. Yakınma, öz-soygeçmişteki risk faktörleri nedeniyle yapılan ileri incelemelerde (ritm holter, efor testi ve kardiyak görüntüleme) tüm hastalara spora katılım açısından engel teşkil edecek bir durum saptanmadı ve tamamına spor yapmaya uygunluk raporu verildi.

Sonuç: Çalışmamızda, çocuk ve adölesanlarda spora katılım öncesi yapılan kardiyak değerlendirme sonucunda, sporu engelleyebilecek klinik açıdan anlamlı bir kardiyak anormalliğe rastlanmamıştır. Çoğu olgu, ayrıntılı öykü alma, fizik muayene ve temel tetkiklerle birinci veya ikinci basamak sağlık hizmetlerinde güvenle değerlendirilebilecek düzeydedir. Bu doğrultuda, yalnızca şüpheli öykü, fizik muayene veya EKG bulgusu saptanan bireylerin ileri inceleme amacıyla çocuk kardiyoloji birimine yönlendirilmesi uygun bir yaklaşım olacaktır.

Anahtar Kelimeler: Çocuk; çocuk kardiyolojisi; spor öncesi değerlendirme

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RETROSPECTIVE ANALYSIS OF MOLLUSCUM CONTAGIOSUM RESULTS IN SKIN EXCISION BIOPSIES

ABSTRACT

Aim: This study aimed to evaluate the retrospective analysis and clinicopathological correlation of biopsies of cases diagnosed with Molluscum Contagiosum on the skin.

Material and Method: Hematoxylin & Eosin stained sections and immunohistochemical (IHC) stained preparations, if any, of 85 cases excised due to skin lesions between 2004-2025 were retrospectively re-evaluated. Age, gender, localization, number of lesions, macroscopic size of the cases were obtained from the pathology report, and HIV test results, if any, were obtained from the hospital automation.

Results: The mean age of 85 cases was 31.59, and their ages ranged from 2 to 64. 42 of the cases were female (49.4%) and 43 were male (50.6%). HIV test was not performed in 59 cases (69.4%) and there was no positive result (n: 26, 30.6%) in those that were performed. Most of the lesions were single (n: 71, 91.8%), and there were multiple lesions in 7 cases (7.2%). The lesions were most frequently in the genital area and their localizations are summarized in Table 1. The largest macroscopic dimension of the lesions was 2.4 cm, the smallest lesion was 0.1 cm and the average was 0.64 cm. The macroscopic dimension in women (0.8 cm) was significantly larger than the macroscopic dimension in men (0.47 cm) (p=0.005).

Conclusion: Molluscum Contagiosum is a lesion most commonly seen in the genital area and can be observed in different localizations. It has been observed that the macroscopic size reaches significantly larger sizes in women than in men. It can present as a single or multiple lesion in the clinic. Molluscum Contagiosum is a lesion that should be kept in mind in the differential diagnosis when evaluating skin biopsies, as it can present in different age ranges, sizes and clinical presentations.

Table 1: Distribution of lesions in cases according to their localizations

Localization	Frequency	Percentage %
FOOT	9	10,6
HAND	12	14,1
GENITAL REGION	26	30,6
PUBIC	13	15,3
TORSO	6	7,1
THIGH	3	3,5
BACK	5	5,9
LEG	4	4,7
FACE	5	5,9
ARM	2	2,4
Total	85	100,0

Keywords: Molluscum Contagiosum, skin lesions, localization

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THE ROLE OF THE KETOGENIC DIET IN DRUG-RESISTANT EPILEPSY

ABSTRACT

Epilepsy is a chronic neurological disorder characterized by recurrent seizures. Although there is no comprehensive prevalence and incidence study representing the general population of Turkey, existing regional research reports that the prevalence of epilepsy ranges between 5 and 7 per 1,000 individuals. Epilepsy significantly reduces an individual's quality of life and also affects familial, social, and economic dimensions. Drug-resistant epilepsy, in particular, constitutes the most challenging patient group in clinical management due to its poor response to antiepileptic drugs. The ketogenic diet (KD), which has been used for therapeutic purposes since the 1920s, is considered an alternative approach in cases of drug-resistant epilepsy. This nutritional model, which includes high fat, low carbohydrate, and adequate protein content, induces physiological ketosis by altering energy metabolism in the brain, thereby producing biochemical and neurological effects that suppress seizure activity. The KD has been reported to reduce seizure frequency by more than 50%, especially in childhood epilepsies, and to completely eliminate seizures in some cases. The KD should also be considered a multifaceted metabolic intervention. As it is restrictive in taste and difficult to sustain, various KD variants with lower fat content, such as the medium-chain triglyceride (MCT) diet, the modified Atkins diet (MAD), and the low glycemic index treatment (LGIT), have been developed to improve patient adherence. Additionally, lower-ratio KD protocols such as 3:1, 2:1, or 1:1 are determined based on the patient's age, individual tolerance, level of ketosis, and protein requirements. Close monitoring of the biochemical changes that occur during KD implementation is important for the early identification and prevention of potential diet-related side effects. The KD also has certain disadvantages. It is not suitable for individuals with renal failure, those at risk of cardiovascular disease, or pregnant and breastfeeding women. In order to better demonstrate the effects of the KD on seizure control and overall patient health, there is a need for large-sample, long-term, and controlled studies. The implementation and sustainability of the KD is not only a medical process but also a psychosocial one. Therefore, the monitoring and management of the diet should be carried out by a multidisciplinary team consisting of physicians, dietitians, and psychologists.

Keywords: epilepsy, ketogenic diet, drug-resistant epilepsy, ketosis

İLACA DİRENÇLİ EPİLEPSİDE KETOJENİK DİYETİN KLİNİK KULLANIMI VE ETKİNLİĞİ

ÖZET

Epilepsi, tekrarlayan nöbetlerle karakterize edilen kronik bir nörolojik hastalıktır. Türkiye genelini temsil eden kapsamlı bir prevalans ve insidans çalışması bulunmamakla birlikte, mevcut bölgesel araştırmalarda epilepsi sıklığının binde 5 ila 7 arasında değiştiği bildirilmiştir. Epilepsi, bireyin yaşam kalitesini önemli ölçüde düşürmekte; ailesel, sosyal ve ekonomik düzeyleride etkilemektedir. Özellikle ilaca dirençli epilepsi, antiepileptik ilaçlara yanıt vermemesi nedeniyle klinik yönetimi en zor olan hasta grubunu oluşturmaktadır. 1920'li yıllardan itibaren tedavi amacıyla kullanılan ketojenik diyet (KD), ilaca dirençli epilepsi vakalarında alternatif bir yaklaşım olarak değerlendirilmektedir. Yüksek yağ, düşük karbonhidrat ve yeterli protein içeren bu beslenme modeli, metabolizmayı fizyolojik ketozise yönlendirerek beynin enerji metabolizmasını değiştirmekte, bu sayede nöbet aktivitesini baskılayan biyokimyasal ve nörolojik etkiler ortaya çıkarmaktadır. KD'nin, özellikle çocukluk çağı epilepsilerinde %50'nin üzerinde nöbet sıklığını azalttığı, bazı vakalarda ise nöbetleri tamamen ortadan kaldırdığı bildirilmektedir. KD, aynı zamanda çok yönlü bir metabolik müdahale olarak ele alınmalıdır. KD, lezzet açısından sınırlayıcı ve sürdürülebilirliği zor bir diyet olduğundan, hastaların diyete uyumunu artırmak amacıyla orta zincirli trigliserit (MCT) diyeti, modifiye Atkins diyeti (MAD) ve düşük glisemik indeksli diyet tedavisi (LGIT) gibi daha düşük yağ içeriğine sahip KD varyantları geliştirilmiştir. Ayrıca, 3:1, 2:1 veya 1:1 gibi daha düşük oranlı KD modelleri, hastanın yaşı, bireysel toleransı, ketozis düzeyi ve protein gereksinimlerine göre belirlenmektedir. KD uygulama süresince vücutta meydana gelen biyokimyasal değişikliklerin yakından izlenmesi, diyete bağlı gelişebilecek olası yan etkilerin erken tanınması ve önlenmesi önemlidir. KD bazı dezavantajlara da sahiptir. Özellikle böbrek yetmezliği olan bireyler ile kardiyovasküler hastalık riski taşıyanlar ve hamile ya da emziren kadınlar açısından uygun değildir. KD'nin nöbet kontrolü ve hasta sağlığı üzerindeki etkilerini daha net biçimde ortaya koyabilmek için, yüksek örneklem sayısına sahip, uzun süreli ve kontrollü çalışmalara ihtiyaç duyulmaktadır. KD'nin uygulanması ve sürdürülebilirliği, yalnızca tıbbi değil aynı zamanda psikososyal bir süreçtir. Bu nedenle, diyetin izlenmesi ve yönetimi, hekim, diyetisyen ve psikologlardan oluşan multidisipliner bir ekip tarafından yürütülmelidir.

Anahtar Kelimeler: epilepsi, ketojenik diyet, ilaca dirençli epilepsi, ketozis

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DETERMINATION OF NURSING STUDENTS' KNOWLEDGE LEVELS REGARDING MEDICAL DEVICE-RELATED PRESSURE INJURIES

ABSTRACT

Aim: This study was conducted to determine the knowledge level of nursing students regarding medical device-related pressure injuries.

Materials and Methods: This descriptive-cross-sectional study was conducted at a state university between December 2024 and February 2025. A total of 167 students studying in the 3rd and 4th grades of the nursing department of the faculty of health sciences participated in the study. Data were collected face-to-face using an introductory information form and the Medical Device-Related Pressure Injury Knowledge Assessment Test. Mann-Whitney U test and Kruskal Wallis-H Test were used in the analysis of the data. Before starting the research, ethics committee approval (Date: November 12, 2024, Number no: E-30640013-050.04-226532) and institutional permission (Date: November 25, 2024, Number no: E-85246909-044-228328) were obtained. In addition, the participants were informed about the purpose and process of the study, and their informed verbal consent was obtained.

Results: It was determined that 70.1% of the students had heard of the concept of medical device-related pressure injuries, and 67.7% had encountered patients with medical device-related pressure injuries during their clinical practice. It was determined that the total score of the students from the Medical Device-Related Pressure Injury Knowledge Level Assessment Test was 9.06±2.15. It was determined that there was no significant difference between the scores of the students in the Medical Device-Related Pressure Injury Knowledge Assessment Test and their introductory characteristics (gender, age group, parent education level, grade, satisfaction with studying in the nursing department, etc.) ($p>0.05$).

Conclusion: In this study, it was determined that nursing students' knowledge regarding medical device-related pressure injuries was not at the desired level. In line with our study findings, it is recommended that practices that will increase awareness and improve knowledge levels of nursing students regarding medical device-related pressure injuries should be included in their formal education.

Keywords: Nursing, Medical device-related pressure injuries, Student.

HEMŞİRELİK ÖĞRENCİLERİNİN TIBBİ CİHAZ KAYNAKLI BASINÇ YARALANMALARINA İLİŞKİN BİLGİ DÜZEYLERİNİN BELİRLENMESİ

ÖZET

Amaç: Bu çalışma, hemşirelik öğrencilerinin tıbbi cihaz kaynaklı basınç yaralanmalarına ilişkin bilgi düzeylerini belirlemek amacıyla yürütüldü.

Materyal ve Yöntem: Tanımlayıcı-kesitsel tipte yürütülen bu çalışma, bir devlet üniversitesinde Aralık 2024- Şubat 2025 tarihleri arasında yapıldı. Araştırmaya sağlık bilimleri fakültesi hemşirelik bölümünde 3. ve 4. sınıfta öğrenim gören 167 öğrenci katıldı. Araştırmanın verileri, tanıtıcı bilgi formu ve Tıbbi Cihaz ile ilişkili Basınç Yarası Bilgi Düzeyi Değerlendirme Testi kullanılarak yüz yüze toplandı. Verilerinin analizinde Mann-Whitney U testi ile Kruskal Wallis-H Testi kullanıldı. Araştırmaya başlamadan önce etik kurul izni (Tarih: 12.11.2024, Sayı no: E-30640013-050.04-226532) ve kurum izni (Tarih: 25.11.2024, Sayı no: E-85246909-044-228328) alındı. Bununla birlikte katılımcılara çalışmanın amacı ve süreci hakkında bilgi verilip, bilgilendirilmiş sözlü onamları alındı.

Bulgular: Öğrencilerin %70,1'inin tıbbi cihaz kaynaklı basınç yaralanmaları kavramını duyduğu, %67,7'sinin klinik uygulamaları esnasında tıbbi cihaz kaynaklı basınç yaralanması olan hasta ile karşılaştığı belirlendi. Öğrencilerin Tıbbi Cihaz ile İlişkili Basınç Yarası Bilgi Düzeyi Değerlendirme Testinden aldıkları toplam puanın 9,06±2,15 olduğu saptandı. Öğrencilerin Tıbbi Cihaz ile İlişkili Basınç Yarası Bilgi Düzeyi Değerlendirme Testi'nden aldıkları puanlar ile tanıtıcı özellikleri (cinsiyet, yaş grubu, anne-baba eğitim düzeyi, sınıfı, hemşirelik bölümünde öğrenim görmekten memnun olma durumu vb.) arasında anlamlı bir fark olmadığı belirlendi ($p>0,05$).

Sonuç: Bu çalışmada, hemşirelik öğrencilerinin tıbbi cihaz kaynaklı basınç yaralanmalarına ilişkin bilgilerinin istendik düzeyde olmadığı saptandı. Çalışma bulgularımız doğrultusunda, hemşirelik öğrencilerinin örgün eğitimleri sürecinde tıbbi cihaz kaynaklı basınç yaralanmaları konusunda farkındalıklarını artıracak ve bilgi düzeylerini geliştirecek uygulamalara yer verilmesi önerilmektedir.

Anahtar Kelimeler: Hemşirelik, Tıbbi cihaz kaynaklı basınç yaralanmaları, Öğrenci.

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NOVEL PREOPERATIVE CT-DERIVED PARAMETERS TO ENHANCE SEMS OUTCOMES IN OBSTRUCTIVE COLORECTAL CANCER

ABSTRACT

Aim: This study aimed to determine whether preoperative computed tomography (CT)-derived morphological parameters can predict clinical success of self-expanding metallic stents (SEMS) in patients with malignant colorectal obstruction, thereby aiding clinicians in making informed decisions on patient selection and procedural planning.

Materials and methods: Between 2016 and 2021, we retrospectively examined 66 patients diagnosed with acute malignant colonic obstruction who received SEMS placement. Preoperative CT scans were reviewed to measure tumor length, wall thickness, and the narrowest lumen diameter. Two ratios were then calculated: SEMS length to tumor length, and SEMS diameter to lumen diameter. Clinical success was defined as effective bowel decompression within 96 hours of stent placement and no stent-related reintervention within three months.

Results: Of the 66 patients, 47 (71.2%) achieved clinical success. Longer tumor length, higher tumor thickness-to-lumen diameter ratio, and smaller lumen diameter emerged as significant predictors of failure ($p<0.05$). Conversely, a larger SEMS length-to-tumor length ratio correlated with better outcomes ($p=0.009$). Patient age, tumor wall thickness, and colonic angulation did not show significant associations with SEMS success ($p>0.05$). These findings suggest that precise morphologic assessment on CT may guide optimal stent sizing and placement.

Conclusion: Our results highlight the value of preoperative CT-based measurements—particularly tumor length, lumen diameter, and tumor thickness-to-lumen diameter ratio—in predicting SEMS efficacy for malignant colorectal obstruction. Tailoring stent selection according to these parameters could reduce complications, enhance decompression, and potentially improve stent patency over time. Larger, prospective multicenter studies are warranted to validate these observations and refine best practices, ultimately enhancing patient outcomes in both palliative settings and as a bridge to surgery.

Keywords: Colorectal Obstruction, Self-Expanding Metallic Stents, Computed Tomography, Tumor Morphology

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NANOCOMPOSITES OF gCN/BiOCl/Ag_2MoO_4 ARE DESIGNED FOR SUPERIOR SUNLIGHT SENSITIVITY, ENHANCING THE PHOTOCATALYTIC BREAKDOWN OF OG DYE

ABSTRACT

In this investigation, a nanocomposite consisting of porous graphite carbon nitride (g-C_3N_4)[1], BiOCl[2], and Ag_2MoO_4 was synthesized through coprecipitation[3] to establish a heterojunction interface. The compounds underwent characterization using XRD, EDX, SEM, UV–vis, and FT-IR analysis. The results demonstrated that the composite displayed exceptional photocatalytic efficacy in the degradation of Orange G (OG) and exhibited enhanced photostability. The OG solution was degraded by over 90% within 60 minutes, surpassing the degradation achieved by each semiconductor individually. Trapping experiments indicated that holes played a significant role in OG photodegradation. This research introduces a promising material for potential applications in the photocatalytic treatment of water pollution.

Keywords: *nanocomposite photocatalyst; coprecipitation; degradation; OG.*

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RISK FACTORS AND IMPACT OF TAXANE TOXICITY IN LUNG CANCER TREATMENT

ABSTRACT

Introduction

This work focuses on evaluating the side effects induced by chemotherapy with taxanes in patients with bronchial cancer. Taxanes, such as paclitaxel and docetaxel, are key antineoplastic agents used in the treatment of various cancers, including bronchial cancer. However, their use is associated with significant side effects that can impair patients' quality of life and limit treatment efficacy.

Material and methods

Our work is based on a retrospective epidemiological analysis that used patient data from multiple oncology facilities' cancer registries at the Oran city level. Lung cancer patients were questioned and database information on the most common side effects, such as peripheral neuropathy, hypersensitivity reactions, and gastrointestinal disorders, while considering their frequency and severity based on administered doses, patient age, and the number of treatment cycles received.

Results

In this study, we included 142 patients with broncho-pulmonary carcinoma receiving taxanes. We discovered a considerable imbalance in treatment responses, with nonresponders outnumbering responders. Peripheral neuropathy was identified as the most serious side effect, and categorization by treatment tolerance revealed heterogeneity in individual responses and unfavorable impact profiles.

Conclusion

The research aims to establish correlations between these adverse effects and patient clinical characteristics by focusing on a specific population of bronchial cancers patients. The ultimate goal is to enhance understanding of taxane-induced toxicity, identify risk factors, and propose tailored strategies to optimize their use while minimizing negative patient impacts.

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ADVANCING SURGICAL PRECISION: A NOVEL APPROACH USING PERSONALIZED 3D PRINTING IN COMPLEX SPINAL OSTEOTOMY FOR ANKYLOSING SPONDYLITIS-RELATED KYPHOSCOLIOSIS

ABSTRACT

INTRODUCTION: Ankylosing spondylitis (AS) is a chronic rheumatic inflammatory disease primarily impacting the spine and sacroiliac joint, leading to gradual flexibility loss and severe kyphoscoliosis. Pedicle subtraction osteotomy (PSO) has traditionally corrected thoracolumbar kyphoscoliosis associated with AS, demanding technical expertise and often reserved for experienced surgical teams. The overall rate of complications is 69.2% such as long incisions, soft tissue disruption, extended operative durations, and notable blood loss[1].Precise technologies are crucial for effectively addressing this deformity. Personalised digital surgical planning and 3D printing guidance templates have proven feasible, effective, and applicable in treating severe adult rigid deformities.[2]

METHODS: This study introduces a novel approach for performing asymmetric wedge PSO in severe thoracolumbar kyphoscoliosis secondary to AS. Surgical-guiding templates,designed considering surgeon requirements, patient-specific factors, and healthcare efficiencies, aided severe spinal deformity correction. The study involved 2 groups of patients undergoing surgery with 3D printing assistance or the freehand technique. Stratified manufacturing and a superimposed prototyping mode enabled 3D printing's conversion of computerised data (e.g., CT scans) into 3D objects. Comprehensive patient data, including age, gender, diagnosis, operation time, blood loss, fusion levels, screw density, complications, Cobb angle, and correction rate, were collected and analysed.[3]

RESULTS: The 3D printing group demonstrated significantly improved screw accuracy and reduced blood loss compared to the freehand group.Conversely complications,including nerve root or spinal cord injuries,sagittal translation and coronal imbalance were observed in 61% of patients in the freehand group due to screw misplacement.[3]

DISCUSSION: Incorporating 3D planning and templates facilitated surgery by providing insights into case-specific anatomy, aiding vertebral level identification, visualising malformed vertebrae, and most importantly enabling direct translation of planned PSO using 3D-printed individualised templates. The 3D-printed guide template showed superior accuracy and safety in screw placement compared to the traditional freehand technique, especially in treating scoliosis in children and adolescents.[4]

CONCLUSION: The integration of 3D virtual planning, 3D-printed spine models, and osteotomy-guiding templates has optimised osteotomy procedures,suggesting potential enhanced safety in future spinal osteotomies.

Keywords - 3D printing; kyphoscoliosis; spine surgery

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PLATELET-RICH PLASMA THERAPY- ENHANCED OVARIAN REJUVENATION: A PROMISING APPROACH TOWARDS OVARIAN INSUFFICIENCY AND FERTILITY PRESERVATION

ABSTRACT

INTRODUCTION

Ovarian aging is a natural process marked by a reduction in both the quantity and quality of oocytes within the follicular pool. Ovarian function naturally ceases around the age of 50, marking the onset of menopause. Women are born with a finite number of eggs, and this reserve begins to deplete from birth onward.This age-related decline in follicle count significantly impacts fertility and is becoming an increasingly common reason for women to pursue fertility treatments.

Platelet-rich plasma (PRP) therapy for the ovaries could be a promising treatment option for patients with a poor prognosis for fertility.

METHODS

This literature review involved a comprehensive search through various database such as Google scholar, pubmed and has comprised data of patients intended for PRP treatment of the ovaries.Blood samples were collected, PRP was prepared, and intraovarian infusions were administered to all participants. The effectiveness of PRP was assessed through a two-month follow-up, during which levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (E2), and anti-Mullerian hormone (AMH) were measured in all individuals.

RESULTS

The objective of this study was to assess the effectiveness of intraovarian PRP injections in women experiencing ovarian dysfunction caused by poor ovarian response (POR), premature ovarian insufficiency (POI), perimenopause, and menopause.

The average number of oocytes increased after the PRP injection. Additionally, the study revealed a decline in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels, while estradiol (E2) and anti-Mullerian hormone (AMH) levels showed a notable increase after the 2 month of follow-up, which further resulted in successful conception and live births. Women with menopause noticed the return of the menstrual cycle after the PRP administration.

DISCUSSION

The regenerative healing properties of PRP are due to its high concentrations of various growth factors, including transforming growth factor-β, insulin-like growth factors 1 and 2

(IGF-1 and IGF-2), and vascular endothelial growth factor (VEGF). These growth factors play a crucial role in promoting tissue repair and regeneration.No allergic reactions, hypersensitivity issues, or complications related to anesthesia were reported among the patients involved in the study.

All participants showed improvements in ovarian function,by changes in their hormonal levels, successful pregnancies, live births, and the return of their menstrual cycles.

CONCLUSION

Ovarian rejuvenation through autologous intraovarian infusion of PRP can be regarded as a promising treatment option to restore the reproductive functions of the ovaries.

However further research is essential to establish treatment protocols and understand long-term effects.

Keywords: Platelet-rich plasma, ovarian dysfunction, fertility treatment, reproductive health, growth factors.

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UNPACKING THE COMPLEXITIES OF DATING VIOLENCE: A MODERATED-MEDIATION ANALYSIS OF OPTIMISM, SELF-CONFIDENCE, HONESTY AND EMOTIONAL DISTRESS IN YOUNG ADULTS

ABSTRACT

This study examined the relationship among optimism, self-confidence, honesty, and emotional distress in young adults experiencing dating violence. The cross-sectional research took place in different public and private universities in Lahore, Pakistan, where young adults' ages 18-26 years, both men and women were recruited by using non-probability purposive sampling technique. Data was collected by using mental toughness scale (Anthoney & Saleem., 2020), self-esteem scale (Saleem & Zafar, 2014) and psychosocial and emotional reactions scale (Rehman et al., 2024). By using a moderated-mediation model, we found that the relationship between optimism and emotional distress is complex and influenced by both mediation and moderation effects. Specifically, self-confidence partially mediated the relationship between optimism and emotional distress, such that high optimism increased self-confidence, which in turn decrease emotional distress. However, honesty moderated this relationship, such that high honesty decreased emotional distress caused by optimism. The results also showed that the conditional effect of optimism on emotional distress varied across different levels of honesty. These findings have significant implications for counsellors who want to offer individualized treatment strategies and preventive measures to help clients to avoid major outcomes from their psychological and emotional responses to dating violence.

Keywords: Optimism, Self-Confidence, Honesty, Psychosocial and Emotional Reactions, Young Adults, Dating Violence

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ECO-FRIENDLY GREEN SYNTHESIS, SURFACE FUNCTIONALIZATION, AND PERFORMANCE OPTIMIZATION OF REDUCED GRAPHENE OXIDE (rGO) FOR HIGH-EFFICIENCY ADSORPTION OF RHODAMINE B DYE: A DETAILED EXPERIMENTAL INVESTIGATION AND IN-DEPTH MECHANISTIC ANALYSIS USING DENSITY FUNCTIONAL THEORY (DFT)

ABSTRACT

Graphene oxide (GO) was synthesized from recycled graphite using a widely recognized method and subsequently reduced through an environmentally friendly approach. The reduction process was optimized to enhance the structural and textural properties of reduced graphene oxide (rGO), with particular attention to key parameters influencing its surface characteristics. The synthesized rGO and its composite with chitosan were systematically characterized using multiple analytical techniques to confirm successful modification, improved porosity, and enhanced functional properties.

The adsorption performance of these materials was investigated for the removal of dye pollutants from aqueous solutions. Comparative studies revealed that the composite material exhibited significantly improved adsorption capacity and interaction with dye molecules compared to rGO alone. Kinetic studies were conducted to understand the adsorption mechanism, indicating that the process followed a well-defined adsorption model, highlighting the strong affinity between the composite material and the target dye. Additionally, the influence of pH on adsorption efficiency was explored, providing insights into the optimal conditions for maximum removal.

Theoretical calculations were performed to further elucidate the adsorption mechanism at the molecular level. Density Functional Theory (DFT) analysis revealed that the incorporation of chitosan introduced additional active sites, enhancing adsorption energy and electronic interactions with dye molecules. The computed adsorption energies and charge transfer properties aligned with experimental findings, confirming the improved adsorption behavior of the composite material.

Overall, the combination of experimental and theoretical approaches provided a comprehensive understanding of the adsorption process, emphasizing the potential of the composite material as an effective and sustainable adsorbent. The enhanced adsorption capacity, favorable kinetic properties, and strong molecular interactions suggest its promising application in wastewater treatment and environmental remediation.

Keyswords: Adsorption ,Reduced Graphene Oxide (rGO), Aloe Vera Extract, Green Reduction.

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THE IMPORTANCE OF SOME BIOMARKERS IN THE DIAGNOSIS OF H1N1 VIRAL PNEUMONIA COMPLICATED BY ARDS

ABSTRACT

In severe cases, influenza A (H1N1) virus is complicated by viral pneumonia, which can lead to respiratory failure and the development of acute respiratory distress syndrome (ARDS) with high mortality.

Purpose of the study to share our achievements in the development, course and diagnosis of ARDS by studying a number of biomarkers in H1N1 viral pneumonia. We retrospectively studied the medical records of 22 male patients treated in the intensive care unit of Mediclub Hospital from October to December 2019, who had laboratory-confirmed influenza A and developed viral pneumonia. 4.54% patient also had bronchial asthma; 13.6% had non-insulin-dependent diabetes, and 18.2% had hypertension. Patients were 43.8±2.34 years old; weighing 77.8±1.37 kg; height was 167.13±1.42 cm. 5 patients (68.2%) developed grade 1 respiratory acidosis, severe hypoxemia and required mechanical ventilation. The study was conducted in 3 stages: Stage I - day 1 of the disease (day of admission to the intensive care unit); Stage II - days 3-5 of the disease; Stage III covers the 7th-10th day of the disease (recovery period).The main complaint of the patients was general weakness, high fever with an increase in temperature to 38-40°C, dry non-productive cough, dyspnea. Upon admission to the clinic, the patients underwent appropriate diagnostic tests: chest X-ray, computed tomography, ECG, echocardiogram. Peripheral and central hemodynamics were strictly controlled in the laboratory. Inflammation parameters, septicaemia, coagulograms, dyspnea panel, blood gas composition and metabolism, myocardial oxygen demand (MOD) and respiratory-carrico index=PaO2/FiO2 (CI) and the concentration of several biomarkers were also studied.

The MOD in stage I was 18.34±0.86 sh, which is 1.24 times more than in stage II; Although it decreased dynamically by 1.38 times compared to stage III, it remained 2.3 times more than the lower limit of the norm. PaO_2-I m was 56.25±1.65 mmHg, dynamically in stage II this indicator was 1.37 times (p_0<0.01); In stage III, it increased by 1.6 times (p_1<0.01) and reached the normal limit. $PaCO_2$ was 61.75±1.61 mmHg in stage I, 1.3 times in stage II (p_0<0.01); In stage III, it decreased by 1.52 times (p_1<0.01) and reached the normal level and is statistically significant. In addition, the neutrophil-to-lymphocyte ratio (NLR) was studied, which is an effective marker for predicting the development of ARDS. In 8 patients (36.4%), NLR>3.13; these patients had a more severe course of the disease. A combined test for protein A (MxA)/CRP resistant to myxovirus was also used to differentiate the causes of pneumonia. The IL-6 biomarker was also determined in the blood to assess the severity and prognosis of the disease. According to preliminary results, the concentration of IL-6 in stage I was very high and amounted to 249.05+63.95 pg/ml, which was 24.9 times higher than the norm. 4.63 times in stage II (p_0<0.05); In stage III, although it decreased by 8.89 times (p_1<0.05), it remained 2.8 times higher than the norm and was statistically significant. Stages I and II of ARDS were detected in 3 patients, stages III-IV – in 2 patients. The CI is normal - 500 mm Hg. Its decrease is considered one of the main criteria of ARDS. In patients with advanced ARDS, the CI in stage I was 101.13±5.56; against the background of the treatment, this indicator in stage II was 1.53 times; In stage III, it increased by 2.65 times (p1<0.001), but did not reach the normal level. Mortality was noted in 2 patients (9.1%). Cause of death: acute respiratory disease of the lower respiratory tract. Against this background, pneumonia of viral origin H1N1 and ARDS developed.

Thus, it can be concluded that biomarkers, along with a number of instrumental studies, have diagnostic value in determining the clinical course and severity of ARDS. Thus, the combined MxA/CRP test helps diagnose viral and bacterial infections by simultaneously measuring virus-specific markers and CRP. Among the effective markers that determine the degree of development and severity of ARDS, we consider the concentration of NLR and IL-6 to be prognostic.

Keywords: biomarkers, ARDS, pneumonia, respiratory failure, respiratory-carrico index, myocardial oxygen demand

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EVALUATION OF THE FUNCTION OF THE VATER'S MOUTH IN CHOLEDOCHODUODENAL ANASTOMOSES WITH VEGDS

ABSTRACT

Choledochoduodenal anastomosis (ChDA) is one of the surgical methods for restoring bile outflow in mechanical jaundice. However, the functional state of the nipple of the mammary gland after this operation may change. Video esophagogastroduodenoscopy (VEGDS) is one of the main diagnostic methods for assessing the function of the Vater's papilla after ChDA.

Our purpose is to evaluate the functional status of the nipple of Vater after choledochoduodenal anastomosis using VEGDS and to investigate its relationship with postoperative complications**.** The study material was collected in 2024 in the Department of Surgery of the Liver, Biliary Tract and Pancreas of the Academician M. Topchubashov Scientific Center of Surgery. The operation "Choledoxoduodenal Anastomosis" was performed on patients undergoing treatment with a diagnosis of cholelithiasis complicated by mechanical jaundice - 24 patients and iatrogenic damage to the bile ducts - 8 patients. 37.5% of patients were men and 62.5% were women. The average age of patients was 58.44

± 11.34 years, and their weight was 72.18 ± 21.16 kg. The diagnoses were established on the basis of routine laboratory and instrumental studies. The study was conducted in 3 stages. Stage I - preoperative period; Stage II - 1 day after surgery; Stage III covers 3 days of the operation. According to the results of the study, the concentration of total bilirubin in stage I was 176.2±52.16 mmol/l. At stage II, this indicator decreased by 1.37 times ($p<0.01$) compared to stage I; At stage III, compared to stage I, it decreased by 4.41 times ($p<0.05$) and is statistically significant. In parallel, 3 months after the operation, the patients underwent VEGDS to assess the morphofunctional changes in the papilla of Vater, the patency of the anastomosis and the rate of bile flow into the intestine. According to the results of the examination, hypertrophic changes in the papilla of Vater after ChDA were observed in 6.25% of patients; uncontrolled reflux of bile into the intestine and choledochoduodenal reflux in 9.4% of patients; 18.75% of patients had anastomotic stricture and bile stasis. In 65.6% of patients, VEGDS reveals a 5x5 mm ChDA in the bulboduodenal junction area; Bile flow through the anastomosis is normal, the membrane of the descending part is unchanged. The ampulla of Vater has a spherical shape, bile flow is not determined.

Thus, the results of VEGDS showed that monitoring the state of the anastomosis in the early postoperative period is an important examination method for preventing complications. Monitoring the functional state of the Vater's papilla using VEGDS after choledochoduodenal anastomosis plays an important role in postoperative management. VEGDS helps to optimize the treatment strategy based on timely identified morphological and functional changes.

Keywords: *Choledochoduodenal anastomosis, Vater's nipple, gallstones, mechanical jaundice, iatrogenic injury, Video esophagogastroduodenoscopy, biliary tract*

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AN OVERVIEW OF CAD; ETIOLOGICAL FACTORS AND SURGICAL MANAGEMENTS

ABSTRACT

The most leading cause of death is CAD. CAD is a disease of coronary artery characterized by calcium or fat deposition, vascular spasm and clot formation. Arthrosclerosis leads to different cardiovascular diseases which include cardiac muscular damage, hypertrophy, ischemic heart disease and other cardiac abnormalities. CAD is usually related to ischemic heart disease, coronary heart disease, myocardial infarction, angina pectoris and congested heart failure. ECG, MRI, Echo, angioplasty, X-ray, PET, CT scan and cardiac markers are different diagnostic workouts. This article is to review different etiological factors of CAD. These factors are modifiable, non-modifiable, environmental factors, conventional, or traditional, psychological and disease related conditions. Modifiable factors are age, high blood pressure, diabetes mellitus, lack of ordinary activity, obesity and cholesterol rich diet. Non- modifiable factors are family history, age and gender. Environmental factors are tobacco, air pollutants, inhaled gases and pesticides. Moreover, psychological factors include depression, anxiety and stress, social isolation and social inactivity. Non-pharmacological therapy includes lifestyle modifications and precautionary measures. Smoking cessation, low cholesterol diet and exercise are lifestyle modifications to prevent the risk of CAD. Pharmacological therapy for CAD includes different agents i.e. anti-platelet agents, anti-coagulating agents, thrombolytic agents, beta blockers, ACE antagonists and lipid lowering agents. When pharmacological therapy fails to treat a patient, then the second option is surgical management. This article also reviews the surgical managements of CAD. Surgical managements for CAD patients involve angioplasty and CABG. Angioplasty is an alternate of CABG because CABG is more complicated surgical procedure than angioplasty.

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FORMULATION AND EVALUATION OF OTF OF CETIRIZINE FOR RAPID SYSTEMIC ACTION

ABSTRACT

Allergy has become one of the most common chronic disorder worldwide, affecting nearly 40% of the global population Hypersensitivity reactions are the root cause of allergies, autoimmune diseases, and transplant rejections. Cetirizine, a second-generation H1 histamine blocker, is widely used to manage allergy-related conditions, particularly hay fever and skin welts in patients. Oral thin films (OTFs) are a pharmaceutical dosage form designed to rapidly dissolve within seconds when placed in the oral cavity. One of the main advantages of oral films is that they may be provided without the need for distilled water, preparing oral thin films convenient to use anywhere and whenever. Oral thin films have low disintegration duration and a high dissolution period, which results in a quick onset of action. The solvent casting method is used to prepared films by initially dissolving the excipients; the mixture was stirred for 15 minutes to achieve a clear solution. The films were dried in a hot air oven at a temperature not exceeding 50°C. Once dried, they were gently peeled from the glass plates. The pre-formulation and post-formulation studies, including Organoleptic analysis, solubility testing, stability assessment, drug content analysis, and microscopic examination were conducted. Each OTF was packaged in silver-coloured aluminium foil to protect it from moisture, heat, and light, with twenty films placed in a box, meeting all necessary packaging requirements. Oral thin films are better than conventional dosage forms because of flexibility, rapid onset of action, improved bioavailability, and increased patient compliance. Oral thin films are customizable, according to specific patient need.

Keywords: Autoimmune disease, rapid systemic action, Solvent Casting method, bioavailability, H1 blocker, patient compliance

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QUANTUM CHICKENS AND THEIR SOCIAL BEHAVIOR DYNAMICS IN PARALLEL UNIVERSES

ABSTRACT

This study represents a groundbreaking exploration of the social behavior of chickens in parallel universes through the principles of quantum mechanics. The research provides a detailed analysis of how chickens exhibit flock behaviors while in a quantum superposition state and investigates the influence of quantum entanglement on these behaviors. Experiments conducted at the University of Helsinki revealed remarkable findings, demonstrating that chickens are capable of interacting socially with their counterparts in parallel universes via quantum entanglement. The experimental results delved deeply into how quantum states affect not only individual chicken behavior but also the dynamics of the entire flock. These interactions showcased extraordinary coordination and communication capabilities among chickens at the quantum level, highlighting the potential consistency of social structures across different realities. Furthermore, the study revealed that the organizational principles governing chicken flocks remain stable and coherent, even in the presence of dimensional variability. The findings contribute to quantum biology by introducing novel perspectives on the interplay between quantum mechanics and behavioral science. Beyond that, this research opens new avenues for understanding the impact of parallel universes on social dynamics and organizational structures. It raises compelling questions about the role of quantum mechanics in interpreting and predicting complex social behaviors, paving the way for interdisciplinary studies that bridge quantum physics, biology, and social science.

Keywords: Quantum Biology, Chicken Behavior, Parallel Universes

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EVALUATING 3,5-DISUBSTITUTED INDOLE DERIVATIVES AS PIM1 KINASE INHIBITORS: IN SILICO DESIGN AND ANALYSIS OF NOVEL THERAPEUTICS FOR HEMATOLOGICAL CANCER MANAGEMEN

ABSTRACT

The World Health Organization (WHO) has recognized cancer as one of the most lethal diseases of our era, with an alarming increase in mortality rates. In response to this urgent challenge, researchers are actively investigating new therapeutic molecules. Among the promising targets for the treatment of hematological cancers, proviral integration moloney (Pim) kinases have garnered significant attention. This study focuses on a series of thirty-four 3,5-disubstituted indole derivatives, which were systematically evaluated as potential inhibitors of Pim1 kinase using advanced methodologies, including two-dimensional quantitative structure-activity relationship (2D-QSAR) analysis and molecular docking techniques.

The thorough investigation of these compounds produced promising results, highlighted by a Q^2 value of 0.71, an R^2 value of 0.82, and an $rtest^2$ value of 0.96. The modeling process utilized 28 compounds as a training set and 6 compounds as a test set. Additionally, leveraging computational simulations, four novel compounds were designed in silico, indicating potential for further investigation. To assess the stability of the newly designed compound X1 and the most active compound (compound 28), molecular docking studies were performed. The results indicated that compound X1 demonstrated superior stability compared to compound 28.

Furthermore, the newly designed compounds were evaluated for their in silico toxicity profiles, ensuring compliance with the five Lipinski rules, which evaluate specific molecular characteristics related to drug-likeness and oral bioavailability, thereby confirming the feasibility of these compounds for subsequent experimental validation. In conclusion, this study explored the potential of 3,5-disubstituted indole derivatives as Pim1 kinase inhibitors, aiming to develop effective treatments for hematological cancers. The findings revealed promising activity, with the newly designed compound X1 exhibiting enhanced stability relative to the most active compound in the series. Further experimental validation in laboratory settings is essential to establish the therapeutic efficacy of these compounds in practical applications.

Keywords: 3,5-disubstituted indole derivatives, QSAR, Cancer, Molecular docking, Pim kinases.

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EXPLORING ADVANCED COMPUTATIONAL APPROACHES FOR IDENTIFICATION OF ANTI-PROSTATE CANCER COMPOUNDS: 2D-QSAR, ADMET PREDICTION, MOLECULAR DOCKING ANALYSIS

ABSTRACT

Prostate cancer is a vital global health concern, it is among the most prevalent cancers affecting men. While various therapeutic options are available to manage this disease, the development of resistance to existing pharmaceutical treatments highlights the critical need for new anti-prostate cancer drugs.

This research seeks to evaluate the potential bioactivity of newly designed 1-(indolin-1-yl) éthan-1-one derivatives through in-silico approaches, with an emphasis on investigating their inhibitory interactions with TRIM24 PHD-bromodomain.

For that purpose, combined computational approaches were employed, including 2D-QSAR, molecular docking. The multiple linear regression (MLR) method were utilized to conduct a quantitative structure-activity relationship analysis on a collection of 37 1-(indolin-1-yl) éthan-1-one derivatives. The analysis of 2D-QSAR results demonstrated that the inhibitory activity could be predicted with high precision with coefficients of determination (R^2) of 0.82 and 0.78 for the training and test datasets, respectively. The developed models underwent rigorous validation through internal and external procedures.

Furthermore, the assessment of ADMET properties established the likelihood of these newly designed ligands being suitable as drug candidates. Four of the selected ligands were submitted to the molecular docking study to evaluate their affinity to the TRIM24 PHD-bromodomain receptor.

Amongst the newly proposed molecules, the ligands P4 and P5 have demonstrated potential as promising candidates for inhibiting prostate cancer. To assess the binding stability of the chosen ligands with the enzyme under study, a Molecular dynamics simulations approach is currently underway.

Keywords: Prostate cancer. 2D-QSAR. ADMET. Molecular Docking. TRIM24 PHD-bromodomain. 1-(indolin-1-yl) éthan-1-one.

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UNDERSTANDING DISEASE-DRUG INTERACTIONS: IMPLICATIONS FOR TREATMENT AND PATIENT SAFETY

ABSTRACT

Disease-drug interactions (DDIs) represent a significant clinical concern, wherein the presence of an underlying disease alters the pharmacokinetics and pharmacodynamics of a drug, leading to potential therapeutic failure or adverse reactions. These interactions can occur due to changes in drug absorption, distribution, metabolism, and elimination caused by physiological alterations in disease states. For example, liver or kidney diseases can impair drug metabolism and excretion, while cardiovascular diseases can influence drug distribution and efficacy. Similarly, chronic conditions like diabetes, hypertension, or infections can affect the body's response to medications, necessitating careful management of pharmacological treatments.

The mechanisms of DDIs are complex, involving alterations in enzyme activity (e.g., cytochrome P450), transporter proteins, and receptor interactions. Additionally, diseases may cause physiological shifts, such as electrolyte imbalances, acid-base disturbances, or inflammatory responses, further complicating drug interactions. Polypharmacy, the use of multiple medications, increases the likelihood of DDIs, particularly in elderly patients and those with comorbidities, where the risks of adverse effects and therapeutic failure are heightened.

This review highlights strategies to identify and manage these interactions, including dose adjustments, therapeutic drug monitoring, and personalized medicine approaches. Healthcare professionals must remain vigilant in considering disease-drug interactions when prescribing, monitoring, and educating patients to ensure safe and effective treatment outcomes.

Keywords: drug interactions, disease, adverse effects, therapeutic failure, monitoring

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LEGAL AND ETHICAL ISSUES IN ORGAN TRANSPLANTATION: THE INDIAN PERSPECTIVE

ABSTRACT

Organ transplantation is a groundbreaking medical advancement that offers hope to patients with end-stage organ failure. However, in India, the process is hindered by ethical dilemmas, legal loopholes, and systemic inefficiencies. This paper examines key challenges, including organ trafficking, informed consent, cultural resistance, and the persistent gap between organ demand and availability. Despite the Transplantation of Human Organs and Tissues Act (THOTA), 1994, and its amendments, enforcement challenges and socio-economic disparities continue to limit access to transplantation services. Cases like the 2023 Uttar Pradesh kidney trafficking scandal highlight the urgent need for stricter regulations and improved oversight. Additionally, emerging technologies such as blockchain, artificial intelligence, and 3D bioprinting present new opportunities to improve transparency and efficiency but also introduce ethical and accessibility concerns. To create a fair and effective transplantation system, this study advocates for stronger legal enforcement, technological advancements, cultural awareness, and international collaboration. By addressing these critical issues, India can move toward a more ethical, transparent, and equitable organ transplantation framework.

Keywords- Organ Transplant, India, Ethical dimensions, Legal challenges, artificial intelligence.

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BRIDGING THE GAP: PUBLIC AND PRIVATE HEALTHCARE INSURANCE IN INDIA'S PATH TO UNIVERSAL HEALTH COVERAGE

ABSTRACT

India's healthcare insurance landscape is shaped by the interplay between public and private sectors, each with distinct advantages and challenges. Public healthcare insurance schemes enhance accessibility but struggle with infrastructural deficits, administrative inefficiencies, and delayed reimbursements. Conversely, private insurance offers innovative, consumer-focused solutions but remains prohibitively expensive for many. Regulatory shifts, including evolving IRDAI guidelines and the integration of digital health technologies like telemedicine and AI, are redefining the sector. A comparative analysis underscores key disparities in urban and rural healthcare access, income-based inequities, and the potential of public-private partnerships to create an integrated and sustainable system. Persistent challenges, such as delays in private claim settlements under PMJAY that hinder life-saving treatments, highlight the need for policy reforms. Strengthening transparency, leveraging technology, and enacting robust legal frameworks can enhance affordability and efficiency. This study envisions a future where healthcare insurance in India evolves into a more inclusive and equitable system, ensuring universal health coverage by 2030.

Keywords: Healthcare Insurance, Public-Private Partnership, Ayushman Bharat, Digital Health, Universal Health Coverage

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WHAT WE KNOW ABOUT PSORIASIS SO FAR?

ABSTRACT

Background Restoration of the dysbiotic gut microbiome has emerged as a promising aid and a better therapeutic approach.

Objective New evidences suggest that the microbiome may play a pathogenic role in psoriatic disease. The aim of the present project is to investigate whether a dietary intervention could ameliorate the clinical manifestations and modulate the gut microbiota of individuals with psoriasis.

Materials and methods Nutrition plays an important role in the development of psoriasis and it can modulate microbiome composition.

Results Among environmental factors, diet plays a central role therefore incorrect nutritional habits and excessive body weight can increase clinical symptoms or even trigger the disease. Such diet-based and nutraceutical approaches to targeting the microbiome may produce a milder side effect profile than current systemic medications. Thus, interventions aimed at the microbiome may be a valuable adjunct for preventing or managing psoriatic disease and its comorbidities.

Conclusion Nutrition plays an important role in the development of psoriasis and its comorbidities. Ultimately, a better understanding of the psoriatic microbiome can lead to the development of new therapeutic modalities that target the shifting microbiota. Thus, interventions aimed at the microbiome may be a valuable adjunct for preventing or managing psoriatic disease and its comorbidities.

Keywords: psoriasis, microbiome, microbiota, Deniplant nutraceuticals

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MATHEMATICAL MODELING OF SEPSIS DIAGNOSIS

ABSTRACT

Aim. The aim of this study was to identify markers and develop a mathematical formula for the early diagnosis of NEC with septic complications (NEC + Sepsis). **Materials and methods.** The design of scientific work is presented by prospective studies. The study involved 100 full-term neonates diagnosed with NEC, with a gestational age of 37-42 weeks. Demographic and clinical data were collected from patients with relevant abdominal and systemic symptoms. Using ROC (Receiver Operating Characteristic curve) analysis, the correct parameters of the model were determined. **Results.** The ROC curve analysis was used to calculate the specificity and sensitivity of nitric oxide (NO) and total bilirubin (TBil) for the early diagnosis and differentiation of NEC with sepsis and severe NEC without sepsis. The highest sensitivity and specificity values were observed with the use of numerical data for NO (92.86%; 93.98%) and TBil (90.09%; 80.00%). Among 83 patients with NEC without sepsis, higher levels of NO and TBil were observed compared to 17 patients with septic complications. Serum NO levels in patients with sepsis were significantly lower compared to those in patients even at stage I NEC. By identifying the low threshold values of nitric oxide (NO <37.80 μmol/L), a mathematical formula was developed for the early detection of septic complications of NEC in full-term newborns. **Conclusion.** Based on the results of our study, we can say that NO and TBil are new biomolecular markers for early diagnosis of sepsis. Extreme low values of serum concentrations of NO and TBil observed in NEC + Sepsis can be used as predictors of sepsis early diagnosis and differentiation from diseases with similar symptoms.

Keywords: sepsis; necrotizing enterocolitis; full-term newborns; differential diagnosis.

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ABCB1 c.3435 C > T (rs1045642) AS A BIOMARKER FOR CARBAMAZEPINE EFFICACY IN ALGERIAN PATIENTS WITH EPILEPSY

ABSTRACT

Background: Epilepsy is a chronic brain disease that affects 70 million people worldwide. In Algeria, about 1% suffer from this disease and are often treated with anti-seizure medications. Carbamazepine is the most prescribed anti-seizure medication due to its affordability and availability. However, one third (1/3) of patients are resistant to antiepileptic drugs, including carbamazepine, and develop serious side effects.

Previous studies have suggested that genetic variations are remarkably associated with reduced bioavailability in epileptic cells, contributing to anticonvulsant resistance and the development of many adverse effects that complicate patients' lives. The Adenosine-Triphoshate-Bending-Cassette-B1 (ABCB1) gene is one of the most studied genes in Carbamazepine pharmacogenetics, it plays an important role in its metabolism. This study aims to evaluate the influence of ABCB1 c.3435 C>T polymorphism on the response to carbamazepine treatment in epileptic patients.

Methods: Ninety-eight epileptic patients under Carbamazepine treatment were identified and invited to participate in this study at the neurology department of the University Hospital of Oran (CHUO); the sampling period extended from 2022 to 2024. Clinical data from all patients were collected, then blood samples were taken, followed by DNA extraction by the salting-out method and finally amplification and digestion of exon 26 of the ABCB1 gene by Polymerase-Chain-Reaction Restriction Fragment Length Polymorphism (PCR-RFLP). Statistical analyses were performed using the regression test.

Results: Our findings show no significant association between the *ABCB1* c.3435C>T genotypes with carbamazepine resistance ($p = 0,1$). The sample size in this study might be limitation; therefore, expanded investigations on Algerian population are needed.

Conclusion: Although this study indicates no significant correlation of the *ABCB1* c.3435C>T polymorphism with influencing CBZ Pharmacoresistance and therapeutic outcomes, larger-scale-studies are required to confirm these results and assess their reliability.

Keywords: Epilepsy**;** *ABCB1* c.3435 C>T; Carbamazepine; Pharmacoresistance; Algerian population; Personalized medicine; Genetic Testing.

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THE EVOLUTION OF DENTAL ZIRCONIA: FROM CONVENTIONAL TO HYPER-TRANSLUCENT.

ABSTRACT

Zirconia is one of the materials with several advantages including excellent mechanical and biological behaviors that provide numerous indications in various clinical situations. Because the opaque appearance of zirconia negatively affects the aesthetic outcome, layering materials have been proposed to mask this appearance. However, porcelain chipping is considered one of the most common technical problems in veneered zirconia crown. To overcome the problem of poor optical properties, translucent monolithic zirconia was introduced to fabricate multi-unit monolithic crown without increased risk of porcelain fracture or reduced aesthetic properties of the core material. However, this material must be further studied in vitro and in vivo to determine its long-term ability to maintain its exceptional properties. The aim of this paper is to provide an overview of the dental zirconia revolution, including its types, properties, applications and cementation procedures.

Keywords: Zirconia, dental prostheses, ceramics, translucency, cementation, monolithic.

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EVALUATION OF THALAMUS, HIPPOCAMPUS AND CEREBELLUM VOLUMES AND THREE-DIMENSIONAL VISUALIZATION IN MULTIPLE SCLEROSIS PATIENTS

ABSTRACT

Objective: In this study, we aimed to evaluate the volumes of thalamus, hippocampus and cerebellum in MS group and control group according to gender, age, expanded disability status scale (EDSS) and MS type and to determine the relationship with cerebrospinal fluid (CSF).

Materials and methods: The study included 100 MS group individuals and 25 healthy individuals as control group. The individuals were divided into two groups according to their age groups as below 40 years and 40 years and above. Absolute volumetric measurements (cm^3) were performed on all individuals using the VolBrain automated software, and visualizations were conducted with the ITK-SNAP program.

Results: While thalamus volume was found to be significantly smaller in MS patients compared to the control group ($p<0.05$), no significant difference was found in hippocampus volume ($p>0.05$). CSF volume was significantly higher in the MS group compared to the control group ($p<0.05$). White matter (WM), cerebrum, cerebellum, cerebellum and cerebellum volumes were significantly lower in the MS group compared to men ($p<0.05$). In age groups,WM , gray matter (GM), cerebrum, cerebellum and cerebellum volumes were found to be significantly lower in the MS group aged 40 years and older compared to those aged below 40 years ($p<0.05$). In contrast, CSF volume was found to be significantly higher in the group aged 40 years and over compared to those under 40 years ($p<0.05$). EDSS score and CSF volume were negatively correlated with cerebrum, cerebellum and WM volumes ($p<0.05$).

Conclusion: Cerebrum, cerebellum, GM and WM volumes decrease with increasing age in MS. As these volumes decrease, the EDSS score worsens. We think that the increase in CSF and decrease in thalamus volume in MS patients can be evaluated as biomarkers in the diagnosis of MS.

Keywords: Cerebellum; Hippocampus Multiple Sclerosis; Thalamus; volBrain

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THE RELATIONSHIP BETWEEN BREAKFAST HABITS OF SCHOOL-AGE CHILDREN AND MOTHERS' NUTRITIONAL KNOWLEDGE AND ATTITUDES

ABSTRACT

Objectives and Study: Breakfast, as a main meal, holds significant nutritional value. Skipping breakfast can lead to malnutrition, reduced dietary intake, and increased consumption of unhealthy foods. Children who miss breakfast often experience slower cognitive processing and learning speeds. As primary caregivers, mothers play a vital role in shaping their children's breakfast and overall nutritional habits. This study aimed to explore the relationship between breakfast habits and maternal nutritional knowledge and attitude among school-aged children.

Methods: The study involved 250 children aged 6–10 years. Data were gathered using a breakfast food frequency questionnaire, along with a survey assessing maternal demographic characteristics, nutritional knowledge, and attitudes. Children's height and weight were measured, with height-for-age and BMI-for-age classified using World Health Organisation z-scores.

Results: Among the children, 1.6% were stunted, 18.8% malnourished, 8.4% severely malnourished, 55.2% had normal weight, and 17.6% were overweight or obese. Only 6% of children did not have breakfast. No significant relationship was observed between breakfast habits and weight status ($p>0.05$). However, children whose mothers included sausage and salami in meals were more likely to be overweight or obese ($p<0.05$). Similarly, mothers unaware of healthy drink options tended to have overweight or obese children ($p<0.05$). Children of mothers who skipped breakfast were more likely to do the same ($p<0.05$).

Mothers who undervalued breakfast or three main meals had children who skipped breakfast more often ($p<0.05$). While no link was found between children's nutritional status and energy/macronutrient intake at breakfast ($p>0.05$), mothers who prioritized daily milk and egg consumption for their children encouraged higher energy and protein intake at breakfast ($p<0.05$). Additionally, children of mothers who avoided rewarding them with chips and chocolate had higher protein intake($p<0.05$).

Conclusions: Maternal nutrition education plays a critical role in shaping children's breakfast habits and overall nutrition. Children often mirror their mothers, highlighting the role of maternal example in promoting healthy eating habits.

Keywords: breakfast, maternal nutrition attitude, nutritional status,

OKUL ÇAĞI ÇOCUKLARINDA KAHVALTI YAPMA ALIŞKANLIĞI İLE ANNELERİN BESLENME BİLGİ VE TUTUMLARI ARASINDAKİ İLİŞKİ

ÖZET

Ana öğün olarak kahvaltı, beslenme açısından önemli değere sahiptir. Kahvaltının atlanması, yetersiz beslenmeye, düşük diyet alımına ve sağlıksız yiyeceklerin daha fazla tüketilmesine yol açabilir. Kahvaltı yapmayan çocukların genellikle bilişsel işlevleri düşer ve öğrenme hızları yavaşlar. Birincil bakım verenler olarak anneler, çocuklarının kahvaltı alışkanlıkları ve genel beslenme düzenleri üzerinde önemli bir etkiye sahiptir. Bu çalışma, okul çağındaki çocuklarda kahvaltı alışkanlıkları ile annelerin beslenme bilgi ve tutumları arasındaki ilişkiyi araştırmayı amaçlamıştır.

Yöntem: Çalışma, 6–10 yaş arası 250 çocuğu kapsamıştır. Veriler, kahvaltı besin sıklığı anketi ile annelerin demografik özelliklerini, beslenme bilgilerini ve tutumlarını değerlendiren bir anket kullanılarak toplanmıştır. Çocukların boy ve kiloları ölçülmüş; yaşa göre boy ve yaşa göre BKİ değerleri, Dünya Sağlık Örgütü z-skorları kullanılarak sınıflandırılmıştır.

Bulgular: Çocukların %1,6'sı bodur, %18,8'i yetersiz beslenmiş, %8,4'ü ciddi derecede yetersiz beslenmiş, %55,2'si normal kiloda, %17,6'sı ise fazla kilolu veya obezdi. Çocukların sadece %6'sı kahvaltı yapmıyordu. Çocukların kahvaltı alışkanlıkları ile ağırlık durumu arasında anlamlı bir ilişki bulunmamıştır ($p>0.05$). Ancak, öğünlerde sosis ve salam kullanan annelerin çocuklarının fazla kilolu veya obez olma olasılığı daha yüksekti ($p<0.05$). Benzer şekilde, sağlıklı içecek seçeneklerini bilmeyen annelerin çocuklarında fazla kilo veya obezite görülme oranı daha fazlaydı ($p<0.05$). Kahvaltı yapmayan annelerin çocukları da kahvaltıyı atlama eğilimindeydi ($p<0.05$). Kahvaltı veya üç ana öğünün önemini küçümseyen annelerin çocukları da daha sık kahvaltı atlamaktaydı ($p<0.05$). Çocukların beslenme durumu ile kahvaltıdaki enerji/makro besin alımı arasında bir ilişki bulunmasa da ($p>0.05$), çocuklarının günlük süt ve yumurta tüketimini önemseyen annelerin çocuklarının kahvaltıda daha fazla enerji ve protein aldığı görüldü ($p<0.05$). Ayrıca, çocuklarını cips ve çikolata ile ödüllendirmeyen annelerin çocuklarının kahvaltıda protein alımı daha yüksekti ($p<0.05$).

Sonuç: Annelerin beslenme eğitimi, çocukların kahvaltı alışkanlıkları ve genel beslenme durumları üzerinde kritik bir rol oynamaktadır. Çocuklar genellikle annelerini örnek alır, bu da sağlıklı beslenme alışkanlıklarının kazandırılmasında annelerin rol model olmasının önemini ortaya koymaktadır.

Anahtar sözcükler: anne beslenme tutumu, beslenme durumu, kahvaltı

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THE INHIBITORY EFFECTS OF *Aronia melanocarpa* on NO, iNOS, and COX-2 in LPS-STIMULATED BV-2 CELLS

ABSTRACT

Objective: This study aimed to evaluate the potential anti-inflammatory effects of *Aronia melanocarpa* extract on BV-2 microglial cells stimulated with lipopolysaccharide (LPS), an established in vitro model of neuroinflammation. With growing interest in plant-based compounds for the prevention and management of neurodegenerative diseases, *Aronia melanocarpa*—a berry rich in anthocyanins, flavonoids, and other polyphenols—was selected due to its previously reported antioxidant, immunomodulatory, and anti-inflammatory properties.

Materials and Methods: Murine BV-2 microglial cells were cultured in Dulbecco's Modified Eagle Medium (DMEM) supplemented with 10% fetal bovine serum and 1% penicillin-streptomycin at 37°C in a humidified 5% CO_2 incubator. Neuroinflammation was induced using 1 µg/mL LPS for 24 hours. Cells were subsequently treated with *Aronia melanocarpa* extract at concentrations of 10, 25, and 50 µg/mL. Nitric oxide (NO) levels in the supernatants were quantified using the Griess reagent assay. The expression levels of pro-inflammatory markers—inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2)—were assessed at both mRNA and protein levels using quantitative real-time PCR (qPCR) and Western blot analysis, respectively.

Results: Treatment with *Aronia melanocarpa* extract significantly reduced LPS-induced NO production in a dose-dependent manner ($p < 0.05$). Additionally, both iNOS and COX-2 gene and protein expression were markedly suppressed.

Conclusion: These findings suggest that *Aronia melanocarpa* extract exerts strong anti-inflammatory effects on activated microglia and may serve as a promising natural neuroprotective agent. Further in vivo studies are necessary to validate its therapeutic potential and clarify its mechanisms of action.

Keywords: *Aronia melanocarpa*, microglia, BV-2 cells, neuroinflammation, iNOS, COX-2, nitric oxide

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PRODUCTION AND CHARACTERIZATION OF A WOUND DRESSING BASED ON POLYVINYL ALCOHOL (PVA) AND CHITOSAN (CS) INCORPORATED WITH PTERIDIUM AQUILINUM (PA) FERN EXTRACT

ABSTRACT

Objective:

In this study, it was aimed to produce a wound dressing containing Pteridium aquilinum (PA) fern extract using the electrospinning method with natural polymers Polyvinyl Alcohol (PVA) and Chitosan (CS), and to characterize the structural, biological, and functional properties of the obtained dressings in detail.

Materials and Methods:

PA extract was prepared by ethanol extraction of the fern. The extract was added in specific ratios to PVA and CS-based solutions and the homogeneous mixture was transformed into a nanofibrous wound dressing using the electrospinning method. The produced nanofiber structures were comprehensively characterized by FTIR (Fourier Transform Infrared Spectroscopy), SEM (Scanning Electron Microscopy), tensile testing, release analysis, antioxidant activity by DPPH, MTT cell viability assay, and antibacterial tests.

Results:

FTIR analyses showed that the PA extract was successfully integrated into the polymer matrix. SEM images revealed a uniform and homogeneous fiber structure. Tensile tests indicated that the mechanical strength was at a sufficient level for wound dressing applications. The release profile of the PA extract was controlled and sustainable. The MTT assay confirmed that the nanofibrous structure did not exhibit toxic effects on cell viability. Antioxidant and antibacterial test results demonstrated that the PA extract possessed properties supportive of wound healing.

Conclusion:

The PVA/CS-based wound dressings containing PA extract produced via the electrospinning method have the potential to support wound healing due to their biodegradable and biocompatible nature. Especially, the antioxidant and antibacterial effects provided by the natural extract make this material suitable for biomedical applications.

Keywords: Polyvinyl Alcohol, Chitosan, Fern, Electrospinning, Wound Dressing

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STIGMA ASSOCIATED WITH ADDICTION: PSYCHOLOGICAL CONSEQUENCES AND INTERVENTION RECOMMENDATIONS

ABSTRACT

AIM

Addiction-related stigma is a multi-layered problem that severely hinders the recovery process of addicted individuals and their re-participation in social life. The aim of this study is to evaluate the types of stigma (social, structural, internalised, etc.) that occur in the context of addiction, the psychological effects of these stigmas and effective intervention strategies to reduce stigma with a holistic approach through a literature review.

MATERIAL AND METHODS

This study is a qualitative review and current national and international literature addressing addiction-related stigma has been examined. In this context, existing academic literature has been analyzed from a broad perspective. The study has been structured in line with published systematic reviews and empirical studies.

FINDINGS

Stigmatization leads to numerous negative outcomes among individuals with addiction, including low self-esteem and self-worth, feelings of guilt, social isolation, avoidance of help-seeking, and resistance to treatment. At the structural level, exclusion from healthcare services, discriminatory practices, and inadequate policies further reinforce stigma. In the context of Turkey, cultural norms and media discourse stand out as significant factors that exacerbate stigmatization. Psychoeducation, contact-based approaches, language reform, and social advocacy emerge as effective intervention strategies to reduce stigma.

CONCLUSION

Reducing the stigma associated with addiction is important not only for the mental health of individuals but also for the general health level and social integrity of the society. In this direction, multilevel psychosocial interventions, rights-based approaches and political arrangements should be addressed together; a transformation that covers all segments of society should be targeted.

Keywords: Addiction, Stigmatization, Social Perception, Psychosocial Intervention.

BAĞIMLILIKLA İLİŞKİLİ DAMGALAMA: PSİKOLOJİK SONUÇLAR VE MÜDAHALE ÖNERİLERİ

AMAÇ

Bağımlılıkla ilişkili damgalama, bağımlı bireylerin iyileşme süreçlerini ve sosyal yaşama yeniden katılımlarını ciddi biçimde sekteye uğratan çok katmanlı bir sorundur. Bu çalışmanın amacı, bağımlılık bağlamında ortaya çıkan damga türlerini (toplumsal, yapısal, içselleştirilmiş vb.), bu damgaların psikolojik etkilerini ve damgalamayı azaltmaya yönelik etkili müdahale stratejilerini literatür taraması yoluyla bütüncül bir yaklaşımla değerlendirmektir.

MATERYAL VE YÖNTEM

Bu çalışma nitel bir derleme araştırması olup, bağımlılıkla ilişkili damgalamayı ele alan güncel ulusal ve uluslararası literatür incelenmiştir. Bu doğrultuda mevcut akademik literatür geniş bir perspektiften analiz edilmiştir. Çalışma yayımlanmış sistematik derlemeler ve ampirik çalışmalar doğrultusunda yapılandırılmıştır.

BULGULAR

Damgalama, bağımlı bireylerde benlik saygısı ve özsaygı düşüklüğü, suçluluk, sosyal izolasyon, yardım aramaktan kaçınma ve tedaviye direnç gibi birçok olumsuz sonuca yol açmaktadır. Yapısal düzeyde ise sağlık hizmetlerinden dışlanma, ayrımcı uygulamalar ve politik yetersizlikler damgalanmayı pekiştirmektedir. Türkiye özelinde toplumsal normlar ve medya dili, damgalamayı arttıran faktörler olarak dikkat çekmektedir. Damgalamayı azaltmada psikoeğitim, temas temelli yaklaşımlar, dil reformu ve sosyal savunuculuk etkili müdahale yolları olarak öne çıkmaktadır.

SONUÇ

Bağımlılıkla ilişkili damgalamanın azaltılması, sadece bireylerin ruh sağlığı açısından değil, toplumun genel sağlık düzeyi ve sosyal bütünlüğü açısından da önemlidir. Bu doğrultuda çok düzeyli psikososyal müdahaleler, hak temelli yaklaşımlar ve politik düzenlemeler birlikte ele alınmalı; toplumun tüm kesimlerini kapsayan bir dönüşüm hedeflenmelidir.

Anahtar Kelimeler: Bağımlılık, Damgalama, Toplumsal Algı, Psikososyal Müdahale.

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EFFECTS OF EATING DISORDERS DIAGNOSED DURING PREGNANCY AND PRE-PREGNANCY ON MATERNAL AND BABY HEALTH

ABSTRACT

PURPOSE

This study aims to examine the effects of diagnosed eating disorders (Anorexia Nervosa, Bulimia Nervosa, Binge Eating Disorder) during pregnancy and the pre-pregnancy period on maternal and fetal health. Special emphasis is placed on “pregorexia,” a condition in which pregnant women restrict caloric intake and engage in excessive physical activity to avoid weight gain.

MATERIALS AND METHODS

A systematic literature review was conducted using databases such as PubMed, Web of Science, Scopus, and PsycINFO. Observational and cross-sectional studies examining the relationship between anxiety, depression, and eating disorders in relation to pregnancy and lactation were included. Methodological quality was assessed using CASP, NICE, and the Newcastle-Ottawa scales. The data were analyzed in terms of epidemiological findings, clinical consequences, and nutritional therapy recommendation.

FİNDİNGS

The prevalence of eating disorders during pregnancy ranges between 5.1% and 7.5%. Behaviors similar to anorexia and pregorexia in pregnant women are associated with anemia, hypertension, increased cesarean rates, postpartum depression, and impaired mother-infant bonding. For the fetus, risks include low birth weight, microcephaly, premature birth, low Apgar scores, sudden infant death syndrome, and stillbirth. Pregorexia is characterized by calorie counting, excessive exercise, skipping meals, self-induced vomiting, and use of laxatives or diuretics. Nutritional deficiencies, dehydration, and electrolyte imbalances are also common. Medical nutrition therapy includes regular weight monitoring, individualized dietary planning, and psychiatric support to address the underlying psychological issues.

CONCLUSION

Eating disorders during pregnancy are a multifactorial condition that significantly threatens both maternal and fetal health. Psychological stress, body image distortion, and fear of weight gain are key contributors. Early identification of at-risk pregnant women, a multidisciplinary approach to care, and implementation of personalized nutrition and mental

health interventions are crucial for protecting maternal and fetal well-being. Furthermore, more research and the development of specific clinical guidelines for managing eating disorders in pregnancy are needed.

Keywords: Pregnancy, Anorexia nervosa, Bulimia nervosa, Pregorexia

GEBELİKTE VE GEBELİK ÖNCESİ DÖNEMDE TANI ALMIŞ YEME BOZUKLUKLARININ ANNE VE BEBEK SAĞLIĞI ÜZERİNE ETKİSİ

ÖZET

AMAÇ

Bu çalışmanın amacı, gebelikte ve gebelik öncesi dönemde tanı almış yeme bozukluklarının (Anoreksiya Nevroza, Bulimiya Nevroza, Tıkanırcasına Yeme Bozukluğu) anne ve fetüs sağlığı üzerindeki etkilerini incelemek; özellikle "pregoreksiya" adı verilen, gebelikte kilo almaktan kaçınmak için enerji alımını kısıtlayan ve aşırı egzersiz yapan kadınların durumuna dikkat çekmektir.

MATERYAL VE YÖNTEM

Bu çalışma için PubMed, Web of Science, Scopus ve PsycINFO veri tabanları kullanılarak sistematik bir literatür taraması yapılmıştır. Gebelik ve emzirme dönemiyle ilişkili olarak anksiyete, depresyon ve yeme bozukluklarını konu alan gözlemsel ve kesitsel çalışmalar incelenmiştir. Metodolojik kalite değerlendirmesi CASP, NICE ve Newcastle-Ottawa ölçekleriyle gerçekleştirilmiştir. Bulgular, epidemiyolojik veriler, klinik etkiler ve tıbbi beslenme tedavisi önerileri doğrultusunda analiz edilmiştir.

BULGULAR

Yeme bozukluklarının gebelikte görülme sıklığı %5,1 ila %7,5 arasında değişmektedir. Pregoreksiya ve anoreksiya benzeri davranışlar, annede anemi, hipertansiyon, sezaryen doğum oranlarında artış, doğum sonrası depresyon ve anne-bebek bağlanmasında bozulma gibi sonuçlara yol açmaktadır. Fetüste ise düşük doğum ağırlığı, mikrosefali, erken doğum, düşük Apgar skoru, ani bebek ölümü ve ölü doğum riski artmaktadır. Pregoreksiya; kalori takıntısı, aşırı egzersiz, öğün atlama, kusma ve laksatif/diüretik kullanımını içeren davranışlarla kendini gösterir. Bu süreçte elektrolit bozuklukları, dehidrasyon ve mikrobesin eksiklikleri sık görülmektedir. Tıbbi beslenme tedavisi kapsamında kilo takibi, bireysel diyet planlaması ve psikiyatrik destek önerilmektedir.

SONUÇ

Gebelikte yeme bozuklukları, hem annenin hem de bebeğin sağlığını ciddi şekilde tehdit eden çok faktörlü bir durumdur. Psikolojik stres, beden algısı bozukluğu ve kilo alma korkusu bu durumun temel nedenlerindendir. Risk altındaki gebelerin erken tanılanması, multidisipliner yaklaşımla desteklenmesi ve bireysel beslenme planlarının uygulanması anne ve bebek sağlığı açısından büyük önem taşımaktadır. Ayrıca, bu alanda daha fazla araştırmaya ve gebelere yönelik özel klinik kılavuzların geliştirilmesine ihtiyaç duyulmaktadır.

Anahtar kelime: Gebelik, Anoreksiya nevroza, Bulimiya nevroza,Pregoreksiya

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MEDITERRANEAN DIET AND SUSTAINABILITY

ABSTRACT

OBJECTIVE

The primary objective of this study is to evaluate the Mediterranean diet in terms of sustainability and to highlight the positive impacts of this dietary model on both environmental and individual health. Today, industrialization, population growth, and modern lifestyles exert significant pressure on the environment, leading to the rapid depletion of natural resources. In this context, the adoption of healthy lifestyles that are both eco-friendly and sustainable is essential—not only for protecting individual health but also for ensuring a livable world for future generations.

MATERIAL AND METHOD

This research was conducted through a review of relevant literature. Reports on sustainable nutrition by international organizations such as FAO and UNEP, scientific articles, and current publications on the Mediterranean diet were used as primary sources. Additionally, based on the Mediterranean diet pyramid, food groups, consumption frequencies, and environmental impacts were analyzed. This is a theoretical study aiming to evaluate the relationship between sustainable nutrition and environmental factors.

FINDINGS

The Mediterranean diet primarily consists of plant-based foods including olive oil, seasonal fruits and vegetables, whole grains, and legumes, with limited consumption of meat and dairy products. Olive oil plays a central role in the diet, contributing significantly to health with its antioxidant and anti-inflammatory properties. This model reduces environmental impact through a low carbon and water footprint and supports biodiversity by encouraging organic agriculture. From a health perspective, it helps reduce the incidence of chronic diseases such as diabetes, cardiovascular conditions, obesity, and metabolic syndrome.

CONCLUSION

The Mediterranean diet stands out as a sustainable nutritional model that supports both individual health and the future of the planet. By integrating environmental sustainability with personal well-being, this diet offers an ideal solution. Adopting and incorporating this model into daily life is crucial for preventing potential food, water, and environmental crises in the future. The emphasis on local, seasonal, and minimally processed foods, limited

consumption of animal products, and meal habits that foster social interaction are among the strong aspects of this model.

Keywords: Mediterranean diet, sustainability, sustainable nutrition, olive oil

AKDENİZ DİYETİ VE SÜRDÜRÜLEBİLİRLİK

ÖZET

AMAÇ

Bu çalışmanın temel amacı, Akdeniz diyetinin sürdürülebilirlik açısından değerlendirilmesi ve bu beslenme modelinin hem çevresel hem de bireysel sağlık üzerindeki olumlu etkilerinin ortaya konulmasıdır. Günümüzde sanayileşme, nüfus artışı ve modern yaşam biçimleri çevre üzerinde ciddi baskılar yaratmakta; bu da doğal kaynakların hızla tükenmesine yol açmaktadır. Bu bağlamda, sağlıklı yaşam tarzlarının çevre dostu ve sürdürülebilir olması, yalnızca bireylerin sağlığını korumakla kalmayıp aynı zamanda gelecek nesillere yaşanabilir bir dünya bırakmak açısından da önem taşımaktadır.

MATERYAL VE YÖNTEM

Bu araştırma, ilgili literatürün incelenmesi yoluyla yürütülmüştür. FAO ve UNEP gibi uluslararası kurumların sürdürülebilir beslenme raporları, bilimsel makaleler ve Akdeniz diyeti ile ilgili güncel yayınlar esas alınmıştır. Aynı zamanda Akdeniz diyeti piramidi temel alınarak besin grupları, tüketim sıklıkları ve çevresel etkileri analiz edilmiştir. Çalışma, teorik bir inceleme olup sürdürülebilir beslenme ve çevresel faktörler arasındaki ilişkiyi değerlendirmeyi amaçlamaktadır.

BULGULAR

Akdeniz diyeti, büyük oranda bitkisel bazlı gıdalardan oluşmakta olup; zeytinyağı, mevsimlik sebze-meyveler, tam tahıllar, baklagiller, sınırlı miktarda et ve süt ürünlerini içermektedir. Diyette zeytinyağının merkezi bir rolü bulunmaktadır; antioksidan ve anti-inflamatuar özellikleriyle sağlığa büyük katkı sağlar. Bu model, düşük karbon ve su ayak izi ile çevre üzerindeki olumsuz etkileri azaltmakta; ayrıca organik tarımı destekleyerek biyolojik çeşitliliğe katkıda bulunmaktadır. Sağlık açısından ise diyabet, kalp hastalıkları, obezite ve metabolik sendrom gibi kronik hastalıkların görülme sıklığını azaltmaktadır.

SONUÇ

Akdeniz diyeti hem bireysel sağlığı destekleyen hem de gezegenin geleceğini koruyan sürdürülebilir bir beslenme modeli olarak ön plana çıkmaktadır.

Bu diyet modeli, çevresel sürdürülebilirlik ile bireysel sağlığı bütünleştirerek ideal bir çözüm sunar. Gelecekte karşı karşıya kalınabilecek gıda, su ve çevre krizlerinin önlenmesi adına, toplumun bu diyeti benimsemesi ve günlük yaşamına entegre etmesi büyük önem taşımaktadır. Yerel, mevsimsel ve az işlenmiş ürünlerin tercih edilmesi, hayvansal ürünlerin sınırlı tüketimi ve sosyal etkileşimi teşvik eden yemek alışkanlıkları, bu modelin güçlü yönlerindendir.

Anahtar Kelimeler: Akdeniz diyeti, sürdürülebilirlik, sürdürülebilir beslenme, zeytinyağı

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INVESTIGATION OF THE RELATIONSHIP BETWEEN GENETIC POLYMORPHISMS AND PARKINSON'S DISEASE: A CASE-CONTROL STUDY

ABSTRACT

Objective:

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor symptoms and dopaminergic neuronal loss. While environmental factors contribute to disease onset, increasing evidence highlights the significant role of genetic susceptibility. This study aimed to investigate the association between selected genetic polymorphisms and Parkinson's disease risk in a Turkish population.

Materials and Methods:

A total of 100 individuals were enrolled in this case-control study, including 50 clinically diagnosed PD patients and 50 age- and sex-matched healthy controls. Genomic DNA was extracted from peripheral blood samples using a standard phenol- chloroform protocol. Genotyping of candidate polymorphisms—including IL-15 rs10519613, COMT Val158Met (rs4680), and SNCA Rep1—was performed using polymerase chain reaction (PCR) followed by restriction fragment length polymorphism (RFLP) analysis and/or real-time PCR. Allele and genotype frequencies were statistically compared using chi-square tests. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to determine the strength of associations.

Results:

The IL-15 rs10519613 polymorphism showed a significant association with PD susceptibility ($p<0.05$), where the minor allele was more frequent in the patient group. COMT Val158Met exhibited a trend toward association, while SNCA Rep1 did not reach statistical significance.

Conclusion:

The findings support a possible role of specific immune-related and dopamine- regulating gene polymorphisms in PD pathogenesis. Understanding genetic predispositions may contribute to early risk assessment and development of personalized therapeutic strategies in Parkinson's disease.

Keywords: Parkinson's disease, genetic polymorphism, IL-15, COMT, SNCA, neurodegeneration

INVESTIGATION OF THE RELATIONSHIP BETWEEN GENETIC POLYMORPHISMS AND PARKINSON'S DISEASE: A CASE-CONTROL STUDY

ÖZET

Amaç:

Parkinson hastalığı (PH), motor semptomlarla karakterize ilerleyici bir nörodejeneratif hastalık olup dopaminerjik nöron kaybı ile ilişkilidir. Çevresel faktörler hastalığın gelişiminde rol oynasa da, son yıllarda genetik yatkınlığın belirleyici etkisi giderek daha fazla vurgulanmaktadır. Bu çalışmanın amacı, bazı genetik polimorfizmler ile Parkinson hastalığı riski arasındaki olası ilişkileri araştırmaktır.

Gereç ve Yöntem:

Bu olgu-kontrol çalışmasına 50 Parkinson hastası ile yaş ve cinsiyet açısından eşleştirilmiş 50 sağlıklı birey dâhil edilmiştir. Bireylerden elde edilen periferik kan örneklerinden standart fenol-kloroform yöntemiyle genomik DNA izole edilmiştir. **IL-15 rs10519613**, **COMT Val158Met (rs4680)** ve **SNCA Rep1** polimorfizmleri; polimeraz zincir reaksiyonu (PCR) ile çoğaltılmış, ardından RFLP analizi ve/veya gerçek zamanlı PCR yöntemi ile genotiplenmiştir. Alel ve genotip frekansları ki-kare testi ile karşılaştırılmış, olasılık oranları (OR) ve %95 güven aralıkları hesaplanmıştır.

Bulgular:

IL-15 rs10519613 polimorfizmi, Parkinson hastalığı ile anlamlı ilişki göstermiştir ($p<0.05$); minör allel hasta grubunda daha yüksek sıklıkta bulunmuştur. COMT Val158Met genotipi anlamlılık sınırında etkili olurken, SNCA Rep1 polimorfizmi istatistiksel olarak anlamlı bulunmamıştır.

Sonuç:

Bu çalışma, bağışıklık yanıtı ve dopamin metabolizmasıyla ilişkili bazı genetik polimorfizmlerin Parkinson hastalığı gelişiminde rol oynayabileceğini göstermektedir. Genetik yatkınlıkların anlaşılması, erken risk tahmini ve bireyselleştirilmiş tedavi yaklaşımlarına katkı sağlayabilir.

Anahtar Kelimeler: Parkinson hastalığı, genetik polimorfizm, IL-15, COMT, SNCA, nörodejenerasyon

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ANTIDEPRESSANT EFFECTS OF SOME PHENYLPROPIONIC ACID DERIVATIVES IN CHRONIC UNPREDICTABLE MILD STRESS-INDUCED RAT MODEL OF DEPRESSION

ABSTRACT

Objective: There is growing evidence that inflammation is essential in the occurrence and progression of stress-related diseases. Chronic stress has been linked to the development of depressive-like behaviors by increasing the level of proinflammatory cytokines. In this study, we aimed to some 2-phenylpropionic acid derivative compounds examine potential antidepressant activity.

Material and Methods: Adult male Sprague-Dawley rats weighing 250-300 g were used in the experiments. The antidepressant efficacy of compounds coded **1a** and **1b**, which effectively inhibit COX-1 and COX-2 enzymes, were evaluated in rats with chronic unpredictable mild stress (CUMS)-induced depression model. The rats were administered compounds **1a** and **1b** (50 mg/kg/day p.o.) during the last 4 weeks of the CUMS protocol. Fluoxetine (30 mg/kg) was used as a positive control. Depression parameters of the animals were investigated by sucrose preference test, modified forced swimming (MFST), and splash tests. The motor activities of the animals were evaluated using activity tests. Following the

behavioral studies, serum levels of ACTH, IL-1β, IL-6, and TNF-α were measured in the serum obtained from the rats using the ELISA method.

Results and Conclusion: Compounds **1a** and **1b** significantly increased the reduced sucrose intake and grooming duration in stressed rats. The same compounds shortened immobility time, increased swimming time, and did not change the climbing time of stressed rats in the MFST. It was also found that the treatment significantly decreased the stress-increased levels of ACTH, TNF-α, and IL-1β. Compounds **1a** and **1b** significantly improved the reduced motor activity of stressed animals. These findings showed that the mentioned compounds have antidepressant-like effects and pointed out that serotonergic mechanisms and suppression of TNF-α and IL-1β-mediated inflammatory processes may mediate this activity. Further detailed studies are needed to clarify their mechanisms of action.

Keywords: Antidepressant, Stress, Inflammation, Modified forced swimming test, Sucrose preference test

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EFFICACY OF CRANIOSACRAL THERAPY IN PATIENTS WITH GONARTHROSIS

ABSTRACT

Purpose: Craniosacral therapy (CST) is a type of manual therapy applied with light touches. CST may accelerate the healing process by affecting the autonomic nervous system. The aim of this study was to investigate the effects of craniosacral therapy on pain, heart rate variability, joint stiffness, physical function, quality of life and kinesiophobia in patients with gonarthrosis.

Method: The study included 24 volunteers between the ages of 40 and 85 with a diagnosis of gonarthrosis. The participants were divided into two groups: home exercise group (n=12), CST+ home exercise group. For 6 weeks; the home exercise program was applied every day, and CST was applied 1 day a week. Pain was assessed with "Visual Analog Scale (VAS)", kinesiophobia with "Tampa Kinesiophobia Scale", quality of life with "SF-36 Quality of Life Questionnaire", pain, stiffness and physical function with "WOMAC Osteoarthritis Index" and heart rate variability with Polar H10 model heart rate monitor before and after treatment. IBM SPSS Statistics 26.0 program was used for data analysis.

Results: At the end of the treatment, there was a significant difference in VAS, SF-36, WOMAC Osteoarthritis Index in the CST+home exercise program group compared to the pre-treatment group. ($p<0.05$) No statistically significant change was detected in Tampa Kinesiophobia Scale and heart rate variability scores. ($p>0.05$) The difference analysis between the groups was significant in favor of the CST+home exercise group. In the KST+home exercise group, a significant increase was observed in pain and joint stiffness reduction, physical function, mobility level and general quality of life compared to the pre-treatment period.

Conclusion: This study showed that craniosacral therapy in addition to a home exercise program in patients with gonarthrosis may be effective in reducing pain, joint stiffness, and improving quality of life and functional status. Since this is the first study on CST in this diagnosis, we think that more participants are needed.

Keywords: craniosacral massage, knee osteoarthritis, osteoarthritis, exercise

GONARTROZ TANILI HASTALARDA KRANİYOSAKRAL TERAPİNİN ETKİNLİĞİ

ÖZET

Amaç: Kraniyosakral terapi (KST), hafif dokunuşlarla uygulanan bir manuel terapi türüdür. KST, otonom sinir sistemini etkileyerek iyileşme sürecini hızlandırabilir. Bu çalışmanın amacı, gonartrozu olan hastalarda kraniyosakral terapinin; ağrı, kalp hızı değişkenliği, eklem sertliği, fiziksel fonksiyon, yaşam kalitesi ve kinezyofobi üzerine etkilerini araştırmaktı.

Yöntem: Araştırmaya 40-85 yaşları arasında gonartroz tanısı olan gönüllü 24 kişi dahil edildi. Katılımcılar ev egzersiz grubu (n=12), KST+ev egzersiz grubu olmak üzere iki gruba ayrılmıştır. 6 hafta boyunca; ev egzersiz programı her gün, KST ise haftada 1 gün uygulanmıştır. Ağrı "Vizüel Analog Skala (VAS)", kinezyofobi "Tampa Kinezyofobi Ölçeği", yaşam kalitesi "SF-36 Yaşam Kalitesi Anketi", ağrı, sertlik ve fiziksel fonksiyon "WOMAC Osteoartrit İndeksi" ve kalp hızı değişkenliği Polar H10 model kalp hızı monitörü ile tedavi öncesi ve sonrası değerlendirildi. Veri analizleri için ise IBM SPSS Statistics 26.0 programı kullanıldı.

Bulgular: Tedavi sonunda KST+ev egzersiz programı grubunda VAS, SF-36, WOMAC Osteoartrit İndeksi'nde uygulama öncesine göre anlamlı farklılık saptandı. ($p<0,05$) Tampa Kinezyofobi Ölçeği ve kalp hızı değişkenliği skorlarında istatiksel açıdan anlamlı değişiklik tespit edilmedi. ($p>0,05$) Gruplar arası fark analizi KST+ev egzersiz grubu lehine anlamlıydı. KST+ev egzersiz grubunda; ağrı ve eklem sertliğinde azalma, fiziksel fonksiyon, mobilite düzeyi ve genel yaşam kalitesinde uygulama öncesine göre anlamlı artış gözlendi.

Sonuç: Bu çalışma; gonartrozu olan hastalarda ev egzersiz programına ek olarak uygulanacak KST'nin kişinin ağrısını, eklem sertliğini azaltmada etkili olabileceğini, yaşam kalitesi ve fonksiyonel durumunu iyileştirebileceğini göstermiştir. KST üzerine bu tanıda yapılan ilk çalışma olduğundan ötürü daha fazla katılımcıyla yapılacak çalışmalara ihtiyaç olduğunu düşünmekteyiz.

Anahtar Kelimeler: kraniyosakral masaj, diz osteoartriti, osteoartrit, Egzersiz

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IMMUNIZATION IN DOUBT: ADDRESSING THE ROOTS OF VACCINE HESITANCY

ABSTRACT

Introduction: Before the advent of vaccines, infectious diseases were among the leading causes of mortality worldwide. Historical attempts to induce immunity date back to the 15th century, but it was not until 1872 that Louis Pasteur developed the first laboratory-based vaccine, marking a turning point in medical science. Vaccines have since become one of the most effective public health tools, saving millions of lives. Nevertheless, concerns about vaccine safety—such as alleged links between the MMR vaccine and autism, or uncertainties surrounding COVID-19 vaccines—have contributed to growing vaccine hesitancy in various populations.

Objective: This review aims to critically examine the benefits and risks of vaccination, providing a balanced perspective to better inform public understanding and support evidence-based decision-making.

Methodology: A narrative review was conducted, drawing on diverse scientific literature and global expert opinions. The analysis focuses on the efficacy, safety, benefits, risks, and both short- and long-term potential side effects of vaccines.

Results: Vaccines are essential for individual and community immunity, significantly reducing the burden of infectious diseases. While short-term safety profiles are well-established, some uncertainty remains regarding rare or long-term adverse effects, which continues to influence public perception.

Conclusion: Although long-term data on vaccine safety are still evolving, the overwhelming evidence supports vaccination as a critical component of disease prevention. Continued research is needed to address knowledge gaps, but in the face of persistent infectious threats, vaccination remains an indispensable public health strategy.

Keywords: Vaccines, immunity, infectious diseases, vaccine safety, vaccine hesitancy, public health, side effects.

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PYRAZOLE-BENZIMIDAZOLE DERIVATIVES TARGETING MCF-7 BREAST CANCER CELLS AS POTENTIAL ANTI-PROLIFERATIVE AGENTS. 3D QSAR AND *In-silico* INVESTIGATIONS VIA MOLECULAR DOCKING AND MOLECULAR DYNAMICS SIMULATIONS

ABSTRACT

Breast cancer is a complicated type of cancer that mainly occurs in women and poses a global threat due to its genetic diversity, making accurate diagnosis challenging. The accepted approaches are categorized by the subtype of cancer and by the level of metastasis. This study focuses on a predictive drug discovery strategy for compounds that may modulate interaction with HER-2 and EGFR, two important receptors in cancer treatment. We employed a 3D QSAR methodology, complemented by molecular docking, ADMET analysis, and molecular dynamics simulations, to evaluate the antiproliferative effects of pyrazole-benzimidazole derivatives on MCF-7 cells as targeted therapies. External validation confirmed the predictive accuracy of the generated models. The best CoMSIA (Comparative Molecular Similarity Indices Analysis) and CoMFA (Comparative Molecular Field Analysis) models exhibited significant Q^2, R^2, and R^2_{pred} values, emphasizing the role of electrostatic and hydrophobic fields in inhibiting breast cancer cell growth. These findings served as the basis for the design and prediction of the biological effects of a number of powerful inhibitors. Additionally, ADMET analysis was conducted to evaluate the drug-likeness of the newly designed ligands, while the stability of the complexes is confirmed by molecular dynamics simulations, which validate the binding stability of the selected chemicals. MMPBSA, PCA analysis, and FEL investigations provide further support for this assertion, reinforcing the robustness of our conclusions.

Keywords: 3D- QSAR; ADMET; Breast Cancer; Pyrazole-benzimidazole Derivatives; Molecular Docking; Simulation Dynamic; PCA; EFL; MMPBSA analysis.

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RATIONAL DESIGN OF POTENT AND SELECTIVE SURVIVIN INHIBITORS BASED ON MX-106 HYDROXYQUINOLINE DERIVATIVES: A 2D-QSAR, MOLECULAR DOCKING, DYNAMICS, AND ADMET STUDY

ABSTRACT

Given the central role of survivin (BIRC5) in tumor cell regulation, the development of novel inhibitors targeting this protein represents a promising strategy in cancer therapy. This study presents the rational design of innovative survivin inhibitors, derived from the hydroxyquinoline scaffold of our previously identified lead compound, MX-106. Nine new derivatives were designed, with predicted inhibitory activity superior to that of the most active molecule in the original series. These compounds showed marked inhibition of MDA-MB-435 cancer cell proliferation in vitro, while also displaying greater metabolic stability. The evaluation of their potential was based on an integrated approach combining 2D-QSAR modeling, molecular anchoring, molecular dynamics and analysis of ADMET properties. The results obtained identified nine promising candidates (Pred1-Pred9), likely to act as potent inhibitors of survivin according to MLR models. A thorough evaluation of their pharmacokinetic properties is recommended to validate their potential as innovative anticancer agents targeting survivin, following the example of MX-106.

Keywords: *Breast cancer, QSAR, ADMET properties, tumor cells, molecular dynamics, selective survivin inhibitors, molecular docking, MX-106 hydroxyquinoline scaffold.*

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THE AFRICAN UNION ON SOCIOPOLITICAL STABILITY IN AFRICA: ACHIEVEMENTS AND CHALLENGES, 2002-2022

ABSTRACT

Since the transformation of the Organisation of African Unity (OAU) to African Union (AU) in 2002, the AU has taken up the ambitious mandate of promoting peace, security, and democratic governance across the continent. However, despite the existence of key frameworks such as the African Peace and Security Architecture (APSA) and the African Governance Architecture (AGA), the continent has continued to witness troubling levels of political instability, armed conflict, and democratic backsliding. The persistence of military coups, post-electoral violence, and weak rule of law in various member states highlights a critical paradox: while the AU has designed robust mechanisms for intervention and accountability, the actual impact of these mechanisms remains inconsistent and often limited in scope and reach. One way to address this shortfall is by strengthening the AU's financial autonomy through sustainable internal funding mechanisms that reduce its overreliance on external donors, thereby enhancing its operational independence and responsiveness. This paper critically evaluates the African Union's performance in fostering socio-political stability in Africa between 2002 and 2022. It explores the extent to which the AU has been successful in mediating conflicts, supporting democratic transitions, and responding to governance crises. Through an analysis of interventions in regions such as the Sahel, the Horn of Africa, and Central Africa, the study interrogates the effectiveness of AU-led peacekeeping operations, diplomatic engagements, and normative frameworks. It further examines how structural limitations, such as insufficient enforcement powers and fragmented political will among member states, undermine the AU's role as a continental stabilizing force. In response, this paper suggests the establishment of a peer review and compliance mechanism to reinforce adherence to democratic principles and sanction member states that breach agreed norms. Drawing from qualitative and quantitative data, this study poses critical questions that guide its analysis: How effective has the AU been in preventing and resolving conflicts across the continent? What factors most significantly hinder its governance and peace efforts? And what institutional or policy reforms are necessary to strengthen the AU's role in building resilient democratic systems and preventing future crises? A key reform area is the enhancement of early warning systems and rapid response capacities within APSA to enable swift intervention in emerging conflicts. Additionally, this paper advocates for broader stakeholder engagement by involving civil society, youth, and local actors in peacebuilding and governance processes to ensure grassroots support and long-term legitimacy. By addressing these questions, this

paper aims to contribute fresh insights to the discourse on continental governance and offer integrated, actionable pathways for enhancing the AU's credibility, capacity, and impact in ensuring peace and political stability in Africa.

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FAMILY DETERMINANTS OF CHILDREN'S PARTICIPATION IN THE POLISH NATIONAL PROJECT: „PE WITH UPE: ACTIVE RETURN TO SCHOOL AND ACTIVE TODAY FOR HEALTH IN THE FUTURE”

ABSTRACT

This study examines the 'PE with UPE' program (2021-2024), a national intervention in Poland designed to counteract the pandemic-related decline in children's physical fitness. Led by the University of Physical Education in Warsaw, the program integrated teacher training, free extracurricular sports with monitoring, and data collection on the socio-demographic and health context of families of over 500,000 children (6-19 years). Parental online questionnaires provided socio-economic and health data, while trained teachers conducted anthropometric and fitness assessments across three program phases. Participation was significantly influenced by higher parental education and lower urbanicity. The participant cohort was primarily composed of younger boys reporting adequate physical activity. These results underscore the importance of targeted strategies for future physical activity programs, particularly focusing on older children, girls, and those from families with less educational capital.

Key words: WF Z AWF, BMI, physical activity, Poland.

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EPIDEMIOLOGICAL INVESTIGATION OF INTESTINAL PARASITES IN CHILDREN HOSPITALIZED MOULAY ABDELLAH HOSPITAL SALE (MOROCCO)

ABSTRACT

The objective of this study is to determine the prevalence of intestinal parasites in children of Sale city (Morocco) and identify the most frequent species. A parasitological examination was performed on 125 stool samples collected. They are issued by children hospitalized Moulay Abdellah Hospital Sale (Morocco). Each sample was subjected to a direct microscopic examination in physiological saline and iodine, an enrichment method Balenger and MIF.

Roughly one out of three contains one or more intestinal parasites. *Giardia intestinalis* (20.90%) and *Blastocystis hominis* (35.82%) are the most frequent, followed by *Entamoeba coli* (16.42%), *Endolimax nana* (8.96%) and *Entamoeba histolytica* (1.49%). *Enterobius vermicualris* (5.97%), *Ascaris lumbricoides* (4.48%), *Strongyloides stercoralis* (1.49%) and *Taenia saginata* (2.99%). The intestinal parasitism is significantly related to age, not the sex.

Keywords: Parasitological examination, intestinal parasites, children, Moulay Abdellah Hospital, Sale (Morocco).

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DIMENSIONS OF LOWER TEETH IN BULGARIAN POPULATION

ABSTRACT

Objectives. Sex determination in forensic anthropology is an essential step for medicolegal purposes and crucial for identification as the number of possible matches is reduced to 50%. The identification of sex is of significance not only in cases of mass fatality incidents where bodies are damaged beyond recognition but also in situations where only fragments of jaw bones with teeth (or teeth alone) are found. Teeth, being the central component of the masticatory apparatus of skull, are excellent material in living and nonliving populations for anthropological, genetic, odontologic and forensic investigations, because they are the hardest and chemically the most stable tissue in the body. The aim of the present study was to determine the sex differences in odontometric dimensions of mandibular teeth in Bulgarians.

Material and methods. The study included 169 subjects of Bulgarian origin in the age group of 20 – 40 years. Buccolingual, mesiodistal and cervicoincisal dimensions of mandibular teeth were measured by Dentistry Sliding Vernier Caliper and analyzed with SPSS 23.0. Inclusion criteria were presence of complete set of fully erupted and periodontally healthy mandibular teeth, non-carious and non-worn mandibular teeth, no dental history of any crown restorations or bridges, normal occlusion. Exclusion criteria were history or clinical evidence of cleft palate, orthognathic surgery or trauma, history or clinical features suggestive of endocranial disorders, metabolic disorders, developmental disorders and history of prolonged illness.

Results. Cervicoincisal dimensions in mandibular premolars and molars were significantly higher in males compared to females. In the right and left first premolars and in the left second premolar there was high degree of significance ($P< 0,001$), while in the right second premolar and the molars the degree of significance was moderate ($0,01>P>0,001$). The mean values in males were significantly higher than in females. Significant differences with weak degree of significance ($P<0,05$) were found in mesiodistal dimensions in mandibular canines and left first molars, while in right first molars differences were with moderate degree of significance ($0,01>P>0,001$). Buccolingual dimensions in lower first molars showed differences with high degree of significance ($P<0,001$) in favor of men while second molars showed differences with weak degree of significance in ($P<0,05$). Mandibular lateral incisors were significantly higher in females than males and the differences were with high degree of significance ($P< 0,001$).

Conclusions. The results of the present measurements exhibited significant sex differences in mandibular teeth in Bulgarians. Our results showed that mandibular canines and molars exhibited the greatest sexual dimorphism. In accordance with similar odontometric studies, teeth may differentiate both genders and thus determine the need for further investigations in this field.

Keywords: sex differences; odontometric dimensions; mandibular teeth; Bulgarians

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AMELIORATIVE EFFECT OF JAMUN (*Syzygium cumini*) SEED AND ORANGE (*Citrus sinensis*) PEEL EXTRACTS AGAINST LEAD INDUCED ALTERATION IN LIVER BIOMARKERS OF RATS

ABSTRACT

The protective effects of jamun seed extract (JSE) and orange peel extract (OPE) on lead induced alteration in liver biochemical parameters were investigated. One hundred twenty Wistar rats were divided into six groups (A-F). Group A (control): No treatment was given, Group B: lead nitrate (10 mg/kg b wt.) was given, Groups C: rats were given 10 mg/kg b wt. Lead nitrate and 200 mg/kg b wt. Jamun seed extract, Group D rats were given 10 mg/kg b wt. Lead nitrate and 200 mg/kg b wt. orange peel extract, Groups E: 200 mg/kg b wt. orange peel extract, and Group F rats were given a dose of 200 mg/kg b wt. jamun seed extract. The treatments were conducted for 14 days. On 7th and 14th day, blood samples were collected from each group and liver biochemical parameters were analyzed. In lead nitrate treated rats liver biomarkers levels (serum alkaline phosphatase, serum SGOT, serum SGPT, serum bilirubin and serum lactate dehydrogenase) were increased at 7 day and 14 day whereas serum albumin levels decreased on 7 day to 14 day as compared to control. JSE and OPE exerts hepatoprotective effects against lead induced alternation in liver biomarkers as the changes in serum alkaline phosphatase, serum SGOT, serum SGPT, serum albumin, serum bilirubin and serum lactate dehydrogenase were recovered to near control values.

Keywords: Lead, Liver biomarkers, Jamun seed extract, Orange peel extract, Protective

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BLOCKCHAIN-BASED SUSTAINABLE TRANSPORTATION FRAMEWORK IN IOVT

ABSTRACT

The rapid evolution of the Internet of Vehicular Things (IoVT) has enabled intelligent transportation systems (ITS) to become more connected, data-driven, and adaptive. However, the increasing demand for real-time vehicle communication, secure data sharing, and environmentally sustainable operations presents significant challenges. This paper proposes a blockchain-based sustainable transportation framework that leverages distributed ledger technology to enhance data integrity, trust, and decentralized coordination among vehicles, infrastructure, and service providers. By integrating smart contracts, the framework automates green routing decisions, verifies eco-driving behaviors, and incentivizes sustainable actions such as reduced emissions or energy-efficient travel. The architecture supports real-time data collection from IoVT devices and enables secure, transparent transactions among stakeholders without reliance on centralized authorities. A case study involving electric vehicle routing and carbon credit allocation is presented, and simulations are conducted to evaluate performance in terms of latency, throughput, and environmental impact. Results demonstrate that the proposed framework enhances security and trustworthiness in vehicular communication and contributes to measurable environmental sustainability. This research provides a foundational step toward integrating blockchain technologies into next-generation eco-friendly ITS solutions.

Keywords: IoVT, BLOCKCHAİN, SUSTAİNABLE TRANSPORTATİON.

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FROM CUP TO CURE: SILVER NANOPARTICLES SYNTHESIZED FROM BUTTERFLY PEA AND GINGER HERBAL TEA FOR DIABETES AND OBESITY MANAGEMENT

ABSTRACT

Herbal teas made from plants other than *Camellia sinensis*, like ginger (*Zingiber officinale*) and butterfly pea (*Clitoria ternatea*), offer notable health benefits, including anti-inflammatory, antioxidant, antibacterial, and immunomodulatory properties. This study employed green synthesis methods to produce silver nanoparticles (AgNPs) using extracts from ginger and butterfly pea as reducing and capping agents. The characterization of the AgNPs through UV-Vis spectroscopy, X-ray diffraction (XRD), and Fourier-transform infrared spectroscopy (FTIR) confirmed their successful synthesis. Antimicrobial tests against *Bacillus subtilis* and *Escherichia coli* showed that the green-synthesized AgNPs had greater efficacy than those made using traditional methods. Additionally, the preparation of herbal tea involved drying the ingredients at 60°C for 2 to 3.5 hours, with varying amounts of ginger powder (1–3%). The best results were achieved with 3.5 hours of drying and a 3% concentration of ginger, yielding 4.25% moisture content and 5.04% ash content. These findings highlight that ginger and butterfly pea herbal tea can be a healthy beverage and a sustainable method for producing biologically active silver nanoparticles with significant antimicrobial and therapeutic properties.

Keywords: Silver Nanoparticles, Herbal tea, X-ray diffraction (XRD), Moisture content, Ginger, Antimicrobial Activity, Butterfly pea.

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BIOCHEMICAL BASIS FOR INSECTICIDE RESISANCE

ABSTRACT

Insecticide resistance presents a major challenge to effective pest management in agriculture and public health. The biochemical basis for this resistance primarily involves enhanced detoxification of insecticides, target site insensitivity, and reduced penetration. Key enzymatic systems such as cytochrome P450 monooxygenases, esterases, and glutathione

S-transferases play pivotal roles in metabolizing and inactivating insecticides. Additionally, mutations in target proteins such as acetylcholinesterase, voltage-gated sodium channels, and nicotinic acetylcholine receptors reduce insecticide binding and efficacy. Altered expression of genes associated with these mechanisms further contributes to resistance development. Understanding these biochemical pathways is essential for designing sustainable pest control strategies, monitoring resistance, and developing next-generation insecticides that can circumvent current resistance mechanisms.

Keywords: Insecticide, Resistance, Cytochrome P450, Monooxygenases and Esterases

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EXPERIMENTAL PRODUCTION AND COMPARISON OF BIOGAS USING CO-DIGESTION OF ORGANIC WASTE

ABSTRACT

Environmental pollution is one of the major problems plaguing the modern world today. The environment and the various elements in the environment need energy to meet their need. So there is a need to produce energy from different sources. Solid Waste is one such material that can be used as a source for deriving energy. The studies on conversion of solid waste to energy have results several alternatives including the biogas generation from biodegradable organic waste. There are several alternatives in the estimation of biogas yield from the bio degradable fraction of solid waste. The different types of biodegradable organic waste may comprises of cow dung, pig waste, poultry manure, food waste, vegetable waste, kitchen waste etc. The present study focuses on production of biogas using cow dung with vegetable waste and poultry manure. In this study, by doing experimentation it is observed that the production of biogas from co-digestion of different organic waste is more than individual waste. The highest yield of biogas is obtained from co-digestion of cow dung with poultry manure than co-digestion of cow dung with the vegetable waste. Waste produced after the production of biogas is used as natural fertilizers for the growth of crops and fields and it gives good yield. By experimentations like energy recovery from solid waste, the conservation of non renewable energy resources may be possible and it also helps to protect our environment.

Keywords: Environmental pollution, Modern world today, Energy recovery, Natural fertilizers, Bio-gas, Cow dung and Solid waste

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WATER, SANITATION AND HYGIENE IN HEALTH CARE FACILITIES IN THE PROVINCE OF AL-HOCEIMA (MOROCCO): STATUS AND PROSPECTS

ABSTRACT

Introduction: Adequate water, sanitation and hygiene (WASH) services are essential for the provision of basic health care to prevent infection and the spread of disease. The aim of this study was to assess and quantify the availability, quality and needs of these services in health facilities in the province of Al-Hoceima.

Method: The assessment was national in scope, took place over a period from May to November 2022, and was carried out on a sample of healthcare facilities selected on a simple random basis. In the province of Al-Hoceima, 19 facilities were surveyed (3 Med V hospital wards, 2 private clinics, Targuist local hospital, 4 CSU, 7 CSR, 2 DR).

Data were entered directly onto cell phones using a CS-Pro computer application, and processed using SPSS statistical software. Graphs were produced using Excel spreadsheets.

Results: The results showed that for the supply and availability of drinking water, 10% of ESS had no source and 39% had a water source located 500 meters away. For the availability of improved and usable sanitation facilities, the results showed that 8.6% were non-functional. Only 16.4% of ESS had a secure area for the storage of medical and pharmaceutical waste (MPW), and only 2.5% had instructions, guidelines or protocols for cleaning.

Conclusion: The results show that the situation regarding water, sanitation and hygiene in health care facilities is alarming. This calls for action by all the departments concerned.

Keywords: Health Care Facilities (HCF), Water, Sanitation and Hygiene (WASH)

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GREEN TEA AS A THERAPEUTIC AGENT: EXPLORING ITS ANTI-INFLAMMATORY AND IMMUNOMODULATORY ROLES IN RHEUMATOID ARTHRITIS MANAGEMENT

ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder that primarily affects the synovial joints, resulting in progressive joint destruction, pain, and disability. Despite advances in pharmacological therapies, long-term use of synthetic drugs often leads to adverse effects and variable patient responses, highlighting the need for safer adjunctive treatment options. Green tea (*Camellia sinensis*), a widely consumed beverage, has garnered significant attention due to its rich polyphenolic content, particularly epigallocatechin-3-gallate (EGCG), which possesses potent anti-inflammatory and immunomodulatory properties. This review explores the therapeutic potential of green tea in the management of RA, emphasizing its ability to modulate key inflammatory mediators such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and nuclear factor-kappa B (NF-κB). Preclinical and clinical studies have demonstrated that green tea polyphenols can suppress oxidative stress, reduce pro-inflammatory cytokine production, and inhibit the activation of synovial fibroblasts and osteoclasts, thereby preventing joint degradation. Furthermore, green tea influences immune cell regulation by modulating the balance between pro-inflammatory Th17 cells and anti-inflammatory regulatory T cells (Tregs), contributing to immune homeostasis. These multifaceted mechanisms support the integration of green tea as a complementary strategy alongside conventional treatment in RA therapy. While promising, further large-scale, randomized clinical trials are necessary to establish optimal dosage, safety profiles, and long-term effects in human subjects. This abstract underscores the potential of green tea as a natural, cost-effective therapeutic agent in attenuating the pathophysiology of rheumatoid arthritis through its anti-inflammatory and immunoregulatory mechanisms.

Keywords: Green tea, rheumatoid arthritis, epigallocatechin-3-gallate, anti-inflammatory, immunomodulatory, cytokines

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MICRORNA 21 AND PROSTATE IN NIGERIA, A REVIEW STUDY

ABSTRACT

Background: Prostate cancer is a leading cause of cancer-related deaths among men worldwide, with a significant burden in Nigeria. MicroRNAs (miRNAs) have emerged as critical regulators of gene expression, with MicroRNA 21 (miR-21) implicated in the pathogenesis of various cancers, including prostate cancer. This review aims to summarize the current state of knowledge on the role of miR-21 in prostate cancer, with a focus on the Nigerian context.

Methods: A comprehensive literature search was conducted using major databases, including PubMed, Scopus, and Google Scholar. Studies investigating the expression and functional significance of miR-21 in prostate cancer, as well as those reporting on the epidemiology and molecular characteristics of prostate cancer in Nigeria, were included.

Results: The review highlights the overexpression of miR-21 in prostate cancer tissues and its association with tumor progression, metastasis, and poor prognosis. Additionally, the review discusses the potential of miR-21 as a biomarker for prostate cancer diagnosis and monitoring in Nigeria, where access to healthcare and diagnostic facilities is limited.

Conclusion: This review underscores the importance of miR-21 in prostate cancer and highlights the need for further research on its role in the Nigerian context. The findings have implications for the development of miR-21-based diagnostic and therapeutic strategies for prostate cancer in Nigeria.

Keywords: MicroRNA 21, Prostate cancer, Nigerian Men, Biomarker, Molecular marker

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EFFECTIVENESS OF CONCEPT MAPPING IN ENHANCING SCIENCE ACHIEVEMENT OF GRADE 8 STUDENTS

ABSTRACT

Concept mapping functioned as an instructional technique to determine its effectiveness for improving General Science grades among Grade VIII students. The research design consisted of two groups from a government school where 57 female students received instruction. Experimental students numbered 29 and received teaching through concept mapping while control students consisted of 28 and learned through conventional methods. The achievement test for data collection was developed by the researcher and validated by experts before implementation. The KR-20 reliability analysis along with item testing confirmed its validity. Concept mapping education strategies enabled students to score better academically according to results obtained through independent t-test analysis. The strategy enabled students to understand science concepts better because it improved their conceptual understanding which results in better academic performance. The proposed research should expand to additional disciplines along with multiple learning environments.

Keywords: Concept mapping, student achievement, instructional methods, science learning, secondary education, teaching strategies.

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RADIOGRAPHIC, CLINICAL, AND BIOCHEMICAL COMPARISON OF Cr-Co-Ceramic Implant-SUPPORTED SINGLE CROWNS USING SCREW OR CEMENT RETENTION: A COHORT STUDY

ABSTRACT

Background: The analysis that was conducted in this study, comparing two different crown-retention solutions, considered periodontal indices and standardized radiographic measurements and the indices of possible damage which now represent a concrete help in diagnosis and prognosis.

Materials and Methods: The present study was designed to compare peri-implant soft and hard tissue response after 2 years of functional loading between direct screw-retained posterior single crowns in Cr-Co/Ceramic or cement-retained Cr-Co/Ceramic on titanium abutment. 24 non-smoking partially edentulous patients, requiring implant therapy for a prosthetic rehabilitation, were included in the study. The values of Il-1β, IL-6, IL-8 were evaluated, together with the periodontal indices PI, GI, PD, BOP, REC. The PICF was collected with standardized paper strips. Repeated measure ANOVA was used between groups months at 1, 3, and 12 months.

Results: During the time of clinical observation, at t0 (1 month), t1 (3 months) and t2 (12 months), both types of crowns performed satisfactorily from a clinical point of view. In light of the results obtained, it is possible to define that screwed Cr-Co/Cer has slightly higher values than the other.

Conclusions: It is possible to hypothesize, that this difference could lead to a clinically visible difference between these two prosthetic solutions in the longer term. The single screwed crown in Cr-Co shows a different interface with the titanium implant connection compared to the titanium-titanium contact of the connection between the implant and the titanium abutment for the cement-retained prosthetic solution.

Keywords: Cr-Co; Implants; Titanium; Cement-retained; Screw-retained; Ceramic.

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INSULIN RECEPTOR SUBSTRATE 1 (IRS1) AND INSULIN RECEPTOR SUBSTRATE 2 (IRS2) PROTEINS WITH BIOINFORMATICS ANALYSES IN GASTRIC CANCER: WHAT IS EXPLAINABLE?

ABSTRACT

Gastric cancer is among the malignancies responsible for over 700,000 annual deaths worldwide. The incidence of gastric cancer exhibits geographical variability across the globe, with a notably high prevalence in the Eastern part of Türkiye. Insulin receptor substrate (IRS) proteins, particularly IRS1 and IRS2, serve as key regulators of the IGF-1R signaling pathway and play critical roles in tumor progression, therapeutic response, and immune response modulation. This study aimed to elucidate the roles of IRS1 and IRS2 genes in stomach adenocarcinoma (STAD) through bioinformatics approaches. Within this scope, the expression levels of IRS1 and IRS2, their methylation status, and their associations with clinical parameters were investigated using publicly accessible bioinformatics databases. The findings revealed that IRS1 and IRS2 genes are significantly overexpressed in gastric tumor tissues compared to normal tissues, and this elevated expression may serve as a favorable prognostic indicator for overall survival. Furthermore, the positive correlation of these genes with CD8+ T cells and Treg cells suggests their potential functional significance in the tumor microenvironment. Methylation analyses indicated that these genes may also undergo epigenetic regulation. Based on these findings, IRS1 and IRS2 may be considered candidate prognostic biomarkers in gastric cancer; however, further molecular genetic studies are needed.

Keywords: Gastric cancer, IRS1, IRS2, Bioinformatic analysis

GASTRİK KANSERDE BİYOİNFORMATİK ANALİZLERLE İNSÜLİN RESEPTÖR SUBSTRAT 1 (IRS1) VE İNSÜLİN RESEPTÖR SUBSTRAT 2 (IRS2) PROTEİNLERİ NELER ANLATIYOR?

ÖZET

Gastrik kanser, dünya genelinde yıllık >700.000 ölüme sebebiyet veren kanserler arasında sayılmaktadır. Dünya genelinde coğrafik olarak görülme sıklığı değişkenlik gösteren mide kanseri, ülkemizde özellikle Doğu Anadolu bölgesinde yaygın görülmektedir. İnsülin reseptör substrat (IRS) proteinleri, özellikle IRS1 ve IRS2, IGF-1R sinyal yolunun anahtar düzenleyicileri olarak, tümör progresyonu, tedaviye yanıt ve immün cevabın düzenlenmesinde önemli roller oynamaktadır. Bu çalışmada, IRS1 ve IRS2 genlerinin mide kanserindeki (STAD) rollerinin biyoinformatik yaklaşımlarla belirlenmesi amaçlanmıştır. Bu kapsamda, IRS1 ve IRS2'nin ekspresyon düzeyleri, metilasyon durumu ve klinik parametrelerle ilişkileri açık erişimli farklı biyoinformatik veri tabanları aracılığıyla incelenmiştir. Elde edilen sonuçlar, IRS1 ve IRS2 genlerinin mide tümörlerinde normal dokulara kıyasla anlamlı ölçüde daha yüksek ifade edildiğini ve bu yüksek ekspresyonun genel sağkalım açısından olumlu bir prognostik gösterge olabileceğini ortaya koymuştur. Ayrıca, genlerin CD8+ T hücreleri ve T reg hücreleri ile pozitif korelasyon göstermesi, bağışıklık mikroçevresinde önemli işlevsel roller üstlenebileceğini düşündürmektedir. Metilasyon analizleri ise bu genlerin epigenetik düzeyde de regülasyona uğrayabileceğini göstermiştir. Bu bilgilere dayanarak, IRS1 ve IRS2'nin mide kanserinde prognostik biyobelirteç adayları olarak değerlendirilebileceğini göstermekle beraber ileri moleküler genetik çalışmalara ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Gastrik kanser, IRS1, IRS2, Biyoenformatik analiz

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TREATMENT OF A NON-SYNDROMIC OLIGODONTIC CASE WITH A MULTIDISCIPLINARY ORTHODONTIC APPROACH

ABSTRACT

Objective: The aim of this case report is to present the results of a multidisciplinary approach to the fixed orthodontic treatment of a patient with Class III subdivision malocclusion who had polydiastema in the upper and lower jaws as a result of oligodontia and who did not have ideal occlusion.

Material and method: A female patient with a chronological age of 14 years and 6 months presented to our clinic with complaints of anomalies in the number, size and shape of her teeth, polydiastema due to multiple missing teeth and inadequacy in smile aesthetics. Clinical and radiologic evaluation revealed 1 mm overjet, 1.5 mm overbite, unilateral posterior crossbite, Class I canine and molar relationship on the right side, Class III canine and molar relationship on the left side, skeletal Class I malocclusion. Panoramic X-rays revealed persistent deciduous teeth in the anterior region of the mandible and congenital absence of teeth numbered 12, 15, 22, 26, 31, 41, 41, 18, 28, 38, 48. After fixed orthodontic treatment with a multidisciplinary approach, implant surgery and prosthetic treatment were planned. Polydiastemas were closed by extracting the deciduous teeth in the anterior region of the lower jaw and mesializing the teeth numbered 32 and 42 towards the midline, and mesializing the teeth numbered 13 and 23 in the upper jaw and replacing the teeth numbered 12 and 22. Polydiastemas in the upper jaw were collected distal to the canine teeth and implant areas were opened for teeth numbered 13 and 23. The existing gaps were corrected with prosthetic rehabilitation. The treatment lasted 18 months in total.

Results: At the end of the treatment, 2 mm overbite, 2 mm overjet and Class II subdivision relationship were obtained. Smile aesthetics were optimized with the procedures performed in the maxillary and mandibular anterior regions.

Conclusion: With the right indication, unaesthetic occlusion in oligodontic patients can be optimized with orthodontic treatments performed with a multidisciplinary approach.

Keywords: Orthodontics, Oligodontia, Multidisciplinary treatment

SENDROMİK OLMAYAN OLİGODONTİ VAKASININ MULTİDİSİPLİNER ORTODONTİK YAKLAŞIM İLE TEDAVİSİ

ÖZET

Amaç: Bu olgu sunumunun amacı oligodonti sonucu alt ve üst çenelerinde polidiastema gözlenen ve ideal oklüzyonu olmayan Sınıf III subdivizyon maloklüzyona sahip hastanın multidisipliner yaklaşım ile yapılan sabit ortodontik tedavisinin sonuçlarını sunmaktır.

Materyal ve yöntem: Kronolojik yaşı 14 yıl 6 ay olan kadın hasta dişlerindeki sayı, boyut, şekil anomalisi, çoklu diş eksikliklerine bağlı polidiastema ve gülümseme estetiğindeki yetersizlik şikayetleri ile kliniğimize başvurmuştur. Klinik ve radyolojik değerlendirmede 1 mm overjet, 1.5 mm overbite, tek taraflı posterior çapraz kapanış, sağ bölgede Sınıf I kanin ve molar ilişki, sol bölgede Sınıf III kanin ve molar ilişki, iskeletsel Sınıf I maloklüzyon gözlemlendi. Panoramik röntgen filminde alt çene anterior bölgede persiste süt dişleri ve 12, 15, 22, 26, 31, 41, 18, 28, 38, 48 numaralı dişlerin konjenital eksikliği tespit edildi. Multidisipliner yaklaşım ile sabit ortodontik tedavi sonrası implant cerrahisi ve protetik tedavi planlandı. Polidiastemalar alt çene anterior bölgedeki süt dişleri çekilerek 32 ve 42 numaralı dişler orta hatta doğru mezialize edilerek, üst çenede 13 ve 23 numaralı dişler mezialize edilerek 12 ve 22 numaralı dişlerin yerine geçmesi ile kapatıldı. Üst çenedeki polidiastemalar kanin dişlerin distalinde toplanarak 13 ve 23 numaralı dişlere implant boşluğu açıldı. Mevcut boşluklar protetik rehabilitasyonla düzeltildi. Tedavi toplamda 18 ay sürdü.

Bulgular: Tedavi sonunda 2 mm overbite, 2 mm overjet, Sınıf II subdivizyon ilişki elde edilmiştir. Maksiller ve mandibular anterior bölgelerde yapılan işlemler ile gülümseme estetiği ideal hale getirilmiştir.

Sonuç: Doğru endikasyon ile oligodonti hastalarında estetik olmayan oklüzyon, multidisipliner yaklaşımla yapılan ortodontik tedavilerle ideal hale getirilebilmektedir.

Anahtar kelimeler: Ortodonti, Oligodonti, Multidisipliner tedavi

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EVALUATION OF *IN VITRO* BIOLOGICAL ACTIVITY AND QUALITY-SAFETY OF FOOD SUPPLEMENTS CONTAINING *TRIBULUS TERRESTRIS*

ABSTRACT

Food supplements are products that individuals use to support their health and improve their quality of life. In recent years, food supplements have become increasingly popular. One such supplement is *Tribulus terrestris* extract, which is widely recommended and available over-the-counter[1]. It is particularly popular among athletes due to its claimed benefits, such as enhancing athletic performance and improving sexual function[2]. However, some concerns have been raised about the quality and safety of food supplements, including *T. terrestris*. The aim of this study is to provide valuable information to consumers, regulators and manufacturers by evaluating the quality and safety of *T. terrestris* supplements available in Türkiye. Sample collection, *in vitro* activity assays, human health risk assessment conjuction with heavy metal analysis steps were conducted as part of this study. Representative samples of *T. terrestris* supplements were obtained from various local market and online stores in Türkiye using random sampling technique. In order to investigate the quality of *T. terrestris* supplements, activity studies were carried out on the plant extract contained in the supplements. After methanol extracts were obtained, antioxidant activity and total phenolic content were determined. Heavy metal content was determined using the Flame Atomic Absorption Spectroscopy (FAAS) method, specifically analyzing the presence of lead (Pb) and cadmium (Cd). The potential health risks associated with these contaminants were evaluated using toxicity data available in the literature. The findings may offer useful insights for consumers, regulatory authorities, and manufacturers, contributing to a better understanding of the potential health risks associated with these supplements.

Keywords: *Tribulus terrestris*, food supplements, FAAS, antioxidant activity, total phenolic content

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EFFECT OF CARDIOPULMONARY BYPASS ON THYROID HORMONE LEVELS

ABSTRACT

Introduction: Cardiopulmonary bypass (CPB) is a technique that provides systemic circulation and oxygenation during cardiac surgery. However, CPB may cause changes in the hormonal system, especially in thyroid hormones. It is thought that postoperative changes in thyroid hormone levels may have an effect on the healing process and clinical outcomes.

Objective: The aim of this study was to evaluate the effect of CPB (perfusion system) on thyroid hormone levels in patients undergoing CPB-guided cardiac surgery.

Methods: This study included 34 patients who underwent elective cardiac surgery under CPB guidance. Preoperative and postoperative serum thyroid hormone levels [free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH)] were evaluated. Cardiopulmonary bypass time (total perfusion time) and aortic cross clamp time were recorded during CPB in order to show the effect of the perfusion system. The relationship between postoperative changes in thyroid hormone levels and total perfusion time and aortic cross clamp time was evaluated by correlation analysis. Statistical significance level was determined as $p<0.05$.

Results: Demographic and descriptive data of the patients are presented in Table 1. There was a significant difference between preoperative and postoperative day 1 thyroid hormone levels, which decreased in the postoperative period ($p<0.001$) (Table 2). There was no correlation between thyroid hormone levels and perfusion system variables (Table 3).

Conclusion: It was found that CPB had an effect on thyroid hormone levels and decreased in the postoperative period compared to preoperative levels. However, this decrease in thyroid hormone levels was not related to the duration of exposure to perfusion system.

Keywords: Cardiopulmonary Bypass, Open Heart Surgery, Perfusion System, Thyroid Hormone, Thyroid Function.

Table 1. Demographic and descriptive data of the patients

Descriptive and Frequency Statistics				
		Frequency	Percent	
Gender	Male	23	67,6	
	Female	11	32,4	
	Minimum	Maximum	Mean	Std. Deviation
Age (years)	41,00	78,00	61,4118	9,10251
Height (cm)	145,00	180,00	164,7353	9,20247
Weight (kg)	54,00	108,00	78,2647	12,78330
Body surface area (m^2)	1,47	2,24	1,8771	0,17867
Flow (L/min)	3,53	5,38	4,5047	0,40717
Total perfusion time (min)	55,00	200,00	106,4706	34,32045
Cross clamp time (min)	40,00	155,00	83,6176	33,48723
Preop FT3 (pmol/L)	3,50	8,08	4,6097	1,13441
Preop FT4 (pmol/L)	12,06	35,56	18,6315	5,35761
Preop TSH (mU/L)	0,17	6,89	2,4594	1,90660
Postop FT3 (pmol/L)	1,57	6,18	3,3091	1,00746
Postop FT4 (pmol/L)	10,23	25,45	15,4715	3,60561
Postop TSH (mU/L)	0,12	5,85	1,8415	1,49135

FT3: Free triiodothyronine, FT4: Free thyroxine, and TSH: Thyroid-stimulating hormone.

Table 2. Preoperative and postoperative comparison of thyroid hormone levels

Test Statistics[a]			
	Postop FT3 – Preop FT3	Postop FT4 – Preop FT4	Postop TSH – Preop TSH
Z	-5,086[b]	-5,069[b]	-5,087[b]
Asymp. Sig. (2-tailed)	<0,001	<0,001	<0,001

a. Wilcoxon Signed Ranks Test
b. Based on positive ranks.

Table 3. Correlation between thyroid hormone levels and perfusion variables

Correlations							
		Preop FT3	Preop FT4	Preop TSH	Postop FT3	Postop FT4	Postop TSH
Total perfusion time (min)	Pearson Correlation	0,177	0,298	0,255	0,319	0,234	0,187
	Sig. (2-tailed)	0,317	0,087	0,145	0,066	0,183	0,289
Cross clamp time (min)	Pearson Correlation	0,195	0,293	0,167	0,325	0,206	0,098
	Sig. (2-tailed)	0,268	0,092	0,344	0,061	0,244	0,583

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THE EFFECT OF FOOT POSTURE ON DYNAMIC AND STATIC BALANCE IN YOUNG INDIVIDUALS

ABSTRACT

Objective: This study aimed to investigate the effect of foot posture on static and dynamic balance in young individuals.

Methods: The study was conducted between September 15, 2024, and February 15, 2025. A total of 50 volunteer participants aged 18–30 years, who had no history of foot trauma or surgery and no neurological or systemic diseases, were included. Clinical and demographic data were collected using the Socio-Demographic Evaluation Form. Foot posture was assessed using the Foot Posture Index (FPI), static balance with the Flamingo Test, and dynamic balance with the Star Excursion Balance Test (SEBT). All assessments were performed by the same physiotherapist.

Results: Statistical analyses were performed using SPSS version 22.0. The Kolmogorov–Smirnov test was used to assess the normality of data distribution. Chi-square test was used for categorical variables, while Spearman correlation analysis was applied for numerical data. A significance level of $p<0.05$ was adopted. The mean FPI scores for both left and right feet were 0.50±0.68. According to the Flamingo Test, the mean static balance duration was 1.52±2.58 seconds with eyes open and 2.78±4.54 seconds with eyes closed. In the Star Excursion Balance Test, the mean reach distance in the left direction was 71.45±5.10 cm. A statistically significant positive correlation was found between the FPI and static balance (Flamingo Test) ($p<0.01$). However, no statistically significant relationship was observed between the FPI and dynamic balance (Star Test) ($p>0.05$).

Conclusion: This study revealed that foot posture has a significant effect on static balance in young individuals. As foot posture deteriorates, static balance performance tends to decline. However, no significant effect was found on dynamic balance. These findings suggest that foot posture should be taken into account during balance assessment and intervention processes.

Keywords: Foot Posture – Static Balance – Dynamic Balance

GENÇ BİREYLERDE AYAK POSTÜRÜNÜN DİNAMİK VE STATİK DENGE ÜZERİNE ETKİSİ

ÖZET

Amaç: Çalışmanın amacı genç bireylerde ayak postürünün dinamik ve statik denge üzerine etkisini araştırmaktır.

Yöntem: Bu çalışma 15 Eylül 2024 - 15 Şubat 2025 tarihleri arasında yürütüldü. Çalışmaya ayak travması veya operasyonu geçirmemiş, nörolojik veya sistemik herhangi bir hastalığa sahip olmayan, 18-30 yaş aralığında 50 gönüllü olgu dahil edildi. Olgulara ait klinik ve demografik bilgiler Sosyo-demografik Değerlendirme Formu kullanılarak sorgulandı. Olguların ayak postürü Ayak Postür İndeksi (APİ), statik dengeleri Flamingo Testi, dinamik dengeleri ise Yıldız Testi ile değerlendirildi. Olguların tüm değerlendirmeleri aynı fizyoterapist tarafından gerçekleştirildi.

Bulgular: İstatistiksel analiz Statiscal Package for Social Sciences (SPSS) 22 versiyonu ile gerçekleştirildi. Verilerin normal dağılıma uygunluğunun tespiti için "Komolrow – Spinorow" testi kullanıldı. Numeratik verilerin korelasyonu için "Spearman" ve kategorik veriler için "Pearson" korelasyon analizi testi uygulandı. Elde edilen değerlerin anlamlı olup olmadığının yorumlanmasında 0.05 anlamlılık düzeyi ölçüt olarak kullanıldı. Ayak postür indeksine (APİ) göre sol ve sağ ayakta puanların her ikisi de ortalama 0,50±0,68'dir. Denge değerlendirmelerine göre flamingo testi açık gözle ortalama 1,52±2,58; kapalı gözle ise 2,78±4,54 saniye olarak hesaplandı. Yıldız testi sol uzanım mesafesi ortalama 71,45±5,10 cm'dir. Yapılan korelasyon analizleri sonucunda APİ ile statik denge (Flamingo Testi) arasıda pozitif yönde anlamlı bir ilişki gözlemlendi ($p<0,01$). Buna karşın APİ ile dinamik denge arasında (Yıldız Testi) istatistiksel olarak anlamlı bir ilişki bulunmadı ($p>0,05$).

Sonuç: Bu çalışma, genç bireylerde ayak postürünün statik denge üzerinde anlamlı bir etkisi olduğunu ortaya koymuştur. Ayak postürü bozuldukça statik denge performansının da olumsuz yönde etkilendiği gözlemlenmiştir. Ancak, ayak postürünün dinamik denge üzerindeki etkisi istatistiksel olarak anlamlı bulunmamıştır. Bu sonuçlar, postüral bozuklukların statik dengeyi olumsuz etkileyebileceğini ve değerlendirme süreçlerinde ayak postürünün dikkate alınması gerektiğini ortaya koymaktadır.

Anahtar Kelimeler: Ayak Postürü, Statik Denge, Dinamik Denge

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VOCATIONAL SCHOOL HEALTH PROGRAMS STUDENTS EXAMINATION OF OCCUPATIONAL ANXIETY LEVELS

ABSTRACT

The aim of this study is to examine the occupational anxiety levels of the students of vocational school health programs at a foundation university and the factors affecting them. This descriptive study was carried out at Hasan Kalyoncu University Vocational School between April 1 and May 31, 2024. Necessary permissions were obtained from the institution, ethics committee and students before the study. Students studying in the Health Programs of the Vocational School of the University formed the universe of the research. All students who agreed to participate in the research constituted the sample of the research. 464 students who volunteered to participate in the study constituted the sample of the research. Data in the study; It was collected using the Descriptive Characteristics Form and the Professional Anxiety Scale for Associate Degree Students. 80% of the participants were female, 98.7% were single and 35.8% were enrolled in the First and Emergency Aid Program. 50% of them are studying in the first grade and 64.7% of them are Anatolian high school graduates. 76.3% of the students willingly chose their departments and 50% of them did internships. In terms of socio-economic status, 67.7% of them have equal income and expenditure status. The proportion of individuals working in the field of health in the family was 73.5%, and the desire to work in their own department after graduation was determined as 74.1%. The ages of the students range from 16 to 34 years and the average age is 20.94±1.79 years. The analysis of the total score of MKI revealed that the professional anxiety levels of women, those studying in the anesthesia department, first-year students, those who did not do internship and those who did not choose their departments willingly were significantly higher ($p<0.05$). The mean score of MKI was found to be 56.09±13.27. This study reveals that the occupational anxiety levels of the students of vocational school health programs show significant differences depending on various individual, academic and socio-economic factors. The findings emphasize the necessity of targeted guidance programs for better management of students' anxiety levels.

Keywords: Occupation, anxiety, health students

MESLEK YÜKSEKOKULU SAĞLIK PROGRAMLARI ÖĞRENCİLERİNİN MESLEKİ KAYGI DÜZEYLERİNİN İNCELENMESİ

ÖZET

Bu araştırmanın amacı, bir vakıf üniversitesindeki meslek yüksekokulu sağlık programları öğrencilerinin mesleki kaygı düzeylerini ve etkileyen faktörleri incelemektir. Tanımlayıcı tipteki bu çalışma, 1 Nisan- 31 Mayıs 2024 tarihleri arasında Hasan Kalyoncu Üniversitesi Meslek Yüksekokulu'nda uygulandı. Çalışma öncesi kurumdan, etik kuruldan ve öğrencilerden gerekli izinler alındı. Üniversitenin Meslek Yüksekokulu Sağlık Programlarında öğrenim gören öğrenciler araştırmanın evrenini oluşturdu. Araştırmada örneklem seçimine gidilmeyerek araştırmaya katılmayı kabul eden tüm öğrenciler araştırmanın örneklemini oluşturdu. Araştırmaya katılmaya gönüllü olan 464 öğrenci araştırmanın örneklemini oluşturdu. Çalışmada veriler; Tanıtıcı Özellikler Formu ve Ön Lisans Öğrencilerine Yönelik Mesleki Kaygı Ölçeği kullanılarak toplandı. Katılımcıların %80'i kadın, %98,7'si bekar olup, %35,8'i İlk ve Acil Yardım Programı'na kayıtlıdır. %50'si birinci sınıfta öğrenim görmekte ve %64,7'si Anadolu lisesi mezunudur. Öğrencilerin %76,3'ü bölümlerini isteyerek tercih etmiş, %50'si staj yapmıştır. Sosyo-ekonomik durum açısından, %67,7'sinin gelir ve gider durumu eşittir. Ailede sağlık alanında çalışan birey oranı %73,5, mezuniyet sonrası kendi bölümünde çalışma isteği ise %74,1 olarak belirlenmiştir. Öğrencilerin yaşları 16-34 arasında değişmekte olup, yaş ortalaması 20,94±1,79 yıldır. MKÖ toplam puanı analizleri, kadınların, anestezi bölümünde öğrenim görenlerin, birinci sınıf öğrencilerinin, staj yapmamış olanların ve bölümlerini isteyerek tercih etmeyenlerin mesleki kaygı düzeylerinin anlamlı şekilde daha yüksek olduğunu ortaya koymaktadır ($p<0,05$). MKÖ ortalama puanı ise 56,09±13,27 olarak bulunmuştur. Bu araştırma, meslek yüksekokulu sağlık programları öğrencilerinin mesleki kaygı düzeylerinin çeşitli bireysel, akademik ve sosyo-ekonomik faktörlere bağlı olarak anlamlı farklılıklar gösterdiğini ortaya koymaktadır. Bulgular, öğrencilerin kaygı düzeylerinin daha iyi yönetilmesi için hedefe yönelik rehberlik programlarının gerekliliğini vurgulamaktadır.

Anahtar Kelimeler: Meslek, kaygı, sağlık öğrencileri

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CLINICAL OUTCOMES OF FULL-ARCH IMPLANT-SUPPORTED FIXED PROSTHESES IN THE EDENTULOUS MAXILLA: IMPLANT SURVIVAL AND PROSTHETIC COMPLICATIONS

ABSTRACT

Background: Full-arch implant-supported fixed dental prostheses, which the patient must carefully manage in home oral hygiene procedures, is the fixed alternative to a mucosal/implant -supported prosthesis. Clinically, the execution of this rehabilitation requires six implants for the upper jaw. The aim of the present study is to verify the survival-rate of implants for implant fixed prostheses in the edentulous upper jaw.

Materials and Methods: This retrospective study was carried out on patients who received an upper full arch fixed prostheses on six implants for rehabilitation. A total of 36 patients (232 implants) were included and evaluated from a clinical and radiographical point of view. The follow-up period in which the data were collected on the upper full-arch is between 60 and 84 months.

Results: The total implant survival rate is 93.1%, a value which is like previous studies already published on the topic. Considering the use of temporary cement for the stabilization, 3 de-cementations occurred in these 48-72 months of observation. Compared to implant-supported prostheses, the incidence of fracture of veneers or teeth is

considerably higher, considering the extent of the forces that are not attenuated by the prosthetic material due to the presence of the metal framework.

Conclusions: Considering the overall results of the study, the loss of implants after loading is in any case lower than the percentage obtained by the same authors using the same implants, but with a removable prosthetic device. Most of these full-arch achieves good clinical results in this study at 84 months.

Keywords: Full-arch; Implant-supported; Fixed dental prostheses; Cement-retained; Cr-Co; Resin; Composite.

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EVALUATION OF CLINICAL AND BIOCHEMICAL OUTCOMES IN TWO VARIANTS OF SCREW-RETAINED SINGLE IMPLANT CROWNS

ABSTRACT

Background: The gold standard of implant-retained crowns has for many years been the metal-ceramic cement-retained crowns on a screwed-abutments. Today it represents an alternative if the implant positioning does not allow a screw-retained crown. The possibilities currently offered for this kind of rehabilitation in the posterior areas are represented by a chromium-cobalt/ceramic or a titanium/zirconia crown. These two solutions allow different productions workflows and generate different prosthetic interfaces at the implant abutment level. The aim of the study is to verify a significant difference in tissue response can be defined between these two different rehabilitations, 18 months after delivery.

Materials and methods: A total of 20 participants were included in the study, each of whom had at least two implants in the posterior sectors prosthetically treated with one of the two solutions previously illustrated. The values of Il-1β, IL-6, IL-8 were evaluated, together with the periodontal indices placque index (PI), gingival index (GI), probing depth (PD), bleeding on probing (BOP), gingival recession (REC).

Results: During the time of clinical observation, at t0 (1 month from the delivery), t1 (9 months after the delivery) and t2 (18 months after the delivery), both types of crowns performed satisfactorily from a clinical point of view. In light of the results obtained, it is possible to define that there are no statistically significant differences between the two techniques, although Cr-Co/Cer has slightly higher values than the other.

Conclusions: It is possible to hypothesize, and confirm through subsequent or longer-term studies, that this difference could lead to a clinically visible difference between these two prosthetic solutions in the longer term. The single crown in Cr-Co shows a different interface with the titanium implant connection compared to the titanium-titanium contact of the connection between the implant and the Ti-Zir crown.

The ceramic that is layered directly on the Cr-Co does not show a connection interface with it, other than the areas hand-finished by the technician, vice versa, the Ti-Zir crown shows an area in which the milled zirconia product is bonded onto the titanium abutment with a resin-based cement.

The causes of this slight difference could be either the better tissue response to titanium and zirconia, or an increased level of inflammation from the Cr-Co/Ti connection.

Keywords: Cr-Co; Implants; Titanium; Resin; Screw-retained; Milling; Zirconia.

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REPOSITIONING THE TEACHING OF SPOKEN ENGLISH IN THE 21ST CENTURY SECONDARY SCHOOLS IN MINNA METROPOLIS, NIGERIA

ABSTRACT

The standard of spoken English of a majority of senior secondary school students in Minna, Nigeria, where English is taught and used as a second and official language is a major cause of concern to language educators. One of the skills driving 21st century education environment is effective communication. It is, therefore, very important that utmost attention be paid to the teaching and learning of spoken English in the secondary school. The spoken English performance of secondary school graduates does not meet the standard expected of them. The purpose of this paper is to examine the instructional environment of the spoken English class and to proffer repositioning strategies for 21st century spoken English instruction. 33 English language teachers in purposively selected public and private senior secondary schools within Minna metropolis were involved in this study. Investigations conducted using the questionnaire, administered on randomly selected 33 English language teachers showed that teaching aids, especially the ones associated with technology do not exist in public schools. Many private schools do not have these aids either. In the face of technological advances, this paper, recommended some strategies that can help to improve the spoken English language learning environment and consequently reposition the teaching of spoken English in Minna metropolis.

Keywords: Repositioning, Spoken English, Senior Secondary Schools, Repositioning Strategies, Technological tools.

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APPLICATIONS, CHALLENGES, AND LIMITATIONS OF AI USE IN HEALTHCARE: AN ANALYSIS OF AI RESPONSES FOR DRUG INFORMATION

ABSTRACT

OBJECTIVES:

Health professionals are increasingly interested in the potential applications of artificial intelligence (AI) in routine healthcare. The primary focus of the discussions lies on accuracy, validity and reliability of the AI-generated information. This study delves into the multifaceted relationship between AI and healthcare scrutinizing the validity and reliability of AI-generated drug information.

METHODS:

The study investigates responses of ChatGPT to questions on Drug-Drug Interactions (DDIs). A comprehensive, systematic literature search on the use of AI in routine healthcare – especially concerning the use of pharmaceuticals – was performed. Exemplary fields operationalized by 40 standardized questions on DDIs where defined. Multiple responses of ChatGPT were investigated and accuracy and reliability compared to clinical guidelines as gold standard were assessed.

RESULTS:

The probability of obtaining a correct interaction was found to be 75%. For 80% of the correct AI information examples ChatGPT provided the correct information on the level of interaction and scientific evidence base, too. Conversely, the probability of encountering interactions that were both incorrect and insuffcient was 25%. All answers based on generative AI were consistent after multiple repetitions. ChatGPT showed signs of consecutive incorrect answers, similar to the phenomenon known as “hallucinations”, rising questions about the ability of providing accurate information over long periods of inquiries, and whether these imperfections are still inheritable to more sophisticated and specialized systems.

CONCLUSIONS:

AI-generated answers to potentially clinically relevant questions on DDIs are available and widely used. It is convenient, fast and practically free of additional costs but the answers of generative AI show some lack of validity although a satisfying reliability. For a relevant number of cases ChatGPT could not provide evidence-based description of the pharmaceutical mechanism. An error rate of 25% and presence of the “hallucinations” phenomenon implicates that healthcare professionals should not fully rely on ChatGPT as a source of information.

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ADVANCED STRATEGIES FOR THE REMOVAL OF PHARMACEUTICALS FROM WASTEWATER

ABSTRACT

Pharmaceutical pollutants in wastewater have suddenly become a major environmental worry as they stay, build up biologically and have ecotoxic properties. Leading to their release into natural water bodies, where they threaten human health and aquatic ecosystems, conventional wastewater treatment plants (WWTPs) are often useless in complete elimination of pharmaceutical residues. Investigation of next-generation treatment technologies for pharmaceutical removal including adsorption, advanced oxidation processes (AOPs), membrane filtration and biological degradation are necessary. Adsorption with activated carbon and new nanomaterials has demonstrated great efficiency in eliminating pharmaceuticals. Pharmaceuticals are efficiently broken down by AOPs, including photocatalysis into less damaging byproducts. Though they are energy-intensive, membrane technologies like reverse osmosis and nanofiltration have great removal rates. Furthermore, microbial biodegradation in designed systems presents a sustainable and environmentally friendly approach for pharmaceutical breakdown. The literature also draws attention to modern developments in hybrid therapies using several technologies for increased removal capacity. Comparative examination of several methods is given with respect to their cost, effectiveness, environmental impact, and suitability for widescale use. The results highlight the importance of environmentally friendly and effective methods of wastewater treatment to reduce pharmaceutical pollution and preserve water quality.

Keywords: Pharmaceutical removal, wastewater treatment, advanced oxidation processes, adsorption, membrane filtration, biodegradation.

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NUMERICAL SIMULATION FOR THE THERMAL AND SOLUTAL SYSTEM OF UNSTEADY NATURALLY CONVECTIVE FLOW OF CASSON FLUID NEAR A VERTICAL OSCILLATING SURFACE

ABSTRACT

The computational analysis of non-Newtonian fluid flow over an oscillating surface often involves numerical simulations and experimental investigations. Computational fluid dynamics method including finite difference or finite element techniques can be used to crack the governing equations of the fluid flow. In this work, we used the Crank-Nicolson numerical technique to analyze the numerical behavior of unsteady boundary layer flow of Casson fluid with natural convection past over an oscillating vertical plate. The temperature dependent viscosity is assumed for the flow analysis. The impact of chemical reaction and heat generation coefficient are used to examine the mass and heat transferal rates. The investigation of non-Newtonian fluid flow over an oscillating surface is crucial for a wide range of industrial, biomedical, and scientific applications. The governing model of equations is occurred in the form of non-dimensional PDE's and then we use the dimensionless variables in order to achieve the dimensional PDE's. These equations are numerically solved by using the Crank-Nicolson technique. The Crank-Nicolson scheme is used because it has ability to provide accurate and stable solutions and make it a valuable numerical technique in various scientific and engineering disciplines. The findings indicate that the significance of numerous parameters on the mass, velocity and energy regions. The numerical outcomes of skin friction are observed due to fluid parameter, viscosity parameter, Grashof numbers of heat and solutal rates.

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EGGSHELL MEMBRANE: PAST, PRESENT, AND FUTURE IN MEDICAL APPLICATIONS

ABSTRACT

Eggshell membrane (ESM), a natural byproduct of the poultry industry, is gaining popularity for its medicinal potential due to its high collagen, glycosaminoglycan, and bioactive protein content. In the past, ESM was thought to be worthless agricultural waste. But studies have shown that it possesses important biological qualities, like anti-inflammatory, antibacterial, and wound-healing effects.

ESM is currently being studied in great detail in the fields of drug delivery, tissue engineering, and regenerative medicine. Research showed that it is effective in accelerating the healing of wounds, reducing the symptoms of osteoarthritis, and acting as a biocompatible scaffold for tissue restoration. ESM is a desirable substitute for synthetic biomaterials due to its cost-effectiveness and natural abundance. Its purity and functional qualities have also been improved by developments in extraction and processing methods, expanding its range of biomedical uses.

The use of ESM in medical applications appears to have a bright future. Its qualities could be further improved by advances in biofabrication and nanotechnology, which would result in more effective medicinal uses. ESM-based bioinks for tissue engineering 3D printing, sophisticated drug delivery methods, and customized biomaterials for personalized treatment are examples of possible advancements. Notwithstanding its benefits, in order to reach its full potential, issues like standardization, extensive processing, and regulatory permissions must be resolved.

Finally, ESM has evolved from an underutilized waste material to a useful biomedical resource. Its significance in upcoming medical applications will be shaped by ongoing research and technical developments, providing long-term and reasonably priced healthcare solutions.

Keywords: Eggshell membrane, tissue engineering, regenerative medicine, wound healing, osteoarthritis, biomaterials, biofabrication.

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TARGETING KEY ENZYMES IN GLUCOSE METABOLISM: AN IN SILICO APPROACH USING PHYTOCHEMICALS FROM MEDICINAL PLANTS OF PAKISTAN

ABSTRACT

The rising global prevalence of diabetes mellitus has intensified the search for novel, effective, and safer therapeutic agents. A promising strategy involves targeting key enzymes involved in glucose metabolism, such as alpha-glucosidase, hexokinase, and glucose-6-phosphatase, which play critical roles in regulating blood glucose levels. In this study, we employed an in silico approach to investigate the inhibitory potential of phytochemicals derived from traditional medicinal plants of Pakistan against these enzymes. A comprehensive phytochemical library was constructed using published ethnobotanical and phytochemical data. The compounds were subjected to molecular docking analysis against the active sites of the target enzymes using AutoDock Vina. The binding affinities, interaction patterns, and drug-likeness properties of the top-ranked compounds were evaluated to identify promising lead molecules. Several phytochemicals, including berberine, quercetin, rutin, and lupeol, demonstrated significant binding affinities and stable interactions with the catalytic residues of the enzymes. ADMET (absorption, distribution, metabolism, excretion, and toxicity) profiling further supported the therapeutic potential and safety profiles of the selected candidates. These findings highlight the potential of Pakistan's medicinal plant-derived compounds as inhibitors of glucose-metabolizing enzymes and lay the groundwork for future in vitro and in vivo validation. The integration of Ethnopharmacological knowledge with computational drug discovery provides an efficient and cost-effective pathway for identifying novel antidiabetic agents from natural sources. This study contributes to the growing body of research supporting the value of traditional medicine in the development of targeted therapies for metabolic disorders.

Keywords: Glucose Metabolism, In Silico Analysis, Phytochemicals, Medicinal Plants, Diabetes Mellitus, Enzyme Inhibition

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POTENTIAL BIOMARKERS AND THERAPEUTIC TARGETS FOR TNBC

ABSTRACT

Triple negative breast cancer (TNBC) is an aggressive type of breast cancer with high reoccurrence rate. Hence, new therapeutic approach is the need of the hour to combat with the disease. Ubiquitination is a post translational modification that stabilizes and regulates cellular proteins. It is hypothesized that reticence in deubiquitinases (DUBs) may cause cell cycle arrest. Our study focuses the inhibition of USP2 (a Ubiquitin specific protease and a member of the largest class of DUBs). ML364, an inhibitor of USP2 was incubated in dose dependent manner with TNBC cells to measure cell cytotoxicity. Differentially expressed proteins were identified using 2DE and LC-MS/MS analysis. Quantitative PCR was utilized to measure gene expression and to demonstrate further analysis, UALCAN, HPA, and TIMER database were employed. F-box protein (FBXO46), Tripartite motif-containing protein 68 (TRIM68), and Inorganic pyrophosphatase (PPA1) were identified as a potential prognostic biomarker and/or therapeutic target for TNBC. FBXO46, TRIM68, and PPA1 were significantly downregulated by ML364, which causes growth inhibition of cancerous cells. The importance of USP2 and its substrates is highlighted in this study, which offers insight into USP2-mediated signaling in TNBC. Findings of the study propose that ML364 may serve as a viable treatment for TNBC.

Keywords: Triple Negative Breast Cancer, FBXO46, TRIM68, PPA1, ML364, USP2

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SYNDROMES THAT CAUSE CLEFT LIP AND CLEFT PALATE

ABSTRACT

Cleft lip and cleft palate (CL/P) are among the most common congenital craniofacial anomalies, affecting approximately 1 in 700 live births worldwide. While many cases are non-syndromic, up to 30% are associated with a variety of genetic syndromes, where CL/P presents as one of multiple systemic abnormalities. These syndromic cases often have complex etiologies involving chromosomal deletions, single-gene mutations, or inherited developmental disorders. Early identification of a syndromic cause is critical for guiding multidisciplinary management, providing prognostic information, and offering appropriate genetic counseling to families. This review explores the major syndromes associated with CL/P, including Van der Woude syndrome, Treacher Collins syndrome, Stickler syndrome, and others. Each condition is characterized by distinct genetic mechanisms and clinical features, which are essential for differential diagnosis. Advances in genetic testing, particularly next-generation sequencing, have significantly improved the detection and classification of these syndromes. Recognizing the syndromic nature of CL/P is essential for improving long-term outcomes, reducing morbidity, and delivering personalized care to affected individuals and their families.

Advances in genetic technologies, particularly next-generation sequencing and chromosomal microarray analysis, are increasingly uncovering rare and novel syndromes linked to clefting, highlighting the importance of ongoing research in this area. As our understanding of the genetic basis of syndromic CL/P continues to evolve, so too does the potential for precision medicine approaches that tailor treatment and counseling based on the specific molecular etiology.

Ultimately, improving outcomes for individuals with syndromic CL/P requires collaboration across medical genetics, pediatrics, craniofacial surgery, audiology, speech therapy, and psychosocial services. Raising awareness of the syndromic associations with CL/P among clinicians and healthcare providers is a crucial step in ensuring timely diagnosis, comprehensive care, and better quality of life for affected individuals and their families.

Keywords: Van der Woude syndrome, cleft lip, cleft palate, Stickler syndrome.

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ACALYPHA INDICA:PHYTOCHEMICAL CONSTITUENTS, TRADITIONAL USES AND PHARMACOLOGICAL PROPERTIES:A REVIEW

ABSTRACT

Drugs used in Ayurveda and other traditional systems around the world have mostly come from plants. Plants have been used to treat a variety of illnesses, according to data from the Ayurvedic, Siddha, Unani, and homeopathic systems. Both traditional and western medicine rely heavily on medicinal components derived from plants. As a member of the Euphorbiaceae family, Acalypha indica L. is a prevalent weed in tropical regions of Africa and South America as well as Asia, including Yemen, Sri Lanka, India, and Pakistan. Plants with emetic, expectorant, laxative, and diuretic properties can help with asthma, pneumonia, and bronchitis. Their leaves also have antifungal, antiparasitic, and laxative properties.The plant possesses various pharmacological activities such as anti-inflammatory, antimicrobial, anti-ulcer, analgesic, anti- arthritic, HIV-1 reverse transcriptase inhibitory, antiurolithiatic, cytotoxic, anthelmintic, anticonvulsant, antianxiety, anti-malarial, lipid lowering, anti-venom and kidney protective activity. The present review gives a detailed survey of the literature on its phytochemistry, pharmacognosy, traditional uses and pharmacological properties.

Keywords : antiparasitic , Euphorbiaceae , Antifungal , antiurolithiatic .

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THE ROLE OF ARTIFICIAL INTELLIGENCE IN MANAGING DIABETIC RETINOPATHY IN LOW- AND MIDDLE-INCOME COUNTRIES

ABSTRACT

Introduction

According to projections by the International Diabetes Federation, the global prevalence of diabetes mellitus (DM) is expected to reach 700 million by 2045. Diabetic retinopathy (DR), a microvascular complication of DM, remains a leading cause of preventable blindness in the working-age population worldwide. This burden is particularly acute in low- and middle-income countries (LMICs), where healthcare resources are often scarce. A critical limiting factor in effective DR screening and management is the global shortage of ophthalmologists; some regions have fewer than five ophthalmologists per 1,000 patients requiring eye care. Advances in artificial intelligence (AI) offer promising, scalable solutions to support DR detection and management, especially in resource-constrained settings.

Methods

We conducted a narrative review of the current evidence on the use of AI-based technologies for the detection and management of DR. Studies employing AI algorithms on digitized retinal images—including colour fundus photographs (CFP) and optical coherence tomography (OCT)—were examined for their diagnostic accuracy, clinical applicability, and deployment in LMICs. We focused on systems with autonomous or semi-autonomous capabilities for DR screening, prediction, or diagnosis.

Results

AI-enabled DR screening systems demonstrated high sensitivity and specificity in detecting referable DR and showed significant potential for task-shifting in settings with limited access to ophthalmologists. Implementation in primary care and community-based settings led to earlier diagnosis, often at a younger age, and increased screening uptake. However, deployment in LMICs faces several barriers, including inconsistent internet connectivity, unreliable power supply, and inadequate digital infrastructure. Furthermore, a lack of digital health literacy among healthcare workers limits the full integration of these technologies into clinical workflows.

Conclusion

AI-assisted DR screening represents a promising approach to addressing the growing burden of diabetes-related visual impairment in LMICs. By enabling earlier detection and reducing reliance on specialist workforce, these technologies have the potential to significantly reduce preventable blindness. Nonetheless, large-scale, prospective studies and randomized controlled trials are necessary to validate long-term effectiveness, cost-efficiency, and integration strategies. Investments in digital infrastructure and workforce training is vital to ensure sustainable and equitable implementation.

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EVALUATION OF VERTICAL DIMENSIONS IN ORTHOGNATHIC SURGERY USING 3D CEPHALOMETRY AND TFA SUPERIMPOSITION

ABSTRACT

Aim: Cephalometry is fundamental in diagnosis, analysis, and planning of orthodontic surgical treatment as it reveals skeletal relationship between the upper and lower jaw as well as facial aesthetic parameters. Nevertheless, 3D cephalometry has still not become the exam of choice in orthognathic treatment even though today CBCT (Cone Beam Computed Tomography) is routinely used in other branches of dentistry. The aim of this study is to evaluate the advantages and disadvantages of the two methods in orthognathic surgery.

Materials and Methods: In a sample of 13 patients undergoing bimaxillary orthognathic surgery a chin-vertex CBCT exam was prescribed prior to orthodontic treatment (OT)and 12 months after surgery (T1). The DICOM files uploaded to MaterialiseSimplant Ortho software pro 2.1 (Materialise Co., Leuven, Belgium) were analyzed following the multiplane 3D Total Face cephalometry protocol (TFA).

Results: Results comparing pre-op and post-op TFA 3D cephalometry, were then evaluated considering reference values reported in literature. The CBCT, carried out preand post-surgery, were subsequently analyzed employing the superimposition method using cranial base as reference.

Discussion and Conclusions: The TFA 3D cephalometry allows the assessment of various bones not only singularly but also considering the rightproportion with others.The advantages ofTFA cephalometry are mostly due to speed of execution thanks to a user-friendly interfacerequiring a learning curve that is similar to traditional 2D cephalometry methods.This 3D analysis was carried out evaluating the relationship between skeletal structures making the approach especially flexible and dynamic. The 3D visualization allowsthe determination of the extent of skeletal disharmony.

Multiplane 3D TFA allows the clinician to locatewhere major or minor skeletal discrepancies are found with respect to ideal parameters and is alsouseful in classifying skeletal intermaxillary

relation. The superimposition method is highly intuitivebut does not provide information on the quantity and location of osteotomic movement.

Keywords: total face approach; superimposition; orthognathic surgery.

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A BRIEF ANALYSIS OF THE CONTRIBUTION OF EUROPEAN PHYSICIANS TO THE DEVELOPMENT OF MEDICAL SCIENCE

ABSTRACT

Medicine is an exceptionally important field in everyday life. Every modern society has developed a network of medical services. However, these systems were not always as we know them today. In earlier times, individuals made personal efforts to care for their own health. Today, we rely on professionals who undergo formal education and training in specialized institutions to assist those in need.

Technological advancement in the medical field has been gradual and often challenging. Physicians from various European countries—such as Romania, France, and the United Kingdom—have played a vital role in the evolution of modern medicine. Their contributions have shaped the discipline as we understand it today. From the development of vaccines to the invention of advanced medical devices, each discovery has played a part in shaping the society we now live in.

Keywords: medical, medicine, history of medicine

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ATTENTION-GUIDED MULTIMODAL FUSION WITH FUZZY INFERENCE FOR EARLY DEPRESSION DETECTION

ABSTRACT

Timely identification of depression is essential for successful intervention; however, conventional unimodal methods frequently overlook the complex nature of depressive symptoms. This study introduces an innovative framework—Fuzzy Logic-Enhanced Attention-Guided Multimodal Fusion—for improving early detection of depression through the use of textual, visual, and acoustic information. Our method utilizes modality-specific encoders, such as BERT for text input, CNN-RNN combinations for facial expressions, and OpenSMILE-BiLSTM for sound signals, to gather comprehensive feature representations. A discriminative attention-driven fusion module actively highlights modality-specific and cross-modal signals that suggest depressive behaviors. To tackle the uncertainty and subjectivity present in mental health signals, we incorporate a decision layer based on fuzzy logic. This layer establishes fuzzy variables like sadness level, vocal strength, and facial expressiveness, utilizing clear membership functions and a fuzzy inference engine to calculate depression probability scores. We assess our approach using benchmark datasets like DAIC-WOZ and CMU-MOSEI, which include mental health annotations. Experimental findings indicate that our model exceeds leading baselines regarding F1-score, AUC, and interpretability, especially in the context of ambiguous emotional states. Visual representations of attention weights and the activations of fuzzy rules offer insights into how models make decisions, thereby improving trust and clarity. Our work emphasizes the collaborative potential of merging attention-driven multimodal learning with fuzzy logic reasoning in delicate areas such as mental health. This study sets a foundation for stronger, more interpretable, and ethically sound systems for detecting depression that can be used in clinical settings and remote telehealth platforms.

Keywords:MULTIMODAL SENTIMENT ANALYSIS, FUZZY LOGIC, DEPRESSION DETECTION

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FORMULATION AND EVALUATION OF ANTIOXIDANT RICH HERBAL LIQUID TONER

ABSTRACT

The present study focuses on the formulation and evaluation of an antioxidant-rich polyherbal liquid toner utilizing natural ingredients such as Green Tea, Lemongrass, and Hibiscus. The developed formulations were assessed for key parameters including pH, viscosity, homogeneity, spreadability, and dermatological safety. Among the three prepared formulations, batch F3 emerged as the optimized variant, exhibiting a skin-compatible pH (5.55), uniform texture, and optimal viscosity (20.3 cP) that ensured smooth application and non-sticky feel. These properties contributed to improved antioxidant delivery and user comfort. The stability studies indicated that the formulation maintained its integrity under standard storage conditions. Overall, the polyherbal toner demonstrates promising potential as a natural, chemical-free skincare product with notable antioxidant and skin-rejuvenating effects. Further investigations focusing on long-term stability, microbiological safety, and consumer acceptability are warranted to support its scalability and market introduction.

Keywords: Antioxidant, Polyherbal Liquid Toner, Safety, Stability.

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THE AUTHORS SHOULD SHARE CITATIONS OF A PAPER (IC), TO ELIMINATE INCONSISTENCIES IN CITATION METRICS

ABSTRACT

In 1964 Eugene Garfield established the SCI which evolved into the database Web of Science. This innovation presents indexing, disseminating the world's scientific literature, and citatometry, a part of scientometrics, that is based on the number of citations within the text of a scientific publication. Citations present measurable data on impact of a publication and enable us to quantify, analyze, and use it for various purposes. However, for citatometry, from the very beginning, the paper of Oliver Lovry was problematic; it describes a measurement of the concentration of proteins, and its citations exceed several times all citations of any Nobel Prize Winner. There are many scientists today who are included among hundreds of contributors, and each receives the same number of citations at the common paper. As a result, in 2024, there were 6.636 highly cited scientists who work in 1200 institutions in 59 countries. In a paper written by 28 authors and reviewed by 90 reviewers [1] each contributor received above 15.000 citations. On the other hand, Albert Einstein, while he was alive, until 1955, got for all his papers 1564 citations. Professor Ervin G. Erdös [2] was right when he used to say: "There are two kinds of scientists: 1) those who discover and 2) those who measure." Evidently the citatometry is in deep crisis. A partial solution to this problem was recently presented [3]: the authors should share the citations of the paper and obtain individual citations (iC). This approach should reduce the number of hyper cited scientists, and be of help to the funding agencies, academia and the public. To determine significance and impact of a paper, peer review and classical evaluation can be obtained only by reading it. Web of Science tracks over 9,000 journals and it is impossible to find enough evaluators to read over one million papers annually. Perhaps the AI could, one day, analyze data, recognize important discoveries and determine significance of a paper. That should be the end of citatometry and a new era of scientific progress. The delayed recognition of important discoveries, e.g. Rita Levi-Montalcini and Milutin Milanković, shall be significantly reduced. While we are waiting for the AI service, we should decide who might be awarded with citates from a paper – only the authors, not minor contributors. There are some other citation issues to be solved, as well.

Cover Letter

This abstract presents various shortcomings and manipulations in citatometry, a part of scientometrics. Our presentation could be included in the “Research and Publication Integrity and Ethics” at the Medical and Health Sciences, if you have such section. The content of this abstract (383 words) is original, and it was not published.

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FIRST APPLICATION OF NEXT-GENERATION SEQUENCING IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY IN MOROCCO AND REPORT OF A NOVEL FRAMESHIFT MUTATION OF *MYBPC3* GENE

ABSTRACT

Background: Hypertrophic cardiomyopathy (HCM) is a myocardial disease characterized by an unexplained left ventricular hypertrophy (LVH), usually asymmetrical and involving the interventricular septum. HCM is a relatively frequent disorder, affecting one of 500 individuals from the general population. Some patients may not have any symptoms during their whole life, whereas in other cases, HCM may lead to severe symptoms such as syncope or dyspnea, sudden death, or congestive heart failure. It remains the most prevalent cause of inexplained sudden death in athletes during exercise. HCM is a familial disease in at least 50% of cases, with mainly an autosomal dominant mode of inheritance with variable expression and incomplete penetrance. It may be also inherited in autosomal recessive pattern or X-linked manner. HCM are caused by mutations in nearly 22 different genes,>17 genes are involved in autosomal dominant HCM. The most frequently mutations fall within myosin heavy chain 7 (*MYH7*) and myosin binding protein C (*MYBPC3*), both accounting for up to 50% of HCM cases.

Case presentation: The present study reports the molecular results of a series of six unrelated Moroccan patients with HCM using for the first time in Morocco a next generation sequencing (NGS) customized multigene panel to investigate the two major HCM genes *MYH7* and *MYBPC3.* Genetic testing lead to the identification of a novel *MYBPC* mutation (c.1049delA; p.Lys350fs) and three others previously described variants at heterozygous state.

Conclusion: Molecular diagnosis by NGS customized multigenes panel allowed us to set up a fast and firstline upon request cost-efficient strategy in order to screen various genes and diseases including HCM. This approach is well suited to general medical genetics laboratories dealing with almost all types of rare genetic diseases with limited funds for a molecular testing more cost-effective.

Keywords: Hypertrophic cardiomyopathy, Moroccan patients, Next-generation sequencing, Customized panel

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CLINICAL AND RADIOLOGICAL OUTCOMES OF CORRECTIVE EXERCISES AND NEUROMUSCULAR ELECTRICAL STIMULATION IN CHILDREN WITH FLEXIBLE FLATFEET: A RANDOMIZED CONTROLLED TRIAL

ABSTRACT

***Background*:** Flexible flatfeet are common among children being scarcely symptomatic requires no specific treatment and resolves spontaneously. However, flexible flatfoot tends to advance and deteriorate overtime and eventually resulting in significant impairments such as plantar fasciitis and patellofemoral pain syndrome.

Research question: What is the effect of corrective exercises and neuromuscular electrical stimulation in children with flexible flatfeet?

***Method*:** This is a randomized controlled trial with 72 children, seven to twelve years-old, randomly assigned to either intervention or control group (36 children for each group) and engaged in a four months (3 sessions/week) of corrective exercise and neuromuscular electrical stimulation or corrective exercise and sham neuromuscular electrical stimulation respectively. Assessments of Staheli's arch index (through foot print), navicular drop (through navicular drop test) and radiographic indexes (through anterior-posterior and medio-lateral X-ray) of both feet were performed before and after the intervention programs.

***Results*:** Study groups were comparable with respect to all outcome measures at entry ($P>0.05$). Within group comparison showed significant improvements in all measured variables. Further, between groups comparison revealed significant higher improvements ($P < 0.05$) in for right and left feet Staheli's arch index, navicular drop as well as the radiographic indexes in favor of the intervention group.

Significance: Integration of corrective exercises and neuromuscular electrical stimulation is more effective than exercises alone for providing clinical and radiological improvements in children with flexible flatfeet.

Keywords: Foot exercise; Navicular drop; Neuromuscular electrical stimulation; Staheli's arch index.

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EFFECT OF ORAL SENSORIMOTOR STIMULATION ON OROPHARYNGEAL DYSPHAGIA IN CHILDREN WITH SPASTIC CEREBRAL PALSY: A RANDOMIZED CONTROLLED TRIAL

ABSTRACT

BACKGROUND: Children with cerebral palsy show various degrees of dysphagia causing late development of oral motor skills

AIM: To investigate effect of oral sensorimotor stimulation on oropharyngeal dysphagia in children with spastic quadriplegia.

DESIGN: This was a double-masked, randomized controlled clinical trial**.**

SETTING: Out-patient Clinics of Faculty of Physical Therapy, Cairo University and Modern University of Technology and information.

POPULATION: A convenient sample of 71 children age ranged from 12 to 48 months diagnosed with spastic quadriplegia, were randomly assigned into two groups.

METHODS: Children in the control group received 90 minutes conventional physical therapy training five times/week for 4 successive months while those in the experimental group received 20 minutes of oral sensorimotor stimulation before the same program as in control group for 60 minutes. Oral motor function, body weight, segmental trunk control and gross motor function were assessed at base-line and after completing treatment.

RESULTS: In total, 64 (experimental n=32, control n=32) children completed treatment and data collection. The baseline assessment showed non-significant difference regarding all measured variables while with-in group comparison showed significant improvement in the two groups. The post-treatment comparisons revealed significant difference the oral motor function and physical growth in favor of the experimental group ($p < 0.05$). Finally, there was non-significant difference regarding segmental trunk control and gross motor function ($p > 0.05$)

CONCLUSION: Oral sensorimotor stimulation has the capability to improve feeding in children with spastic cerebral palsy diagnosed with oropharyngeal dysphagia.

CLINICAL REHABILITAYION IMPACT: OSMS has effect on some of the essential oral motor skills that contribute toward the improvement of feeding performance in children with spastic CP. The results of our study offer remarkable clinical importance for the children and their families.

Keywords: Cerebral palsy, Oropharyngeal dysphagia, Segmental trunk control, Sequenced trunk co-activation exercises, Spastic quadriplegia.

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EFFICACY OF PLYOMETRIC EXERCISES ON UPPER EXTREMITY FUNCTION, SELECTIVE MOTOR CONTROL AND HAND GRIP STRENGTH IN CHILDREN WITH UNILATERAL CEREBRAL PALSY: A RANDOMIZED CONTROLLED STUDY

ABSTRACT

BACKGROUND: Impairment in unimanual upper limb function is frequent among children with unilateral cerebral palsy (UCP), which affect their ability to perform functional activities.

AIM: To assess the efficacy of plyometric exercises on function of upper extremity, selective motor control (SMC) and hand grip strength (HGS) in children with UCP.

DESIGN: It was a double-masked, randomized controlled clinical trial.

SETTING: Outpatient Clinics of Faculty of Physical Therapy, Cairo University and Center for Physical Medicine, Rehabilitation and Rheumatology, Al-Agouza Hospital, Giza, Egypt

POPULATION: Forty children with UCP, age ranged from 8-12 years, were randomly allocated to two groups equal in numbers.

METHOD: Children were allocated to receive conventional therapy (CONV-group; n=20) or plyometric exercises (PLYO-group; n=20) for 45 minutes. In addition, children of both groups received a selected physical and occupational therapy programs (each lasted for 30 minutes) twice a week over 3-months. The intervention was delivered on non-consecutive days. Upper extremity function, SMC and HGS were assessed by using quality of upper extremity skills test (QUEST), Test of arm selective control (TASC) and Pneumatic Squeeze Bulb Dynamometer respectively.

RESULTS: Overall, 35 children (18 in the CONV-group, 17 in the PLYO-group) completed data collection and treatment. With-in group comparison showed significant improvement in the study groups while post-treatment comparisons revealed significant difference with mean difference of upper extremity function is 9.55 (8.71:10.39), SMC is 2.12 (1.51:2.72) and HGS is 2.91 (2.13:3.68) ($P<0.05$; 95% CI) in favor of the PLYO-group.

CONCLUSIONS: Plyometric exercises have the capability to enhance upper extremity function and strength in children with UCP.

Keywords: Grip strength; Plyometric exercises; Selective motor control; Unilateral cerebral palsy; Upper extremity function.

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EVIDENCE-BASED PRACTICES RELATED TO BREAST MILK AND BREASTFEEDING

ABSTRACT

Breast milk is an ideal source of nutrition for infant health and development. WHO and UNICEF recommend exclusive breastfeeding for the first six months and emphasise that breastfeeding should continue until the age of two. Increasing breastfeeding rates supports public health by reducing the burden on health services. Breastfed infants are less likely to become ill, enabling the health system to use its resources more efficiently. WHO states that the lives of approximately 823,000 babies could be saved each year and significant savings in health costs could be achieved by promoting breastfeeding alone. Breastfeeding not only supports the physical development of infants, but also strengthens the immune system and provides protection against infections. However, mothers may face many difficulties during breastfeeding. Nipple cracks, insufficient milk production, lack of information on breastfeeding techniques and lack of psychological support are among the main factors that threaten the continuity of breastfeeding. In order to prevent and solve such problems, evidence-based nursing practices play an important role in promoting breastfeeding by providing comprehensive guidance and support to mothers. Evidence-based practices are indispensable for increasing the benefits of breast milk and breastfeeding and ensuring its sustainability. Adoption of these practices in health services will lead to positive results at both individual and social levels. Supporting this process by healthcare professionals is one of the most effective steps to strengthen maternal and infant health. In this review, it is aimed to review the current literature on evidence-based practices for breast milk and breastfeeding.

Keywords: Breast Milk, Breastfeeding, Evidence

ANNE SÜTÜ VE EMZİRME İLE İLGİLİ KANIT TEMELLİ UYGULAMALAR

ÖZET

Anne sütü, bebek sağlığı ve gelişimi için ideal bir besin kaynağıdır. WHO ve UNICEF ilk altı ay yalnızca anne sütü ile beslenmeyi önerirken, emzirmenin iki yaşına kadar devam ettirilmesi gerektiğini vurgulamaktadır. Emzirme oranlarının artırılması, sağlık hizmetleri üzerindeki yükü azaltarak toplum sağlığını destekler. Anne sütüyle beslenen bebeklerin daha az hastalanması, sağlık sisteminin kaynaklarını daha verimli kullanmasını sağlar. DSÖ, yalnızca emzirmenin yaygınlaştırılmasıyla her yıl yaklaşık 823.000 bebeğin hayatının kurtarılabileceğini ve sağlık maliyetlerinde ciddi tasarruf sağlanabileceğini belirtmektedir. Emzirme, sadece bebeklerin fiziksel gelişimini desteklemekle kalmaz, aynı zamanda bağışıklık sistemini güçlendirir ve enfeksiyonlara karşı koruma sağlar. Bununla birlikte, emzirme sürecinde anneler birçok zorlukla karşılaşabilmektedir. Meme başı çatlakları, yetersiz süt üretimi, emzirme tekniklerine ilişkin bilgi eksikliği ve psikolojik destek yetersizliği, emzirmenin sürekliliğini tehdit eden başlıca faktörler arasında yer alır. Bu tür sorunların önlenmesi ve çözülmesi için kanıt temelli hemşirelik uygulamaları, annelere kapsamlı rehberlik ve destek sağlayarak emzirmenin teşvik edilmesinde önemli bir rol oynar. Kanıt temelli uygulamalar, anne sütü ve emzirmenin faydalarını artırmak ve sürdürülebilirliğini sağlamak açısından vazgeçilmezdir. Bu uygulamaların sağlık hizmetlerinde benimsenmesi hem bireysel hem de toplumsal düzeyde olumlu sonuçlar doğuracaktır. Sağlık çalışanlarının bu süreci desteklemesi, anne ve bebek sağlığını güçlendiren en etkili adımlardan biridir Bu derlemede, anne sütü ve emzirmeye yönelik kanıt temelli uygulamalara ilişkin güncel literatürün derlemesi amaçlanmıştır.

Anahtar Kelimeler: Anne Sütü, Emzirme, Kanıt

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EXPLORING THE IMPACT OF CURCUMIN ADMINISTRATION FORMS ON BLOOD GLUCOSE LEVELS AND THEIR RELATIONSHIP WITH ENERGY-REGULATING HORMONES

ABSTRACT

Background: Curcumin is a widely used herbal supplement in traditional medicine for preventing and managing diabetes. However, its potential as an effective antidiabetic agent is limited by challenges such as low solubility, poor absorption, and overall low efficacy, all contributing to reduced bioavailability. Recent studies have focused on developing

nanotechnology-based pharmaceutical formulations to overcome these barriers and enhance curcumin's bioavailability, thereby improving its therapeutic effects against diabetes.

Purpose: We aimed to assess the effects of curcumin, nano-curcumin, and encapsulated nano-curcumin on blood glucose levels and insulin resistance in streptozotocin-induced diabetic rats. Furthermore, we compared the relationships between these different curcumin administration forms and key metabolic-regulating hormones, including leptin, ghrelin, nesfatin-1, and irisin, which have a critical role in metabolic regulation, and their interactions were evaluated under impaired glucose metabolism and control conditions.

Material and methods: A total of 56 male rats were divided into 8 groups (n=7) including control, control curcumin, control nano-curcumin, control encapsulated nano-curcumin, diabetic, diabetic curcumin, diabetic nano-curcumin, and diabetic encapsulated nano-curcumin.

Results: Administration of curcumin in the encapsulated nano form significantly improved blood glucose levels and insulin resistance ($p<0.001$). Moreover, the different curcumin administration forms had a notable impact on leptin, nesfatin-1, irisin, and ghrelin levels in both diabetic and control groups ($p<0.001$).

Conclusion: Although the promising effects of curcumin administration on improving diabetes-induced metabolic dysfunction are evident, we strongly recommend that further clinical studies investigating the use of encapsulated nano-curcumin in humans are essential to draw definitive conclusions regarding its therapeutic potential in addressing these diverse metabolic and stress-related disorders.

Keywords: Diabetes mellitus, Curcumin, Nano-curcumin, Encapsulated nano-curcumin, Leptin, Ghrelin, Nesfatin-1, Irisin, Insulin, Blood Glucose Levels

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DIGITAL HEALTH LITERACY AND THE DIGITAL TRANSFORMATION OF HEALTHCARE INSTITUTIONS: A CONCEPTUAL REVIEW

ABSTRACT

Aim: The digitalization of healthcare institutions has significantly transformed especially over the last decade. It determines how the individuals access care and healthcare institutions operate. This process is not only limited to the use of technology alone but also requires individuals to comprehend and utilize digital health systems. Digital health literacy (DHL) has gained increasing importance during the digitalization process of healthcare institutions. As digital health platforms become more prevalent, individuals' DHL levels impact not only their health outcomes but also the performance of healthcare systems. This study aims to discuss DHL not only as an individual-based concept but also as a potential factor that may affect the management processes of healthcare institutions.

Material and Method: This research is based on a conceptual analysis of existing literature, discussing DHL as a factor that influences both personal health behaviour and the operational processes of healthcare institutions.

Results: The conceptual evaluation reveals that individuals' levels of DHL can be a determinant in the effective use of digital health systems. In management processes such as appointment management, information flow, and feedback mechanisms, insufficient digital competencies among users may indirectly limit system performance. In this context, DHL emerges as a variable that can affect both administrative efficiency and patient satisfaction. The relationship between administrative transformation and DHL is bidirectional: individuals' competencies influence institutional functioning, while system design by institutions shapes individuals' usage skills.

Conclusion: This study highlights that DHL is a determinant not only for individual health behaviours but also for the administrative efficiency of healthcare institutions. Considering users' DHL levels in healthcare management strategies is crucial for process efficiency and system integrity. Moreover, for effective adaptation to digital transformation, priority should be given to patient education, the implementation of DHL awareness-raising initiatives, and the design of user-friendly digital systems.

Keywords: Digital health literacy, healthcare management, healthcare institutions, digital transformation

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TURKISH LANGUAGE DEVELOPMENT IN A FRENCH-TURKISH BILINGUAL CHILD WITH FRAGILE X SYNDROME: INTERVENTION-BASED CASE REPORT

ABSTRACT

OBJECTIVE: This case study aims to evaluate the effectiveness of an intensive language intervention program in supporting second language(L2) development in a 7.5-year-old bilingual male child diagnosed with Fragile X Syndrome (FXS).

MATERIALS AND METHODS: The medical history of the case living in France includes FXS and borderline intellectual disability.He was evaluated by a speech-language therapist through formal and informal language assessment in L2 in Turkey. His Turkish expressive vocabulary was limited to 85 words. A formal language assessment was performed with the Turkish version of the Test of Early Language Development(TELD-3-TR). In the TELD-3-TR findings, the receptive and expressive language standard score was<50 (1% percentile). For informal language assessment, natural language sample analysis was performed and lexical repertoire was questioned based on parent reports. Expressive vocabulary was limited to 85 words. In reciprocal interactions, communication was predominantly at the single-word level, with only occasional use of two-word combinations. Difficulties were observed in maintaining reciprocal communication, particularly in semantic and morphosyntactic domains. Considering the child's overall language profile a 10-week intensive therapy program was implemented. The intervention targeted lexical performance, the development of early syntactic structures (e.g., noun+verb), basic sentence forms (subject+object+verb), and reciprocal communication. Additionally, parent guidance was included in the intervention.

RESULTS: Formal and informal assessment findings pre-therapy and post-therapy were compared. TELD-3-TR scores increased to 55 (receptive) and 58 (expressive). His Turkish vocabulary grew to 150 words, with improved verb use. Improvements were observed in morphosyntactic use, responding to "wh-" questions in SOV form, and initiating and sustaining dialogues.

CONCLUSION: This case demonstrates that a short-term, intensive, and targeted language intervention can significantly enhance second language skills in bilingual children with FXS. Observable gains in vocabulary, syntax, and functional communication highlight the child's capacity for progress when supported with structured and individualized therapy.

Keywords: Fragile X Syndrome, Language Intervention, Bilingualism

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EVALUATION OF ANTIPROLIFERATIVE AND APOPTOTIC EFFECTS OF ALOE VERA IN GLIOBLASTOMA MULTIFORME

ABSTRACT

Objective: Glioblastoma multiforme (GBM) is one of the most difficult brain tumors to treat and is often resistant to chemotherapy and radiotherapy. Although our understanding of the clinical course and molecular biology of the disease has advanced over the past few decades, the survival rate of GBM patients is still poor. Chemotherapy resistance and radioresistance in GBM are mostly related to the evasion of apoptosis and rapid proliferation mechanisms by tumor cells. In addition, the blood-brain barrier prevents chemotherapy agents from reaching neoplastic cells, limiting drug efficacy. Since tumor development and progression are physiologically complex processes, monotherapy may not always be the most appropriate treatment strategy. Moreover, anticancer drugs often cause serious side effects. Therefore, natural products should be investigated to improve drug efficacy and overcome tumor resistance. In this context, our study aimed to investigate the antiproliferative activity of Aloe vera extract (AVE) in GBM and to evaluate its potential anticancer effects on apoptotic and migration processes.

Material and Methods: The ethanolic extract of AVE was applied to U87-MG and LN229 human glioblastoma cell lines at concentrations of 35 µg/mL, 70 µg/mL, and 100 µg/mL in triplicate. Antiproliferative activity was analyzed over 24 hours using the xCELLigence Real-Time Cell Analyzer. AVE was applied at IC_{50} values to U87-MG and LN229 cell lines to assess apoptotic processes via Annexin V-FITC/PI apoptosis kit (flow cytometry) and migratory effects via wound healing assay.

Results: The study demonstrated that AVE exhibited antiproliferative activity in both cell lines, with IC_{50} values of 91 µg/mL for U87-MG and 83 µg/mL for LN229. Flow cytometry results revealed that after 24 hours of AVE treatment, the apoptosis rate was 23% in U87-MG and 28.66% in LN229 cells ($p<0.05$). Although AVE exhibited no antimigratory effects in U87-MG cells, it significantly suppressed migration in LN229 cells.

Conclusion: Given the demonstrated antiproliferative and pro-apoptotic effects of AVE in GBM, further investigation is warranted to evaluate its potential as a promising therapeutic candidate

Keywords: xCELLigence, Flow cytometry, Apoptosis, Migration, Aloe vera, Glioblastoma

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SINGLE-CLICK MOLECULAR DOCKING-BASED VIRTUAL SCREENING VIA SWIFTDOCK

ABSTRACT

Molecular docking-based virtual screening (MDVS) is a computational method used to systematically dock libraries of small molecules against a target macromolecule in order to identify potential compounds with the desired biological activity. Several VS tools, such as PyRx, InstaDock, and the MultiDock Screening Tool, have been developed to perform this task, typically utilizing docking software including AutoDock4 (AD4) and AutoDock Vina (ADV). Although a number of automation scripts and software solutions are available to facilitate VS using AD4, none provide a fully integrated, single-click workflow that covers file preparation, docking execution, and extraction of the optimal pose along with its corresponding binding energy. To address this gap, we present SwiftDock (https://github.com/notacoder-dz/SwiftDock), an open-source VS tool designed for Windows users. SwiftDock performs a fully automated, single-click MDVS using AD4, streamlining the entire process. By automatically handling all pre-docking, docking, and post-docking steps within a designated working directory containing protein and ligand files, SwiftDock removes the need for prior expertise or familiarity with the underlying software tools, including MGLTools, OpenBabel, and AutoDock4. Despite its technical limitations, SwiftDock aims to ease access to MD and VS, making these computational techniques more attainable for non-bioinformaticians. Ultimately, SwiftDock is designed to facilitate experimental and therapeutic research, offering a simple, efficient solution.

Keywords: Molecular docking, AutoDock4, Virtual screening, Single-click execution, Automation, SwiftDock.

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FACTORS CONTRIBUTING TO MEDICATION ERRORS DURING ADMINISTRATION BY NURSING STAFF

ABSTRACT

Introduction: The nursing profession has managed to establish itself over the years as an independent and original scientific discipline. "The nurse, midwife is responsible for nursing care within the healthcare professional team." The professional responsibility of the nurse regarding the application of pharmacological therapy cannot be judged solely by considering a specific act, but it is viewed in the entire complexity of actions, which together allow the management of such therapy to ensure the safety and efficacy for the patient. Medication errors during administration occur during the nurse's actions but also result from the influence of organizational work factors.

The aim of the study :To assess the adherence to the rules that help prevent errors in the administration of medications by the nursing staff at the Regional Hospital with the goal of identifying the contributing factors to the occurrence of medication administration errors.

Methodology: This is a descriptive cross-sectional study conducted at the Regional Hospital. The study included 70 nurses. The participants in this study were selected randomly. Data collection was carried out using a self-administered questionnaire, completed by the nurses.

Results: The largest source of errors by nursing staff is the failure to review the therapy sheet in advance (60%), followed by illegible handwriting in the medical chart (57.1%). A significant issue is the administration of medication by a nurse who did not prepare it previously (54.3%), which is the same percentage as errors due to incorrect medical orders. Confusion during the receipt of verbal orders is another error reported by participants (44.3%). 38.6% cited non-compliance with technique protocols as a cause of errors. 37.1% mentioned the presence of medications with similar names as a source of errors, as well as miscalculation of medication doses. Distractions and insufficient knowledge of the nurse follow closely, each at 34.3%. 28.6% reported that receiving verbal orders from doctors is a source of error. 25.7% pointed to the similar external appearance of medications. 31.4% of nurses reported administering medication to the wrong patient. 41.4% indicated they never make this error, 8.6% do so frequently, and 18.6% rarely.

Conclusion: The main source of errors during medication administration is the lack of careful review of the therapy sheet before administration, as well as the administration of medication prepared by another nurse. Nurses fear the opinions of the leading doctor and colleagues if they were to report a medication administration error.

Keywords: Factors, errors, medication administration.

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SOFT TISSUE IMAGING WITHOUT RADIATION: AN ALTERNATIVE TO CBCT VOLUMETRIC RENDERING

ABSTRACT

Aim: The aim of the present study is to evaluate whether a "radiation free" method using 3D facial scan can replace Cone Beam Computed Tomography (CBCT) volumetric rendering of soft tissue of the patient to assess maxillofacial surgery outcomes and compare the reference points and angular

measurements of patient facial soft tissue.

Methods: Facial soft tissue scan of the patient's face, before and after orthognathic surgery and a CBCT of the skull for volumetric rendering of soft tissues were carried out. The 3D acquisitions were processed using Planmeca ProMax 3D (ProFace® software Planmeca USA, Inc.; Roselle, Illinois, USA). The positioned in a natural position during the skull participant were scannering. Three sagittal angular measurements were performed (Tr-NA, Tr-N-Pg, Ss-N-Pg) and two verticals (Go-N-Me, Tr-Or-Pg) on facial soft tissue scan and on the patient's 3D soft tissue CBCT volumetric rendering.

Results: A certain correspondence has been demonstrated between the measurements obtained on the Proface and those on the CBCT.

Conclusion: A radiation free method was to be considered an important diagnostic tool that works in conditions of not subjecting the patient to harmful ionizing radiation and it was therefore particularly suitable for growing subjects. The soft tissue analysis based on the realistic facial scan has shown sufficient reliability and reproducibility even if further studies are needed to confirm the research result.

Keywords: CBCT; Ionizing radiation; Soft tissue; Orthodontics; Diagnosis.

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SYNTHESIS, CRYSTAL STRUCTURE, AND COMPUTATIONAL TECHNIQUES (DFT, HSA, ELF) STUDIES OF MELAMINIUM DIHYDROGEN PYROPHOSPHATE $(C_3N_6H_7)_2$ $(H_2P_2O_7)$

ABSTRACT

The compound namely " Melaminium Dihydrogen-Pyrophosphate (bis(2,4,6-triamino-1,3,5-triazinium dihydrogen-pyrophosphate, MDP, $(C_3N_6H_7)_2$ $(H_2P_2O_7)$, was determined by X-ray powder diffraction and infrared spectroscopy techniques. The material crystallizes in the monoclinic system, space group P1 (Z = 2), with unit cell dimensions: a =10.89321(2) Å, b = 11.2079(1) Å, c = 6.8424(1) Å, α = 104.9691(6), β = 101.4734(8), γ = 83.8050(3), and volume V = 789.501 (16) $Å^3$. The crystal (MDP) structure reveals hydrogen bonds between the phosphoric hydrogen $(H_2P_2O_7)^{2-}$ and the organic compound $(C_3N_6H_7)_2^{2+}$. The arrangement includes symmetric $(H_2P_2O_7)^{2-}$ dimer tetrahedral connected via hydrogen bonding O27 -H••••O24. Quantum chemical simulations were performed using the DFT / B3LYP/lanl2dz/scrf=(solvent=water) /pop= (nbo, savenbos) basis set to determine the energies and structural descriptors of MDP. The bond lengths & angles for MDP, as determined using the DFT method, were thoroughly compared with experimental data obtained from X-ray crystallography, reveals an excellent agreement between the computational results and the experimental data. Specifically, the (SD = standard deviation) for bond lengths is only σ =0.086%, and for bond angles, it is σ =0.0862%. These minimal deviations indicate that the DFT is highly accurate in predicting the molecular geometry of MDP, closely mirroring the structure observed in experimental X-ray data. A hydrogen atom from the anionic phosphate group $(H_2P_2O_7)^{2-}$ was transferred to the organic cation$(C_3N_6H_7)_2^{2+}$, forming a singly protonated melaminium cation. The resulting structure is stabilized by weak O-H----O(P) & N-H----O(P) hydrogen bonds, which create a 3D network and exhibit notable vibrational effects. Furthermore, 3D-MEPs, Fukui function (nucleophilic and electrophilic reactivity), and HAS analyses provided insights into local and global reactivity and intermolecular interactions within $(C_3N_6H_7)^{2+}$ **.....**$(H_2P_2O_7)^{2-}$

Keywords: Crystal structure; electronic structure, Hirschfeld, Infrared, X-ray; Computational (ELF, HSA, DFT),

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STAKEHOLDERS' PERCEPTIONS AND FEASIBILITY OF COLLABORATIVE PSYCHOLOGICAL APPROACH IN THE TREATMENT OF DENTAL PHOBIA: A SURVEY ON THE INDIAN POPULATION

ABSTRACT

Introduction and Objective: Dental phobia contributes to significant oral health disparities due to care avoidance and is often inadequately addressed by conventional interventions. While previous research has explored the prevalence and treatment of dental anxiety, stakeholder perspectives-including those of patients, dentists, and mental health professionals-remain under-investigated. This study evaluated the feasibility and therapeutic potential of a hybrid teledentistry-telepsychiatry model for managing dental phobia in India, aiming to promote a comprehensive, technology-driven, and patient-centred approach. **Methods:** A structured questionnaire was administered to assess stakeholder perceptions of hybrid care models. The study collected both quantitative and qualitative data through Likert scales and open-ended responses. **Results:** Significant gaps in awareness were identified, with 95% of surveyed urban patients unaware of teledentistry-telepsychiatry integration ($p = 0.01$). Perceptions varied significantly by educational level ($p = 0.002$), and the 31-40 age group showed a strong preference for telehealth solutions ($p = 0.02$). Urban dentists acknowledged the benefits of interdisciplinary collaboration but expressed concerns over consent, cost, and time demands. Mental health professionals strongly supported the model, emphasizing its potential to improve access and outcomes. **Conclusion:** Hybrid models integrating teledentistry and telepsychiatry show promise for managing dental phobia; however, critical barriers-particularly lack of awareness-hinder adoption. Addressing these through education, public outreach, and policy reform is essential. Future research should focus on refining and scaling such models to ensure broader accessibility, higher engagement, and improved long-term outcomes.

Keywords: Dental Phobia, Telehealth, Teledentistry, Telepsychiatry, Interdisciplinary Collaboration, India

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KNOWLEDGE, USE AND PERCEPTION OF ARTIFICIAL INTELLIGENCE BY PHARMACY STUDENTS OF TLEMCEN, ALGERIA

ABSTRACT

Introduction: The emergence of Artificial Intelligence (AI) has had a significant impact on digital professions but it is still in its infancy in pharmacy. The objective of this work is to assess the rate and areas of use of AI as well as its perception by pharmacy students at the Faculty of Medicine of Tlemcen.

Materials and methods: This is a cross-sectional descriptive study using an electronic questionnaire shared online first with the delegates of each promotion, who then shared it with the students they represent. It includes questions about the informant and about knowledge, use and perception of AI. The data collected were statistically analyzed using SPSS software.

Results: 95% of the faculty's students are already familiar with AI, the most used of which is Chat-GPT with a percentage of 50.7% followed by Google Bard with 11% use. The study also showed that 6th year pharmacy students are those who use AI the most. Among the students surveyed, 80.9% want to integrate AI into their field, 84% of whom think it will make their job easier and save time.

Conclusion: Pharmacy students in Tlemcen have some knowledge of the principles of AI and the majority show a positive attitude towards the use of this technology.

Keywords : Artificial Intelligence, pharmacy, survey.

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Lawsonia inermis THERAPEUTIC POTENTIAL: A THOROUGH REVIEW

ABSTRACT

The *lawsonia inermis* often called henna, belongs to the *Lythraceae* family and has been shown to have a number of chemicals in its stem, bark, roots, flowers, and seeds that have both industrial and therapeutic uses. The pharmacological actions and adverse effects of *Lawsonia inermis* are thoroughly reviewed in this research. Many bioactive substances, including as flavonoids, coumarins, triterpenoids, steroids, xanthones, polyphenols, alkaloids, quinones, tannins, and catechins, are found in *Lawsonia inermis*. Numerous ailments, such as ulcers, ocular diseases, hair loss, and jaundice, have been traditionally treated using the herb. Additionally, a variety of pharmacological properties have been discovered, such as anti-inflammatory, analgesic, antiparasitic, hepatoprotective, antifungal, anticancer, wound healing, and hypoglycemic effects.

Keywords: pharmacokinetics, bioactive components, pharmacological activities, *Lawsonia inermis*, and therapeutic advantages.

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WOUND HEALING ACTIVITY IN POLY HERBAL

ABSTRACT

Ayurveda, commonly referred to as the “Goddess of All Healing” in Indian culture, is regarded as one of the most potent traditional medical systems with several therapeutic and restorative qualities. Numerous plant extracts and their phytoconstituents are regarded as a possible substitute for wound healing treatments because of their wide range of active ingredients, accessibility, and low risk of adverse effects. Excision and burn wound models were used to assess the wound-healing capabilities of a polyherbal formulation that contained extracts of Psidium guajava and Ficus religiosa. In both of the examined wound models, the formulation showed a considerable response. In terms of epithelialisation time and wound contracting ability, the outcomes were similar. Therefore, this investigation validates the application of a formulation that contains Psidium guajava and Ficus religiosa extract as a wound-healing agent.

Keywords: wound healing, Poly herbal plant, Ayurvedic medicine, Burn Healing.

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LONGITUDINAL QUALITATIVE STUDY ON THE CARE NEEDS JOURNEY MAP OF PRIMARY CAREGIVERS OF PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY (TKA)

ABSTRACT

Background: Total knee arthroplasty (TKA) is a common and effective treatment for advanced knee osteoarthritis, yet it imposes significant demands on primary caregivers throughout the perioperative and rehabilitation phases. Understanding caregivers' evolving needs is critical for optimizing patient outcomes and sustaining caregiver well-being.This study aimed to explore the dynamic care experiences and changing needs of primary caregivers of TKA patients across three distinct phases: the diagnosis period, discharge transition, and rehabilitation phase, and to construct a comprehensive journey map of caregiving needs.

Methods: A longitudinal qualitative study was conducted using purposive sampling. Sixteen primary caregivers of patients undergoing unilateral TKA were recruited from a tertiary hospital in Henan, China. Semi-structured interviews were conducted at three time points: preoperative (T1), pre-discharge (T2), and one month post-discharge (T3), resulting in 43 interviews. Data were analyzed using content analysis and synchronized temporal mapping to identify themes and subthemes along the caregiving timeline.

Results: Four major themes and 27 subthemes were identified: care tasks, emotional experiences, caregiving barriers, and support systems. Caregivers' responsibilities evolved from pre-surgical information gathering to intensive post-surgical care and long-term rehabilitation support. Emotional burdens shifted from anxiety and helplessness to fatigue and psychological strain. Major barriers included knowledge deficits, skill limitations, and inadequate systemic support. The caregiver support network transitioned from hospital-based to community and family-based systems over time. A visual journey map was developed to represent these findings.

Conclusion: Primary caregivers of TKA patients face complex and changing needs across different stages of care. A caregiver-centered, multidisciplinary, and phase-specific support framework is essential to improve the quality of postoperative care and reduce caregiver burden.

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IMPACT OF PSYCHOLOGICAL RESILIENCE INTERVENTION ON NEGATIVE EMOTIONS AND NURSING COMPLIANCE IN CAUTI PATIENTS: AN EVIDENCE-BASED PRACTICE STUDY USING THE DELPHI METHOD

ABSTRACT

This study addresses the widespread psychological adaptation disorders among patients with catheter-associated urinary tract infections (CAUTI) by constructing a psychological intervention program through mixed methods. In the qualitative phase, in-depth interviews with 24 catheterized patients identified three major psychological pain points: "loss of dignity" (42%), "shame-related avoidance behaviors" (33%), and "unmet informational needs" (25%). Based on these findings, an intervention program was designed, incorporating dignity-preserving strategies (e.g., privacy protection checklists) and cognitive behavioral training (CBT modules). A standardized psychological nursing pathway was developed through two rounds of the Delphi method involving 15 experts (CVI = 0.89). In the quantitative phase, a randomized controlled trial was conducted with 100 patients. The Hospital Anxiety and Depression Scale (HADS) assessment revealed that anxiety scores in the intervention group decreased from 8.7 ± 2.1 to 4.2 ± 1.3 ($P < 0.001$), while nursing compliance improved to 89.6% (compared to 67.2% in the control group). The research outcomes have led to the development of the Psychosocial Support Toolkit for CAUTI Patients (including dignity assessment scales and communication guidelines). This study demonstrates that evidence-based psychological interventions centered on patient dignity can effectively transcend the limitations of traditional technology-driven care, offering methodological innovation for the clinical translation of the biopsychosocial medical model.

Keywords: Catheter-associated urinary tract infection; Psychological intervention; Delphi method; Patient dignity; Nursing compliance

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MEDICINE IN DACIA

ABSTRACT

The crisis of allopathic medicine brought a reconsideration of traditional medicine, as patients went in search of new approaches to healing, and doctors to practices in dealing holistically with the human body. In the last few decades, like a mechanic in his workshop, the allopathic doctor has been treating the body, and not the patient, thus the unavoidable happened, unsatisfied with the treatments, patients started searching for alternative ways to heal their bodies. As a consequence, doctors, patients and researchers have become interested in ancient medical practices, linked to the ethnogenesis of one's people, as they would provide a holistic view of healing one in which history, culture and medicine are intertwining. In this context, based on analysis of social documents, we will present an overview of healing, actors and medical practices in the Dacia.

Keywords: History of medicine, Dacia, natural medicine

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SOCIAL RECONSTRUCTION OF A BIOLOGICAL FACT

ABSTRACT

For centuries our sleep has been viewed simply as a biological fact that needs to be satisfied for our body to function properly. With time, as we become aware of how the environment affects our sleep, and how our sleep quality affects our life quality, we stating paying close attention to sleep and asking ourselves if it is socially constructed. The definite scientifically "yes" came only in the 20 century, as sociologists laid the foundation of what today we now as the sociology of sleep. Based on social histories of living practices, we will present ways in which throughout centuries, our biological sleep has been modeled socially and culturally as humans developed new forms of living together – from small nomad groups to the agrarian communities, and from the firs civilizations to today's postmodern societies.

Keywords: sleep, social reality, scooping review

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ROLE OF DIFFERENT SURFACTANTS (TX-100 and Tween-80) IN ENHANCING THE SOLUBILITY OF ANTIBIOTIC DRUGS(levofloxacin) FOR BETTER DRUG DELIVERY SYSTEM

ABSTRACT

This study investigates the role of two commonly used surfactants, Triton X-100 (TX-100) and Tween-80, in enhancing the solubility of the antibiotic drug levofloxacin, a broad-spectrum fluoroquinolone. Levofloxacin's poor water solubility limits its bioavailability and therapeutic efficacy, presenting a challenge for effective drug delivery. Surfactants like TX-100, a nonionic surfactant with an aromatic ether group, and Tween-80, a nonionic surfactant composed of a polyoxyethylene sorbitan ester, are known for their ability to improve drug solubility by reducing surface tension and forming micelles. In this study, the solubility of levofloxacin was analyzed in aqueous solutions of varying concentrations of TX-100 and Tween-80. The results demonstrated a significant increase in levofloxacin solubility with the addition of both surfactants, with Tween-80 showing a more pronounced effect at lower concentrations. The enhancement in solubility is attributed to the formation of micelles by the surfactants, which encapsulate the hydrophobic drug molecules, thereby increasing their aqueous solubility. This research highlights the potential of TX-100 and Tween-80 as solubilizing agents in pharmaceutical formulations, offering a promising approach to improving the bioavailability of levofloxacin. The findings suggest that surfactant-based strategies could be effectively employed to enhance the therapeutic efficacy of poorly soluble drugs.

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PHYTOPHARMACEUTICALS IN CHRONIC DISEASE MANAGEMENT

ABSTRACT

Chronic diseases such as diabetes, cardiovascular disorders, arthritis, and neurodegenerative conditions are among the leading causes of mortality and morbidity worldwide. Conventional therapies, while often effective, are frequently associated with side effects, high costs, and limitations in long-term management. In recent years, phytopharmaceuticals—plant-derived standardized drugs with proven pharmacological effects—have emerged as promising alternatives or adjuncts in chronic disease therapy. This paper explores the therapeutic potential of phytopharmaceuticals in chronic disease management, focusing on their anti-inflammatory, antioxidant, immunomodulatory, and metabolic regulatory properties. Compounds such as curcumin (from *Curcuma longa*), resveratrol (from grapes), berberine (from *Berberis* species), and andrographolide (from *Andrographis paniculata*) have shown significant efficacy in preclinical and clinical studies. These bioactives act through diverse mechanisms, including modulation of signaling pathways (e.g., NF-κB, AMPK), inhibition of pro-inflammatory cytokines, and improvement of insulin sensitivity and lipid profiles. Despite the promising data, challenges persist regarding standardization, bioavailability, clinical validation, and regulatory frameworks. This abstract highlights the importance of integrating traditional knowledge with modern pharmacological research to develop phytopharmaceuticals that meet global standards of safety and efficacy. As chronic diseases demand sustainable and holistic management approaches, phytopharmaceuticals offer a valuable, evidence-based bridge between traditional herbal remedies and contemporary medicine.

Keywords: Phytopharmaceuticals, chronic diseases, plant-based medicine, curcumin, berberine, inflammation, metabolic disorders, herbal therapeutics, integrative medicine, natural compounds

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PHYTOCHEMICAL PROFILING VIA FTIR AND EVALUATION OF ANTIHEMOLYTIC PROPERTIES OF *Adenocarpus decorticans* Boiss. EXTRACTS

ABSTRACT

This study presents the first comprehensive analysis of *Adenocarpus decorticans* Boiss., an endemic medicinal shrub with significant ethnopharmacological importance in Morocco's Rif Mountains and Spain's Sierra Nevada. Systematic evaluation reveals this species as an exceptional reservoir of bioactive compounds with remarkable therapeutic potential. Understanding their exact compositions, particularly in bioactive molecules, is crucial for enhancing the value of plant matrices and their derivatives. Infrared spectroscopy offers advantages such as speed, ease of use, and non-destructiveness, while being environmentally friendly due to minimal or zero solvent usage.

This study explore the application of infrared spectroscopy in characterizing extracts from various parts of these two medicinal plants. It also documente striking tissue-specific phytochemical variations, with leaves showing significant phenolic content (526.90 ± 11.61 mg GAE/g DW) and flavonoids (369.23 ± 7.14 mg QE/g DW), while flowers exhibited superior proanthocyanidin content. These findings highlight the importance of organ-specific analyses when evaluating medicinal plants. The robust antihemolytic capacity demonstrated across multiple assays like hyptonic test with IC_{50} of 1.58 mg/ml, which validates traditional applications and suggests utility in oxidative stress-related disorders. The selective cytotoxicity of leaf extracts against murine multiple myeloma cells (IC_{50} = 276.1 ± 8.12 µg/mL), with minimal toxicity toward normal splenic mononuclear cells, suggests intriguing anticancer properties with potentially favorable therapeutic indices. These results scientifically validate traditional medicine applications and establish a foundation for bioprospecting novel therapeutic agents from *A. decorticans*, positioning it as a valuable botanical resource with significant potential for pharmaceutical development and addressing pressing global health challenges.

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NON COMMUNICABLE DISEASES RISK FACTORS AND THEIR TRENDS IN MEDICAL SYSTEM

ABSTRACT

Non-communicable diseases (NCDs), including cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes, are major global health challenges. These diseases are largely driven by modifiable risk factors categorized as behavioral (tobacco use, physical inactivity, unhealthy diet, harmful alcohol use) and metabolic (raised blood pressure, overweight/obesity, raised blood glucose, high cholesterol). Environmental factors like air pollution also contribute significantly. Trends reveal a mixed picture. While tobacco and alcohol use have declined in some regions, physical inactivity and unhealthy diets remain high or are increasing. Overweight and obesity, hypertension, and diabetes are showing upward trends globally, placing a growing burden on medical systems. Medical systems are responding through awareness campaigns, screening programs, lifestyle modification counseling, and policy interventions. Integrated care approaches and improved surveillance are becoming increasingly important to manage these risk factors and mitigate the rising burden of NCDs worldwide. Addressing these trends requires multi- sectoral efforts to promote healthier environments and individual behaviors.

Keywords: cardiovascular diseases, health challenges, hypertension, risk factors

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ANTICANCER POTENTIAL OF PLUMBAGO ZEYLANICA AS HERBAL MEDICINAL TREATMENT

ABSTRACT

Plumbago zeylanica, a medicinal herb traditionally used in various systems of medicine, has garnered significant attention for its anticancer properties. This review summarizes the current understanding of its potential in cancer prevention and treatment.The plant's roots contain plumbagin, a naphthoquinone identified as a key bioactive compound responsible for its anticancer activity. Studies have demonstrated that plumbagin and crude extracts of P. zeylanica exhibit cytotoxicity against various cancer cell lines, including lung, breast, prostate, gastric, and colon cancers. The mechanisms of action involve the induction of apoptosis, cell cycle arrest, and inhibition of metastasis. Furthermore, P. zeylanica extracts have shown synergistic effects with conventional chemotherapy drugs, enhancing their efficacy while potentially reducing toxicity. Preclinical studies in animal models have also indicated the ability of plumbagin to inhibit tumor growth and metastasis.While these findings highlight the promising anticancer potential of Plumbago zeylanica, further research, including well-designed clinical trials, is warranted to fully elucidate its role in cancer prevention and treatment in humans and to establish optimal dosages and delivery methods.

Keywords: plumbagin, anticancer, Plumbago, chemotherapy, cytotoxicity

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IN SILICO ANALYSIS OF POTENTIAL INTERACTIONS BETWEEN APREMILAST AND ANTI-APOPTOTIC PROTEINS: A MOLECULAR DOCKING STUDY ON BCL-2, BCL-XL, AND SURVIVIN

ABSTRACT

Apoptosis is a fundamental cellular process that plays a vital role in the development, survival, and functionality of multicellular organisms. Apoptosis dysregulation is linked to various diseases, including cancer and degenerative disorders. Apoptosis occurs via two main pathways, the intrinsic and the extrinsic pathways. The intrinsic pathway of apoptosis is regulated by Bcl-2 family proteins, including anti-apoptotic members Bcl-2 and Bcl-xl, which are overexpressed in various cancer types and contribute to chemoresistance. Similarly, survivin, a member of the IAP family, inhibits apoptosis and regulates mitosis, and is upregulated in numerous tumors. This study aimed to evaluate the potential interactions of Apremilast, a PDE4 inhibitor approved for psoriasis and psoriatic arthritis, with Bcl-2, Bcl-xl, and survivin using in silico molecular docking analysis. Three-dimensional structures of Bcl-2, Bcl-xl, and survivin were retrieved from the Protein Data Bank. The structure of Apremilast was optimized, and molecular docking simulations were performed using AutoDock Vina. Interaction profiles, binding affinities, and docking poses were analyzed using Discovery Studio. The Venetoclax–Bcl-2 complex served as a positive control. Docking results indicated strong binding affinities of Apremilast with Bcl-2 (-7.2 kcal/mol), Bcl-xl (-7.5 kcal/mol), and survivin (-6.8 kcal/mol). The interactions included Pi-Alkyl, Pi-Sulfur, Pi-Sigma, hydrogen bonding, and van der Waals forces. Visual analyses showed that Apremilast was well-positioned within the binding pockets. The Venetoclax–Bcl-2 complex displayed a stronger binding score (-10.9 kcal/mol), but Apremilast formed stable complexes through diverse interaction types. This study shows that Apremilast interacts with key anti-apoptotic proteins such as Bcl-2, Bcl-xl, and survivin, indicating potential anticancer effects beyond its known anti-inflammatory role. These findings provide a preliminary rationale for repurposing Apremilast in cancer therapy. If supported by experimental validation, Apremilast may emerge as a candidate agent for targeting apoptosis pathways in tumor cells.

Keywords: Apremilast, Apoptosis, Bcl-2, Bcl-xl, Survivin, Molecular docking

APREMİLAST'IN ANTİ-APOPTOTİK PROTEİNLERLE OLASI ETKİLEŞİMLERİNİN IN SİLİCO ANALİZİ: BCL-2, BCL-XL VE SURVİVİN ÜZERİNE MOLEKÜLER DOCKİNG ÇALIŞMASI

ÖZET

Apoptoz, çok hücreli organizmaların gelişimi, hayatta kalması ve işlevselliği açısından hayati öneme sahip temel bir hücresel süreçtir. Apoptozun düzensizliği, kanser ve dejeneratif hastalıklar dahil olmak üzere çeşitli hastalıklarla ilişkilidir. Apoptoz, intrinsik ve ekstrinsik olmak üzere iki ana yol aracılığıyla gerçekleşir. İntrinsik apoptoz yolu, Bcl-2 ailesi proteinleri tarafından düzenlenir. Bu ailede yer alan Bcl-2 ve Bcl-xl gibi anti-apoptotik proteinler, birçok kanser türünde yüksek düzeyde eksprese edilmekte ve kemoterapiye direnç gelişimine katkıda bulunmaktadır. Benzer şekilde, IAP ailesine ait survivin proteini apoptozu baskılar, mitozu düzenler ve birçok tümörde yüksek düzeyde eksprese edilir. Bu çalışmada, psoriasis ve psoriatik artrit tedavisinde onaylanmış bir PDE4 inhibitörü olan Apremilast'ın, Bcl-2, Bcl-xl ve survivin ile potansiyel etkileşimlerinin in silico moleküler docking analizi ile değerlendirilmesi amaçlanmıştır. Bcl-2, Bcl-xl ve survivin proteinlerinin üç boyutlu yapıları Protein Data Bank'ten elde edilmiştir. Apremilast'ın yapısı optimize edilmiş ve AutoDock Vina programı kullanılarak moleküler docking simülasyonları gerçekleştirilmiştir. Etkileşim profilleri, bağlanma afiniteleri ve docking pozisyonları Discovery Studio ile analiz edilmiştir. Venetoclax–Bcl-2 kompleksi pozitif kontrol olarak kullanılmıştır. Docking analizleri, Apremilast'ın Bcl-2 (-7.2 kcal/mol), Bcl-xl (-7.5 kcal/mol) ve survivin (-6.8 kcal/mol) ile güçlü bağlanma afiniteleri gösterdiğini ortaya koymuştur. Bu etkileşimlerde Pi-Alkyl, Pi-Sulfur, Pi-Sigma, hidrojen bağları ve van der Waals kuvvetleri yer almıştır. Görsel analizler, Apremilast'ın bağlanma ceplerine uygun şekilde yerleştiğini göstermiştir. Venetoclax–Bcl-2 kompleksi daha güçlü bir bağlanma skoru (-10.9 kcal/mol) sergilemiş olsa da, Apremilast'ın çeşitli etkileşim türleriyle stabil kompleksler oluşturduğu görülmüştür. Bu çalışma, Apremilast'ın Bcl-2, Bcl-xl ve survivin gibi temel anti-apoptotik proteinlerle etkileşime girdiğini ve bilinen anti-inflamatuar etkilerine ek olarak potansiyel antikanser özellikler taşıyabileceğini göstermektedir. Bu bulgular, Apremilast'ın kanser tedavisinde yeniden konumlandırılması için ön bilimsel gerekçe sunmaktadır. Deneysel doğrulamalarla desteklenmesi durumunda, Apremilast apoptoz yolaklarını hedefleyen potansiyel bir ajan olarak değerlendirilebilir.

Anahtar Kelimeler: Apremilast, Apoptoz, Bcl-2, Bcl-xl, Survivin, Moleküler docking

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THE RELATIONSHIP BETWEEN POLYPHENOL CONSUMPTION LEVEL AND LIPID PARAMETERS IN INDIVIDUALS DIAGNOSED WITH CARDIOVASCULAR DISEASE

ABSTRACT

Aim: This study aimed to investigate the relationship between polyphenol consumption levels and lipid parameters as well as blood pressure in individuals diagnosed with cardiovascular disease (CVD).

Materials and Methods: A total of 112 individuals diagnosed with CVD and receiving treatment at Tekirdağ Namık Kemal University Research Hospital were enrolled in the study. The frequency of polyphenol consumption was assessed, and daily intake levels were calculated.

Results: The mean daily total polyphenol intake of the participants was 804.98 mg/day. The primary dietary sources contributing to polyphenol intake were identified as non-alcoholic beverages, fruits, and vegetables, respectively. A significant negative correlation was found between polyphenol consumption and total cholesterol (TC), low-density lipoprotein (LDL), triglyceride (TG), and systolic blood pressure (SBP) levels (respectively; $r=-0.380$; $p<0.01$, $r=-0.368$; $p<0.01$, $r=-0.300$; $p<0.01$, $r=-0.221$; $p<0.05$). Among the polyphenol subgroups,

flavonoids (483.94 mg/day) and phenolic acids (246.86 mg/day) had the highest intake levels. Flavonoid intake showed a significant negative correlation with TC, LDL, TG, and SBP levels (respectively; r=-0.412; p<0.01, r=-0.390; p<0.01, r=-0.305; p<0.01, r=-0.204; p<0.05). A significant negative relationship was also observed between phenolic acid intake and TC, LDL, and TG levels (respectively; r=-0.226; p<0.05, r=-0.233; p<0.05, r=-0.210; p<0.05). Lignan intake was negatively associated with TC, LDL, and TG levels (respectively; r=-0.336; p<0.01, r=-0.313; p<0.01, r=-0.237; p<0.05). Stilbene intake was significantly negatively correlated with TG, SBP, and diastolic blood pressure (DBP) levels (respectively; r=-0.230; p<0.05, r=-0.275; p<0.01, r=-0.221; p<0.05). Patients with elevated lipid and blood pressure levels exhibited lower polyphenol consumption.

Conclusion: The findings of this study suggest that higher intake of polyphenols is negatively associated with lipid parameters and blood pressure in individuals with CVD. These findings highlight the potential beneficial effects of polyphenols on cardiovascular health and underscore the importance of nutrition in the management of cardiovascular diseases.

Keywords: Polyphenol, lipid, blood pressure

KARDİYOVASKÜLER HASTALIK TANISI ALMIŞ BİREYLERDE POLİFENOL TÜKETİM DÜZEYİNİN LİPİT PARAMETRELERİ İLE İLİŞKİSİ

ÖZET

Amaç: Bu çalışmanın amacı, kardiyovasküler hastalık (KVH) tanısı olan bireylerde polifenol tüketim düzeyi ile biyokimyasal lipit parametreleri ve kan basıncı arasındaki ilişkinin araştırılmasıdır.

Materyal ve Yöntem: KVH tanısı olan ve Tekirdağ Namık Kemal Üniversitesi Araştırma Hastanesi'nde tedavileri devam eden, toplam 112 birey çalışmaya dahil edilerek, polifenol tüketim sıklığı sorgulandı ve günlük polifenol alımları hesaplandı. Katılımcıların biyokimyasal lipit parametreleri ve kan basınç değerleri retrospektif olarak incelendi.

Bulgular: Katılımcıların günlük ortalama toplam polifenol tüketimi 804,98 mg/gün olarak hesaplandı. Polifenol alımına en çok katkı sağlayan besin gruplarının sırasıyla alkolsüz içecek, meyve ve sebze olduğu tespit edildi. Polifenol tüketimi ile toplam kolesterol (TK), düşük yoğunluklu lipoprotein (LDL), trigliserit (TG) ve sistolik kan basıncı (SKB) düzeyleri arasında anlamlı negatif ilişki saptandı (sırasıyla; $r=-0,380$; $p<0,01$, $r=-0,368$; $p<0,01$, $r=-0,300$; $p<0,01$, $r=-0,221$; $p<0,05$). Polifenoller içerisinde en yüksek düzeyde alt grup alım miktarı flavonoit (483,94 mg/gün) ve fenolik asit (246,86 mg/gün) olarak bulundu. Flavonoit tüketimi ile TK, LDL, TG ve SKB düzeyleri arasında anlamlı negatif ilişki saptandı (sırasıyla; $r=-0,412$; $p<0,01$, $r=-0,390$; $p<0,01$, $r=-0,305$; $p<0,01$, $r=-0,204$; $p<0,05$). Fenolik asit tüketimi ile TK, LDL, TG düzeyleri arasında anlamlı negatif ilişki tespit edildi (sırasıyla; $r=-0,226$; $p<0,05$, $r=-0,233$; $p<0,05$, $r=-0,210$; $p<0,05$). Lignan tüketimi ile TK, LDL, TG düzeyleri arasında anlamlı negatif yönlü ilişki bulundu (sırasıyla; $r=-0,336$; $p<0,01$, $r=-0,313$; $p<0,01$, $r=-0,237$; $p<0,05$). Stilben tüketimi ile TG, SKB, diyastolik kan basıncı (DKB) düzeyleri arasında anlamlı negatif yönlü ilişki tespit edildi (sırasıyla; $r=-0,230$; $p<0,05$, $r=-0,275$; $p<0,01$, $r=-0,221$; $p<0,05$). Lipit ve kan basınç düzeyleri daha yüksek hastalar daha düşük polifenol tüketimine sahipti.

Sonuç: Bu çalışmanın sonuçları, daha yüksek polifenol tüketiminin KVH ile ilişkili biyokimyasal lipit parametreleri ve kan basıncıyla negatif yönde ilişkili olduğunu göstermektedir. Bulgular, polifenollerin KVH üzerinde olumlu etkisini ortaya koymakta ve KVH'de beslenmenin önemini yansıtmaktadır.

Anahtar Kelimeler: Polifenol, lipit, kan basıncı

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ASSOCIATION BETWEEN FINE PARTICULATE MATTER AND DERMATITIS IN ERZINCAN, TÜRKİYE

ABSTRACT

Purpose: Air pollution exposure is a significant environmental risk factor for the development and exacerbation of dermatitis. This study aimed to investigate the effects of fine particulate matter concentrations, measured between January 1, 2018, and December 31, 2018, on dermatitis cases across different age groups (<18, 18-64, >64), focusing on lag0-lag7 periods.

Materials and Methods: The effect of a 10 μg/m³ increase in $PM_{2.5}$ concentrations on dermatitis cases in each age group was assessed using a Generalized Additive Model with a quasi-Poisson link. Daily average $PM_{2.5}$ concentrations, relative humidity (%), temperature (°C), weekdays, official holidays, and the number of dermatitis cases were included in the model. Risks were expressed as relative risks with 95% confidence intervals (95% CIs) for each 10 μg/m³ increase in $PM_{2.5}$. Lag effects (lag0-lag7) were analyzed using a Distributed Lag Non-Linear Model.

Findings: When examining $PM_{2.5}$ exposure by age group, a statistically significant effect was observed in the <18 age group. A 10 μg/m³ increase in $PM_{2.5}$ concentrations was significantly associated with an increase in dermatitis visits in the <18 age group at lag2 (RR:1.0031; 95% CI: 1.0003-1.0060) and lag3 (RR:1.0031; 95% CI: 1.0003-1.0060). These findings suggest that sensitive populations exposed to air pollutants should be specifically considered in the prevention and management of dermatitis cases.

Conclusion: This study suggests that $PM_{2.5}$ exposure may be an independent risk factor for the development of dermatitis, particularly as children appear to be more vulnerable than adults.

Keywords: Dermatitis, fine particulate matter, Generalized Additive Model, Erzincan, Türkiye

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HISTOPATHOLOGICAL, IMMUNOHISTOCHEMICAL, AND BIOCHEMICAL EFFECTS OF BEE BREAD (PERGA) ADMINISTRATION IN EXPERİMENTAL DIABETES

ABSTRACT

Aim: Diabetes mellitus is a major public health issue in modern times. Bee bread (Perga) is widely used in apitherapy due to its bioactive compounds and potential therapeutic effects. This study aimed to investigate the possible antidiabetic effects of bee bread in streptozotocin (STZ)-induced diabetic rats.

Material and Method: A total of 40 male Wistar albino rats were randomly divided into five groups: Control, Perga (0.5 g/kg), Diabetes (STZ, 55 mg/kg), Diabetes + Perga (STZ 55 mg/kg + Perga 0.5 g/kg), and Diabetes + Acarbose (STZ 55 mg/kg + Acarbose 20 mg/kg). Experimental diabetes was induced by a single intraperitoneal (i.p.) injection of STZ (55 mg/kg). Perga and acarbose were administered daily via oral gavage throughout the study. Blood glucose levels were measured at regular intervals via tail vein sampling. At the end of the experiment, pancreatic tissues were evaluated histopathologically and immunohistochemically. In addition, serum levels of ALT, AST, ALP, LDH, total cholesterol, triglycerides, creatinine, urea, and glucose were analyzed.

Findings: STZ administration resulted in significant histopathological damage to pancreatic tissue and a marked decrease in insulin expression. Biochemical analyses revealed notable alterations in metabolic parameters associated with diabetes. Perga administration effectively reduced blood glucose levels and exhibited ameliorative effects on pancreatic histopathology and insulin expression. However, unfavorable changes in certain liver enzyme levels were observed in the Perga-treated group.

Conclusion: The findings suggest that bee bread may exhibit antidiabetic potential in STZ-induced diabetic rats. Nonetheless, the observed hepatic effects and limited biochemical responses indicate that further studies are required to confirm its efficacy and safety.

Keywords: Perga, Diabetes, Streptozotocin, Rat, Antidiabetic effect

Note: The data presented in this study are derived from the master's thesis research currently being conducted by Mehmet ÇUBUKÇU at the Institute of Health Sciences, Van Yüzüncü Yıl University.

DENEYSEL DİYABETTE ARI EKMEĞİ (PERGA) UYGULAMASININ HİSTOPATOLOJİK İMMÜNOHİSTOKİMYASAL VE BİYOKİMYASAL ETKİLERİ

ÖZET

Amaç: Diyabet, günümüzde önemli bir halk sağlığı sorunu olarak öne çıkmaktadır. Arı ekmeği (Perga), sahip olduğu biyoaktif bileşenler sayesinde apiterapide yaygın olarak kullanılmaktadır. Bu çalışmanın amacı, streptozotosin (STZ) ile deneysel diyabet oluşturulan sıçanlarda arı ekmeğinin potansiyel antidiyabetik etkilerini değerlendirmektir.

Materyal ve Yöntem: Çalışmada 40 adet erkek Wistar albino sıçanı rastgele beş gruba ayrılmıştır: Kontrol, Perga (0,5 g/kg), Diyabet (STZ, 55 mg/kg), Diyabet + Perga (STZ, 55 mg/kg + Perga, 0,5 g/kg) ve Diyabet + Akarboz (STZ, 55 mg/kg + Akarboz, 20 mg/kg). Diyabet, tek doz STZ enjeksiyonu [55 mg/kg, intraperitoneal (i.p.)] ile indüklenmiştir. Perga ve akarboz uygulamaları deney süresi boyunca günlük olarak gastrik gavaj yöntemiyle gerçekleştirilmiştir. Deney süresince belirli aralıklarla kuyruk veninden kan glukoz düzeyleri ölçülmüş; deney sonunda pankreas dokuları histopatolojik ve immünohistokimyasal olarak incelenmiştir. Ayrıca serumda ALT, AST, ALP, LDH, total kolesterol, trigliserid, kreatinin, üre ve glukoz düzeyleri analiz edilmiştir.

Bulgular: STZ uygulaması, pankreas dokusunda belirgin histopatolojik lezyonlara ve immunohistokimyasal olarak insülin ekspresyonunda anlamlı azalmaya yol açmıştır. Biyokimyasal parametrelerde diyabete bağlı olarak önemli değişiklikler gözlenmiştir. Perga uygulaması, hiperglisemiyi baskılayarak kan glukoz düzeylerinde azalma sağlamış; pankreatik histopatolojik bulgularda ve insülin immunekspresyonunda iyileştirici etkiler göstermiştir. Ancak, Diyabet 4 Perga grubunda bazı karaciğer enzim düzeylerinde olumsuz değişiklikler saptanmıştır.

Sonuç: Elde edilen bulgular, Perga'nın STZ ile oluşturulan deneysel diyabet modelinde potansiyel antidiyabetik etkiler gösterebileceğini ortaya koymaktadır. Bununla birlikte, karaciğer üzerine gözlemlenen etkiler ve sınırlı biyokimyasal yanıtlar dikkate alındığında, Perga'nın antidiyabetik etkinliğinin daha ileri çalışmalarla desteklenmesi gerekmektedir.

Anahtar Kelimeler: Perga, Diyabet, Streptozotosin, Sıçan, Antidiyabetik etki

Bilgi: Bu çalışma, Van Yüzüncü Yıl Üniversitesi Sağlık Bilimler Enstitüsünde henüz hazırlanmakta olan Mehmet ÇUBUKÇU'nun yüksek lisans tez çalışması verilerinden elde edilmiştir.

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DOES THE DIMENSION OF THE PROSTATE HAVE ANY INFLUENCE ON URINARY INCONTINENCE SUBSEQUENT TO HOLMIUM LASER ENUCLEATION OF THE PROSTATE (HOLEP)?

ABSTRACT

Background: We endeavored to examine the association between prostate dimensions and post-HoLEP complications.

Methods: We conducted a retrospective analysis of the data of 221 individuals who underwent HoLEP from August 2021 to August 2024. The cohort was stratified into two groups based on prostate volume. Those with prostate volume ≤ 80 ml were included in group 1 (n=122) and those with prostate volume >80 ml were included in group 2 (99). The groups were assessed concerning perioperative outcomes, complications and urinary incontinence at a three-month follow-up. Statistical analyses were performed using the chi-square test, T student test and Mann Whitney U techniques.

Results: The peroperative, postoperative parameters are presented in table. The mean age was 68.2±8.7. The mean pre-operative prostate spesific antigene (PSA) was 3.2 ng/dl in group1 and 8.1 ng/dl in group 2 (p<0.001). Surgery time was longer in group 2 than group 1 as expected (<0.001). Postoperative hemorrhaging and the necessity for blood transfusion were more prevalent in group 2 (p<0.001). At the post-operative third month follow-up, 31 subjects in cohort 2 and 17 subjects in cohort 1 persisted in expressing grievances regarding urgency incontinence (p=0.03).

Conclusion: HoLEP is a surgical technique that can be utilized for any prostate independent of dimensions. Nevertheless, the operative duration is extended and postoperative sphincter functionality recovers longer time. There are scholarly articles demonstrating that the prevalence of incontinence diminished in investigations encompassing extended-term follow-up.

	All patients	Prostate volume ≤80 ml	Prostate volume >80ml	P value
Age (years)	68.2 (8.7)	67.3 (8.5)	69.4 (8.8)	0.875^
PSA (ng/dl)	5.2 (6.1)	3.2 (3.1)	8.1 (7.9)	**<0.001**^^
Surgery time(min)	62.4 (28.7)	47.6 (14.7)	82.8 (31.1)	**<0.001**^^
Blood transfusion (n)	14	1	13	**<0.001**^^^
Postop incontinans(n)	52	21	31	**0.003**^^^
Urethral stricture (n)	13	9	4	0.394^^^

^: T test, ^^: Mann Whitney u test, ^^^: Chi-square test

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RECOMBINANT DNA TECHNOLOGY IN PHARMACEUTICAL RESEARCH: DESIGN, DEVELOPMENT AND APPLICATIONS OF BIOPHARMACEUTICALS FOR DISEASE TREATMENT AND PREVENTION

ABSTRACT

Recombinant DNA technology has revolutionized pharmaceutical research by enabling the design, development, and production of biopharmaceuticals that play a pivotal role in disease treatment and prevention. This technology involves the manipulation of genetic material to create recombinant proteins, monoclonal antibodies, and vaccines. By introducing foreign genes into host organisms, such as bacteria, yeast, or mammalian cells, researchers can produce therapeutic proteins in large quantities with high specificity and efficacy. The applications of recombinant DNA technology span a wide range of diseases, including cancer, autoimmune disorders, infectious diseases, and genetic disorders. The development of human insulin, growth hormones, and monoclonal antibodies exemplifies the success of this approach in improving patient outcomes. Furthermore, recombinant DNA technology enables the creation of vaccines that are safer and more effective compared to traditional methods. This technology also facilitates gene therapy, where defective genes are replaced or repaired to treat genetic disorders at the molecular level. As the understanding of genomics and molecular biology advances, the potential for recombinant DNA technology in personalized medicine grows, paving the way for targeted therapies that are tailored to individual genetic profiles. The ongoing research and innovation in this field continue to enhance the efficacy, safety, and accessibility of biopharmaceuticals, ultimately contributing to improved global health outcomes.

Keywords: Recombinant DNA technology, biopharmaceuticals, disease treatment, genetic disorders, monoclonal antibodies, gene therapy.

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EVALUATION OF THE MARGINAL ADAPTATION AND FRACTURE RESISTANCE OF DIGITALLY FABRICATED ENDO-CROWNS MADE FROM TWO DIFFERENT MATERIALS: AN IN VITRO STUDY

ABSTRACT

Background: An endocrown is a restoration that can be defined as a one-piece restoration, which replaces the entire crown of the tooth, retained with an extension at the level of the pulp chamber, and with the occlusal adhesion principles of adhesive restorations. Endocrowns represent, in some contexts, a valid alternative for restoring endodontically treated teeth with severe coronal damage.

Materials and methods: After preparation, and 7 days of storage at 37 °C and 100% humidity, a digital impression was obtained with a Trios 5 scanner, and sent to the lab, where the endocrown design was performed on EXOCAD, same design in two different materials (ZR and LD). From the digital files, 4 epoxy resin framework models were produced as to proceed with the bonding procedures and marginal gap analyses. To proceed with bonding the endocrowns, the internal surface was treated with 5% hydrofluoridric acid (IPS Ceramic Gel Etching; Ivoclar Vivadent AG) for 20 seconds for the LD group, while, for the ZR group, endocrowns were airborne particle abraded (Rocatec System; 3M ESPE). The samples were bonded with PANAVIA SA cement universal (Kuraray), a dual-polymerizing resin cement, under finger pressure for 60seconds.

Results: Statistical tests revealed a statistically significant difference between the different groups. Tukey testing demonstrated that ZR has the highest fracture toughness values compared to LD. At significantly lower values the LD showed fractures (often however with irregular patterns, typical of ceramics) which were sometimes even restorable. Conversely, Zr showed clear fracture margins (with a particularly rough separation surface).

Conclusions: The choice of different materials affected the fracture resistance of this kind of restoration. The possibility of producing these restorations in a full digital workflow, also considering the coronal position of the finishing line compared to other restorations, guarantees a favorable factor.

Keywords: Endo-Crowns; endocrown; intra-radicular retention; post; core; post-core; fiber-post; adhesive; Lithium-Disilicate; Lithium-Disilicate; Katana; Zirconia.

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PRELIMINARY EVALUATION OF THE ADAPTABILITY OF POST-AND-CORE STRUCTURES PRODUCED VIA SLS COMPARED TO LOST-WAX CASTING

ABSTRACT

Background

This preliminary study evaluates the marginal adaptation and primary stability of custom post-cores manufactured by Selective Laser Sintering (SLS) versus traditional lost-wax casting, also considering the limitations of fiber and cobalt–chromium posts in post-endodontic restorations.

Materials and Methods

More fabrication protocols were compared on a single endodontically treated tooth: initiallly a post-core made from the scan of the final impression and modeled via exocad was tested.

Subsequently, 2 pin cores were tested in the same patient: one made using the direct technique with pattern resin and then scanned and one using the lost wax casting technique starting from the same post-core made from pattern resin.

In a different patient, 4 post-core were tested, each resulting from a different technique:

1-Direct post in Pattern Resin, scanned, modeled via exocad and fabricated via SLS

2-Direct post in Pattern Resin, cast using the lost-wax technique

3-Indirect post based on a precision impression and stone model, waxed, scanned, modeled with exocad and fabricated in SLS

4-Indirect post based on a precision impression and stone model, waxed and cast via lost-wax technique

Each post-core was inserted into the post space and assessed for:

- Marginal adaptation so detection of gaps in mesial, distal, buccal and lingual faces

- Primary stability

- Rotational tendency

Evaluations were performed by visual inspection, use of a probe to assess the presence of gaps greater than 50 µm by surface sliding and mobility tests.

Results

The direct SLS-fabricated post exhibited virtually no marginal gaps, excellent primary stability, and zero rotational movement.

Both direct and indirect cast posts showed marginal gaps > 50 µm, detectable micromovements, and required increased cement thickness.

The indirectly scanned post also demonstrated insertion difficulties.

Conclusion

Direct SLS fabrication provides superior marginal adaptation, enhanced primary stability, and greater reproducibility compared to traditional lost-wax casting, representing a promising clinical alternative for custom post-core restorations.

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AN APPRAISAL OF THE REFERENCE RANGE FOR BLEEDING TIME AMONGST CHRISTIANS IN NIGERIA

ABSTRACT

This study aims to create baseline values that reflect the distinct physiological traits of this population by evaluating the reference range for bleeding time among Christians in Nigeria. Bleeding time, an important hemostatic characteristic, varies among groups as a result of genetic, environmental, and lifestyle influences. This study seeks to add useful information to the sparse body of knowledge on hemostatic characteristics particular to the Nigerian Christian population by undertaking a thorough examination of bleeding time in a sample of young Nigerian people. With a cross-sectional design, the study enrols a varied group of healthy adults between the ages of 18 and 30. Bleeding time measurements are made using standardised procedures, and the outcomes are contrasted with accepted global reference ranges, gender, platelet count, and bleeding time variability. This study adds to our understanding of hemostasis in various groups and emphasises the value of individualised reference intervals for diagnostic and therapeutic procedures. The researcher's conclusions have significance for clinical practice, assisting medical personnel in accurately diagnosing bleeding problems and enhancing patient treatment plans for young Christian adults in Nigeria. Healthcare institutions and diagnostic laboratories in Nigeria should adopt bleeding time reference ranges that reflect the local population’s physiological characteristics rather than relying solely on international standards.

Keywords: Bleeding, Christians, pregnancy, clinical practice, hemostasis, Nigeria

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SYNTHESIS AND STUDY OF KINETICS OF $CoFe_2O_4$@SiO_2-CHITOSAN ADSORBENTS FOR REMOVAL OF CADMIUM AND LEAD FROM WATER

ABSTRACT

This work investigated CoFe2O4@SiO2-chitosan magnetic nanocomposites functionalized with chitosan, which served as an efficient adsorbent for the separation of trace amounts of lead (Pb(II)) and cadmium (Cd(II)) in water. The percentage of contaminants extracted from the solution has been determined using atomic absorption spectroscopy (AAS). Furthermore, the pseudo-first-order and pseudo-second-order kinetic models, along with the Freundlich and Langmuir isotherm models, were applied to evaluate the kinetic and equilibrium data for metal adsorption on adsorbents. The magnetic adsorbent demonstrated excellent magnetic properties and high Langmuir adsorption capacities of 255.10 mg/g for lead (Pb(II)) and 236.41 mg/g for cadmium (Cd(II)) ions. The second-order kinetic model and Langmuir adsorption isotherm exhibit the most precise adsorption data match. Results suggested that the coordinative interaction of amino groups in chitosan and metal ions was responsible for the occurrence of chemisorption. The adsorption efficiency after the first cycle for Pb(II) and Cd(II) ions was 93% and 89%, respectively. Furthermore, the adsorbents exhibited outstanding reliability, excellent reusable values, and good application performance, with 82% and 79% for lead (Pb(II)) and cadmium (Cd(II)), respectively, after five cycles of adsorption.

Keywords: Ferrite nanoparticles; silica coating; chitosan coating; chemical kinetics; toxic elements.

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FORMULATION AND EVALUATION OF MICELLE NANOGEL–BASED DRUG DELIVERY SYSTEM FOR LUTEIN IN AGE-RELATED MACULAR DEGENERATION

ABSTRACT

Antioxidants such as lutein have been shown in recent research to significantly reduce the incidence of age-related macular degeneration (AMD), which has been linked to blindness in many older persons. Antioxidants lessen the harm caused by free radicals by stopping oxidation. However, the limited stability, short residence period, and poor solubility of lutein limit their bioavailability in the eyes after topical treatment. This study aimed to develop and characterize a micelle nanogel formulation for lutein administration into the eyes. Because of its enhanced corneal permeability, extended retention on the ocular surface, and reduced requirement for frequent injection, the micelle nanogel delivery system offers a novel therapeutic approach for delivering ocular medications. We developed a lutein micelle at the nanoscale and added it to a gel foundation to boost the ocular permeability and solubility. Evaluations of the micelle nanoformulation included cell line studies, ex vivo permeation tests, mean particle size, entrapment efficiency (EE), zeta potential, in vitro release studies, and Hen's egg test chorioallantoic membrane (HET-CAM). With an entrapment effectiveness of 84.5 ± 1.75%, this nanoformulation demonstrated favourable particle size (205.2 ± 15.36 nm), PDI (0.3 ± 0.20), and zeta potential (− 14.2 to + 11.3 mV). Compatibility was verified by Fourier transform infrared spectroscopy, and TEM showed nanoscale spherical structures. F4 showed improved wound healing qualities, minor ocular irritation, increased fibroblast viability, antioxidant activity (IC_{50}: 55.11 µg/mL), and efficient corneal penetration. Based on the results, The formulations were both safe and effective for delivering drugs to the eyes.

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THE ECOLOGICAL RISK OF CONTAMINATION WITH TOXIC METALS IN THE SOILS, WASTE AND ASH, AROUND THE "TREPÇA" COMPLEX, THE "KOSOVO" THERMAL POWER PLANTS AND THE NEW FERRONICKEL COMPLEX

ABSTRACT

Samples of toxic waste, soil and ash, were collected in the landfill (solid environmental hot-spots) near the "Trepça" Complex, "New Ferronickel" and Kosovo "Thermal Power Plants'', and analyzed by the ICP-OES method to measure the concentration of 10 toxic metals (Pb, Cd, Cr, Ni, Zn, Cu, As, Co, Mn, and Fe). The pollutant with the highest mean concentration (in acidic medium) was Fe (36400.00 mg/kg), followed by the Mn (8683.00 mg/kg), Cr (6575.00 mg/kg), As (4739.00 mg/kg), Pb (3364.00 mg/kg), Zn (2394.00 mg/kg), Ni (922.60 mg/kg), Cu (297.60 mg/kg), Co (46.60 mg/kg). and Cd (61.8mg/kg). To analyze the level of heavy metal pollution in an area, more than one pollution index analysis is needed, so in this study 3 pollution indices were used, namely the geoaccumulation index (I_{geo}), contamination factor (CF_i), and the pollution load index (PLI). The CF_i (contamination factor) values determined for Fe, Mn, Cr, As, Pb, Zn, Ni, Cu, Co and Cd indicated a high degree of contamination in all samples. In all soil samples the PLI values indicated the presence of soil pollution.

Keywords: Trepça, Ferronickel, thermal power plant, toxic metals, ecology risk, soil, waste, ash

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THE INHIBITION OF SOME PHYTOPATHOGENIC BACTERIA BY ACTINOBACTERIA ISOLATED FROM ALGERIAN SAHARAN SOILS

ABSTRACT

Every year, between 10 and 28% of agricultural crops are lost, and this is due to agricultural pests. Among the bacterial pests, there are: *Erwinia amilovora, Agrobacterium tumefaciens, Pseudomonas savastanoi pv savastanoi...*

The traditional chemical means used for the control of these plant pathogens are sometimes ineffective; costly and, above all, recognized for its side effects on the environment and the health of the consumer.

Faced with these problems, the search for new bioactive molecules is more than necessary to fight against these phythopathogens. Among the most promising sources of bioactive substances are microorganisms, especially actinobacteria, which are gram-positive bacteria with a high percentage of G+C, the majority of which tend to form branched mycelium. Actenobacteria characterize the most important part of the microbial community as they are the sources of novel bioactive compounds. This phylum has the capacity to grow in extreme climatic conditions. Due to their high biotechnological applications, this community has always been a fascinating field of research for chemists, pharmaceutical companies, etc. They are known to produce a wide array of chemically diverse bioactive compounds, such as antibiotics, antitumor and anti-infection agents, and thus open up new possibilities in drug research. In this review, we attempt to highlight the diversity of actinobacteria and their multifaceted role in biotechnology applications.

Isolation of actinobacteria carried out on chtin-vitamin B medium; after pretreatment with Ca Co3, followed by incubation at 30C for 21 days; enumeration is done using a colony counter; and purification on ISP2 medium by successive transplanting until pure colonies are obtained. The search for antimicrobial activity carried out by the cross-streak technique on ISP2 medium.

The results of the antibacterial activity indicate a significant important inhibition of some phytopathogenic bacteria.

Keywords: Actinobacteria; Inhibition; phytopathogenic bacteria; bioactive molecules.

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ACTINOBACTERIA AS A PROMISING METHOD OF BIOLOGICAL CONTROL AGAINST PATHOGENIC BACTERIA AND FUNGI

ABSTRACT

Plants are constantly surrounded by a large number of phytopathogenic microorganisms (Bacteria, fungi, protozoa or viruses) and, unfortunately, when a plant is affected by a disease, its growth, fertility and productivity are affected. Symptoms develop and all or part of the body can die, which can cause serious economic and/or ecological damage. In addition, plant pathogenic diseases reduce global agricultural production by 12 to 14%.

Biological control against plant pathogens is one of the promising methods, Actinobacteria are among the microorganisms used, they are known for their abilities to produce secondary metabolites, they can be used as a promising alternative for protection methods.

Indeed, of the 22,000 bioactive molecules isolated from microorganisms, about half of these molecules are produced by actinobacteria, in particular the genus Streptomyces, which alone provides 70% of antibiotics, mainly found in the soil, can be considered the most competent bacterium in nature, which produces many and varied secondary metabolites.

The major interest in actinobacteria is their ability to produce metabolites secondary to different biological activities, namely, antibiotics, antifungals, ... They are recognized by their PGPR activities (stimulation of plant growth, production of Indole-3-acetic acid, and the ability to degrade toxic substances) ...

Keywords: Actinobacteria; bioactive molecules; biological control; phytopathogenes.

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UNVEILING ADAPTIVE COMPONENTS FOR ENVIRONMENTAL HETEROGENEITY IN *Ipomoea carnea* Jacq.

ABSTRACT

Environmental heterogeneity is an important factor that affects species richness and provides conditions for adaptation of existing species. Factors affecting the diversity gradient are climatic variation, biotic interactions, territory, ambient vigor, productivity, available water resources and some other factors that direct the historical process by the evaluation of climatic history and phylogeny of niche conversation. Naturally adapted populations of *Ipomoea carnea* Jacq. were collected from various ecological regions of Punjab province to investigate their adaptive components that have been developed under heterogeneous environmental conditions. Multivariate redundancy analysis (RDA) and correlation analysis were done to evaluate the association of soil physiochemical features with different morpho-anatomical and physiological characteristics. *I. carnea* is an invasive species that can rapidly grow, spread and adapt from xerophytic to aquatic habitats. This species showed better growth and biomass production near water bodies. Additionally, it also exhibited some specific anatomical modifications such as aerenchyma formation, sclerification, xylem ray thickness, leaf thickness and large metaxylem area that enable it to survive under harsh environmental conditions. Populations from highly saline habitats showed higher value of osmolytes and ionic contents (K^+ and Ca^{2+}).Furthermore, the populations from highly saline areas also exhibited the maximum uptake of Na^+ content and the lowest uptake of K^+ and Ca^{2+} content. In conclusion, *I. carnea* showed very specific modifications in morpho-anatomical and physiological traits that reveal its ecological success from aquatic to xerophytic habitats.

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NITRATE ION (NO3-) LEVELS IN FRUITS AND VEGETABLES IN THE CITIES OF PRISHTINA AND GRAÇANICA WERE MEASURED USING THE "Green Test ECO 5 F -ANMEZ" EQUIPMENT

ABSTRACT

This study uses the "Green Test ECO 5 F-ANMEZ" instrument to measure the amount of nitrate ions (NO3-) in fruits and vegetables in Kosovo cities including Prishtina and Gracanica. In order to assess physical and chemical characteristics, such as pH, sugar content, and nitrate levels, in ten distinct plant products, the monitoring was conducted for approximately a month at six sampling locations at nearby marketplaces and warehouses. The purpose of our study is to assess how storage conditions affect the physico-chemical and organoleptic characteristics of fruits and vegetables. With the exception of a few instances of high nitrate levels in fruits like melons and other vegetables, our data demonstrated that nitrate concentrations in the majority of samples were within the allowed limits.

Additionally, by tracking changes in pH, sugar content, and structure over time, our study assessed how refrigeration affected the way fruits and vegetables were stored. Overall, our research indicates that the majority of products satisfy WHO-established local and worldwide quality criteria, and that handling and storage practices are critical to preserving the safety and quality of these agricultural products.

Keywords: refrigeration, pH, nitrate concentration, nitrate ions, fruits and vegetables, Prishtina, Gracanica, Green Test ECO 5 F-ANMEZ, and food quality requirements.

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EVALUATING ASEPTIC INTERVENTIONS AND CATHETER MANAGEMENT STRATEGIES TO PREVENT CATHETER-ASSOCIATED INFECTIONS IN NEONATES

ABSTRACT

Objective: Catheter-associated infections (CAIs) pose a significant challenge in neonatal care, particularly in infants with peripheral venous catheters (PVCs). These infections are frequently caused by Staphylococcus aureus, including methicillin-resistant strains (MRSA), and can lead to extended hospitalizations and serious complications. This study aims to identify the risk factors contributing to CAIs, with an emphasis on catheter insertion duration, aseptic technique adherence, and bacterial species involved. Additionally, it evaluates the role of catheter management and infection control measures in preventing infections in neonatal care units.

Materials and Methods: The study involved 116 neonates from neonatal intensive care units (NICUs), all of whom had PVCs for a minimum of 24 hours. Microbiological samples were collected from the distal end of each catheter upon admission and during catheter removal, following strict aseptic protocols. Bacterial load was measured using the Cleri-Brun-Buisson quantitative culture method, and bacterial species were identified according to EUCAST 2024 guidelines. Antibiotic susceptibility testing, including detection of MRSA through cefoxitine resistance, was also conducted. A catheter tracking sheet was used to gather detailed data on catheter placement, duration, and removal reasons. Compliance with aseptic protocols was evaluated using an aseptic practice monitoring sheet, which helped to identify any connections between lapses in technique and infection occurrence. Statistical analysis, including chi-square tests and logistic regression, was conducted using SPSS to evaluate the risk factors for CAIs.

Results: A total of 200 samples were collected for analysis. The findings revealed a variety of bacterial species colonizing the catheter tips, with Bacillus and Staphylococcus species being the most prevalent. While other bacterial species were also detected, Staphylococcus aureus, particularly methicillin-resistant strains, was identified in a significant number of cases. The study found a clear correlation between longer catheter insertion durations and increased bacterial colonization. Moreover, data analysis from the catheter tracking and aseptic practice monitoring sheets showed that breaches in aseptic techniques were associated with higher bacterial colonization rates. Statistical analysis confirmed that longer catheter dwell times and failure to adhere to aseptic protocols were significant risk factors for the development of infections.

Conclusion: The findings of this study underscore the crucial importance of effective catheter management and strict adherence to aseptic protocols in preventing CAIs in neonatal care settings. The wide variety of bacterial species found highlights the complexity of infection control in these units. The study supports the need for enhanced infection control measures, consistent adherence to aseptic practices, and continuous monitoring of catheter management to reduce the incidence of CAIs in neonatal intensive care units.

Keywords: Catheter-associated infections, Staphylococcus aureus, Bacillus species, Methicillin-resistant S. aureus (MRSA), Neonatal care, Aseptic techniques, Infection control, Neonatal intensive care unit (NICU), Catheter management, Aseptic practice compliance.

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BACTERIAL COLONIZATION AND INFECTION RISKS IN NEONATAL CARE: FOCUS ON PERIPHERAL VENOUS CATHETER MANAGEMENT

ABSTRACT

Purpose: Catheter-associated infections (CAIs) represent a major challenge in neonatal care, particularly in neonates with peripheral venous catheters (PVCs). These infections, often caused by *Staphylococcus aureus*, including methicillin-resistant *S. aureus* (MRSA), can result in prolonged hospital stays and severe complications. This study aims to identify the risk factors associated with CAIs, focusing on catheter insertion duration, aseptic practices, and the bacterial species involved. It also seeks to assess the role of catheter management and infection control strategies in preventing infections in neonatal care units.

Materials and Methods: The study involved 116 neonates from neonatal intensive care units, each with a PVC in place for at least 24 hours. Microbiological samples were collected from the distal ends of catheters upon admission and at the time of catheter removal, following aseptic protocols to ensure sample integrity. Samples were analyzed using the Cleri-Brun-Buisson quantitative culture method to measure bacterial load. Bacterial species were identified following EUCAST 2024 guidelines, and antibiotic susceptibility testing, including resistance to cefoxitine for MRSA detection, was performed. To assess catheter management, a catheter tracking sheet was used to gather detailed information on catheter placement, duration, and removal reasons. An aseptic practice monitoring sheet was also employed to evaluate compliance with aseptic protocols and identify any potential links between lapses in aseptic technique and infection occurrence. Statistical analysis was performed using SPSS, including chi-square tests and logistic regression to evaluate risk factors for CAIs.

Results: A total of 200 samples were collected. The results indicated a diversity of bacterial colonization, with *Bacillus* species and *Staphylococcus* species being the most common pathogens found on the catheter tips. Other bacterial species were also detected, but *Staphylococcus aureus* was present in a significant proportion of the cases. The study identified a correlation between longer catheter insertion durations and increased bacterial colonization. Furthermore, the analysis of clinical data using the catheter tracking and aseptic practice monitoring sheets showed that lapses in aseptic techniques were associated with higher bacterial colonization rates. Statistical analysis revealed that prolonged catheter duration and non-compliance with aseptic protocols were significant risk factors for the occurrence of infections.

Conclusion: This study highlights the importance of effective catheter management and strict adherence to aseptic techniques in preventing catheter-associated infections in neonatal care. The diversity of bacterial colonization observed emphasizes the complexity of infection control in these settings. The findings support the need for improved infection control strategies, adherence to aseptic practices, and continuous monitoring of catheter management to reduce CAIs in neonatal intensive care units.

Keywords: Catheter-associated infections, *Staphylococcus aureus*, *Bacillus*, Methicillin-resistant *S. aureus* (MRSA), Neonatal care, Aseptic techniques, Infection control, Neonatal intensive care unit (NICU), Catheter tracking, Aseptic compliance.

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NEUROPROTECTIVE EFFECTS OF *Rosmarinus officinalis* ETHANOLIC EXTRACT ON COGNITIVE-AFFECTIVE FUNCTIONS AND HIPPOCAMPUS OXIDATIVE STRESS IN WISTAR RATS EXPOSED TO CADMIUM

ABSTRACT

Rosmarinus officinalis is a plant used in the Mediterranean diet and traditional medicine with various antioxidant and cytoprotective bioactivities. The study aims to investigate the neuroprotective effect of the ethanolic extract of Rosmarinus officinalis against cognitive-affective functions and oxidative stress in Wistar rats exposed to Cadmium (Cd).

18 rats of each sex were distributed into three groups: group 1: control): NaCl saline solution (0.9%); group 2: Cd-1 mg/kg + ED; group 3: Cd-1 mg/kg + 200 mg/kg of the ethanolic extract of Rosmarinus officinalis were administered daily for 8 weeks. After the treatment period, the animals were tested in the Y-maze to assess working memory and the Morris water maze to assess learning and spatial memory. The 1 mg/kg dose of Cd+ ED causes impairments in spatial learning and memory in both sexes. In the Y-maze and Morris water maze tests, both males and females expressed a low percentage of alternations, and spatial learning and spatial memory were significantly impaired, suggesting that working memory, learning and spatial memory were affected by Cd at the 1 mg/kg dose + ED. Cd decreased the level of catalase and increased the level of NO in the hippocampus significantly in both sexes ($p < 0.01$). In rats treated with 1 mg/kg of Cd+ or 200 mg/kg of EERO, males and females had high levels of alternation percentages, and spatial learning and memory were improved, with elevated catalase levels and low NO concentrations in the hippocampus in both sexes.

Rosmarinus officinalis exerted a powerful positive effect against Cd-induced cognitive impairment through its antioxidant activity, improving spatial learning and memory.

Keywords : Rosarinus officinalis, cadmium, cognitive affective function, oxidative stress, rats.

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DOSE-DEPENDENT EFFECTS OF CADMIUM ON ANXIETY-LIKE AND DEPRESSIVE-LIKE BEHAVIORS AND OXIDATIVE STRESS IN THE PREFRONTAL CORTEX OF FEMALE RATS

ABSTRACT

Cadmium is a heavy metal that represents a human health problem since daily intake through food, water, and simple inhalation (smoking and occupational exposure) exposes humans to this metal. Several studies have shown a direct effect between cadmium exposure and the development of neurodegenerative disorders. The objective of this study was to assess the dose-dependent effect of this metal on anxiety-like and depressive-like behaviors and oxidative stress in the prefrontal cortex of female rats.

administering daily subcutaneous injections of four different doses of 25, 50, 75 and 100 mg/kg CD while a control group received 0.9% NaCl. Based on behavioral tests (open field, elevated plus maze and forced swimming), behavioral alterations were detected, particularly anxiety levels and depressive-like behavior. Simultaneously, hippocampal oxidative stress markers (catalase, nitric oxide and lipid peroxidation) were assessed to elucidate the involvement of oxidative stress (OS) in the observed effects.

The results show a clear dose-dependent effect of Cd, revealing increased anxiety and depressive-like behaviors at doses of 75 and 100 mg/kg after subchronic Cd exposure. Notably, OS markers showed discernible alterations only at 75 and 100 mg/kg, with no significant variation observed at lower doses (25 and 50 mg/kg).

Our study confirms the dose-dependent effect of Cd exposure, implicating prefrontal cortex OS markers as potential contributors to the observed neurobehavioral changes. Thus, our results highlight OS as a plausible mechanism explaining the underpinnings of the neurotoxic effects observed after cd exposure.

Keywords : Cadmium, dose-dependant, oxidative stress, prefrontal cortex, rats.

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FOSTERING AN INTERDISCIPLINARY AND INNOVATIVE APPROACH TO MEDICAL SCIENCES, HEALTH SCIENCES, AND BIOLOGY: UNITED NATIONS' SUSTAINABLE DEVELOPMENT GOALS INITIATIVE AND EUROPEAN PARTNERSHIP ERA4HEALTH

ABSTRACT

To begin with, United Nations' Sustainable Development Goals initiative emphasizes the paramount role played by knowledge sharing, research collaboration, and partnerships for the goals in fostering innovation, enhancing pivotal connections, and vital expertize in maximizing an interdisciplinary approach to medical sciences, health sciences, and biology research and development programs in universities. The current research delves into the analysis of the importance and role of interdisciplinary and innovative approach to medical sciences, health sciences, and biology, highlighting the reasons why it has become important these days to foster science for all in order to cope with the health issues as well as the environmental problems. What is more, the study centers on several recent reports published by reputable international organizations which address the challenges in achieving the Global Goals, by encouraging trans-disciplinary and interdisciplinary approaches to transformational sustainability by exploring different ways of strategizing sustainability. Furthermore, the focal point is on assessing the benefits and challenges of the European Research Area for Health (ERA4Health). The outcomes of the paper are: firstly, the international reports prompt to the necessity of universities to have interdisciplinary approaches in order to foster the students' keen interest in the dynamic fields of medical sciences, health sciences, and biology, since the links with the economic, financial, and social approaches have become vital; secondly, meaningful connections ought to be made with the help of connected educational curriculum, between topics such as healthcare, medicine, biology, biosciences, leadership, economics, and management; thirdly, the European Partnership addressing ERA4Health is seen as a leading European initiative that encourages creating common research and innovation programs that target effectively health and that involve actively European funding organizations.

Keywords: Medical Sciences; Health Sciences; Biology; European Research Area for Health (ERA4Health); Sustainable Development Goals; Research and Development Programs; Medical Research Publishing; Healthcare; Life Sciences; Environmental Solutions; Universities; Horizon Europe; Public Institutions.

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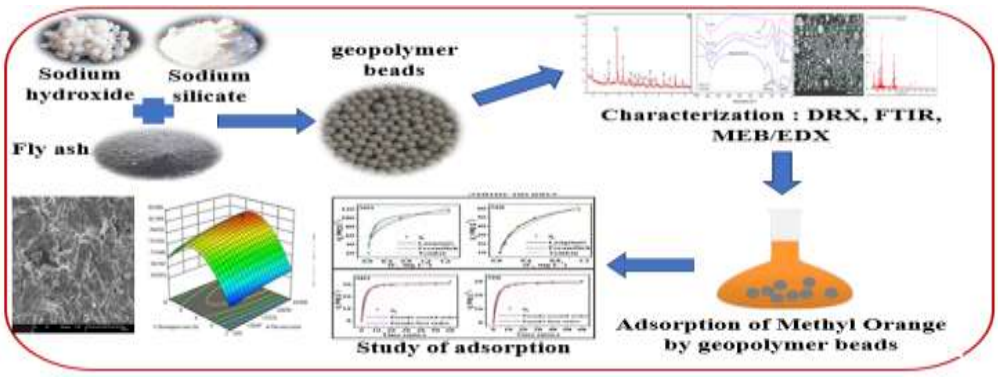
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THE APPLICATION OF SYNTHESIZED GEOPOLYMER WASTE RED CLAY-BASED FOR THE REMOVAL OF ANIONIC DYE FROM INDUSTRIAL WASTEWATER

ABSTRACT

Discharges of various micropollutants (organic and inorganic) into the environment are on the increase. These pollutants are generally toxic, poorly biodegradable, and cause numerous adverse health effects. In this context, this work focuses on the development of a geopolymer based on red clay waste, with a view to its application as an adsorbent in the treatment of an aqueous medium contaminated by Methyl Orange. The synthesized geopolymer was characterized by various analytical techniques. The raw material and the synthesized geopolymers were characterized by various physico-chemical methods. The results of XRF, XRD, and FTIR confirmed the successful synthesis of geopolymer beads, while the SEM/EDX findings revealed the homogeneous surface of the adsorbents. Adsorption tests were carried out by varying various parameters likely to affect adsorption performance, including adsorbent dose, solution pH, contact time, initial Methyl Orange concentration, and solution temperature. The kinetic study revealed that the geopolymer eliminates Methyl Orange relatively quickly. The pseudo-second-order model is the most suitable for presenting the adsorption mechanism. The isotherm for Methyl Orange retention on geopolymer is in perfect agreement with the Langmuir model. Evaluation of the thermodynamic quantities showed that the Methyl Orange adsorption process is favorable, spontaneous, and endothermic. The results we have found allow us to predict that the use of these new generations of geopolymers offers great potential for the retention of cationic textile dyes.

Keywords: Adsorption; red clay waste; Geopolymer Beads; Methyl Orange



Title: geopolymer beads synthesis, characterization, and study of adsorption.

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SIGNAL PROCESSING TECHNIQUES FOR NEUTRON-GAMMA DISCRIMINATION IN SCINTILLATORS

ABSTRACT

Neutron spectrometry using scintillation detectors has gained widespread adoption in radiation detection and medical science, particularly in radiation diagnosis and radiation therapy. These detectors are highly efficient in detecting neutrons across a broad energy spectrum, cost-effective, and feature a straightforward design that facilitates maintenance and operation. Despite these advantages, a critical challenge remains in accurately distinguishing neutron signals from accompanying gamma radiation, which is essential for precise radiation diagnosis and effective radiation therapy treatment planning. Addressing this challenge, various techniques have been proposed to differentiate neutrons from gamma radiation. This work reviews neutron-gamma discrimination methods using different types of organic scintillators and compares these methods based on their accuracy and the type of detector used. Additionally, potential recommendations for the research community are provided.

Keywords: Neutron-gamma discrimination, Machine learning, Pulse Shape discrimination, Scintillation detectors

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ENDOWMENT CONCEPT AS THE SUPPLY OF MEDICAL CARE: AN EXPLORATORY STUDY ON SUSTAINABILITY OF HEALTH INSURANCE AT HIGHER INSTITUTIONS

ABSTRACT

Important here is the term endowment, meaning the devotion of assets or properties, either directly or indirectly, to any charitable or religious institution or cause, or to secure advantage or benefit for a person or persons. The purpose of this study is to explore and represent the importance and utility of an endowment form of sustenance for the infrastructures and/or amenities necessary for beneficiaries at higher institutions. However, the specific aims and objectives of this study are to ensure the availability and sustainability of standardized health services at Khazar University by the application and implementation of a policy of endowment. Khazar University is undoubtedly among the world's fastest growing young universities. Obviously, the university strives endlessly to provide services of global standard to meet the challenges involved in competing with older, well established universities around the world. The study is exploratory in nature and applies a phenomenological approach in presenting the concept of endowment and how it is practiced at many world class universities to provide and sustain the necessary facilities at their various institutions of higher education. Following exploration, this study proposes that stakeholders of Khazar University use endowment to upgrade the university's health and medical services to an advanced level. The study highlights the practical experience of endowment-based universities in different part of the world, including: Al-Azhar University in Egypt; the University of Cordova in Spain; IIU- the Islamic University of Indonesia; universities founded in Turkey; the King AbdulAziz University, and many universities in Malaysia, of which the present study focuses on the International Islamic University, Malaysia.

Keywords: endowment; sustainability, medical care; health center; health insurance; higher institutions.

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COMPUTATIONAL AND BIOINFORMATICS INVESTIGATION OF NOVEL $GABA_A$ LIGANDS WITH ANTICONVULSANT ACTIVITY

ABSTRACT

Epilepsy remains one of the most prevalent neurological disorders, with current antiepileptic drugs often limited by toxicity, resistance, or lack of efficacy. In this study, we used a bioinformatics-based in silico approach to explore the anticonvulsant potential of newly designed molecules inspired by literature-reported compounds. Molecular docking was performed to assess binding affinities toward the $GABA_A$ receptor, a key mediator of inhibitory neurotransmission in the brain and a validated target in epilepsy treatment. The best-ranked molecules were further analyzed via molecular dynamics simulations to evaluate the stability of ligand-receptor interactions. ADMET predictions were conducted to assess pharmacokinetic properties and drug-likeness. This integrated bioinformatics strategy enabled the identification of promising $GABA_A$ modulators, laying the groundwork for future development of safe and effective anticonvulsant agents.

Keywords: Bioinformatics, Anticonvulsant agents, Molecular Docking, $GABA_A$, ADMET, Molecular Dynamics.

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EVALUATION OF BLOOD–BRAIN BARRIER PERMEABILITY AND CNS DRUG POTENTIAL OF HYDRAZONE ESTER DERIVATIVES

ABSTRACT

Crossing the blood–brain barrier (BBB) is a critical requirement for compounds intended for central nervous system (CNS) therapy. In this in silico study, four hydrazone-based ester derivatives were assessed for their ability to penetrate the BBB and exhibit pharmacological activity within the CNS. All four molecules—three methyl esters with varied aromatic substitution and one ethyl ester—were predicted by SwissADME to be **BBB permeable**, indicating that their physicochemical properties fall within CNS-accessible limits. The **topological polar surface area (TPSA)** of 50.69 Å² for all compounds is well below the typical BBB cutoff of 90 Å². In addition, their **moderate lipophilicity** (Log P values between 2.93 and 3.61) supports passive diffusion across lipid-rich biological membranes. These features are further supported by the compounds' small size (MW < 500 g/mol) and low flexibility (5–6 rotatable bonds), optimizing membrane crossing efficiency. The radar plots reinforce this balance between lipophilicity and polarity, placing all four derivatives in the favorable absorption and CNS-permeant zones. These findings suggest that the studied hydrazone esters not only have oral bioavailability but also possess potential for CNS-targeted therapeutic applications, warranting further biological evaluation in neuropharmacology.

The table below summarizes the key findings:

Molecule	TPSA (Å²)	BBB Permeant	Log P	GI Absorption
Mol 1	50.69	Yes	2.93	High
Mol 2	50.69	Yes	3.29	High
Mol 3	50.69	Yes	3.61	High
Mol 4	50.69	Yes	3.29	High

Keywords- Blood–brain barrier, CNS penetration, hydrazone esters, TPSA, Log P, SwissADME, neuropharmacology, oral drugs, passive diffusion

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CHARACTERISTICS OF HEART RATE VARIABILITY DEPENDING ON BLOOD PRESSURE LEVEL

ABSTRACT

A positive correlation between the level of arterial pressure and the risk of cardiovascular complications has been demonstrated. Disorders in the autonomic regulation of cardiac activity play a significant role in the development of fatal complications. Numerous studies have shown results associated with an increase in sympathetic activity and a proportional decrease in vagal inhibition.
Analysis of heart rate variability (HRV) reflects the neurohumoral regulation of the heart and allows for the prediction of complications such as fatal arrhythmias and sudden cardiac death.

The aim of the study was to investigate the characteristics of comparative HRV periodic and spectral parameters among individuals with different blood pressure levels.

Materials and Methods. The study was conducted between 2019 and 2024. Data were collected from 90 individuals aged 19–59 years in an outpatient setting. The participants were divided into three groups:

- **Main group**: Individuals with high normal arterial pressure (HNAP) — systolic arterial pressure (SAP) 130–139 mmHg and/or diastolic arterial pressure (DAP) 85–89 mmHg (n=30);
- **Comparison group**: Individuals with grade I arterial hypertension (HTN) — SAP 140–159 mmHg and/or DAP 90–99 mmHg, with no prior cardiovascular complaints, whose condition was incidentally detected and who had received no treatment before the study (n=30);
- **Control group**: Individuals with normal blood pressure — SAP 120–129 mmHg and/or DAP 80–84 mmHg (n=30).

All participants underwent a standard 12-lead ECG recording for 5 minutes at relative rest during the first half of the day. HRV assessment was performed according to standard measurement units, physiological interpretation, and clinical application standards.

Results. In the group with HNAP, when compared to the control group, HF (high-frequency component) decreased by 4.3% ($p>0.05$), while both LF (low-frequency component) and the LF/HF ratio showed a tendency to increase by an average of 33.0%. A statistically significant difference was found between the groups for LF and LF/HF values ($p<0.05$).

In the group with hypertension, HF decreased by 35.2% compared to the control group ($p>0.05$), LF increased by 30.1% ($p<0.05$), and the LF/HF ratio increased by 118.1% ($p<0.01$), indicating a significant strengthening of sympathetic effects in this group.

When comparing the main group (HNAP) with the hypertension group, HF was 47.6% higher, LF was 7.5% lower, and LF/HF was approximately 40% lower in the main group. A statistically significant difference was found between the groups for HF and LF/HF values ($p<0.05$).

In the analysis of periodic parameters, in the HNAP group compared to the control group, SDNN decreased by an average of 10.0%, RMSSD decreased by 46% ($p<0.05$), and pNN50 decreased by 22.4%, although no statistically significant difference was observed for SDNN and pNN50 ($p>0.05$). In the hypertension group, SDNN decreased by 30.0%, RMSSD by 55.7%, and pNN50 by 33.0% compared to the control group. Statistically significant differences were found between groups for both SDNN and RMSSD values ($p<0.05$). When comparing the main group (HNAP) with the hypertension group, SDNN was 28.7%, RMSSD 22.0%, and pNN50 16.0% higher in the main group, but no statistically significant difference was found between the two groups ($p>0.05$).

Both in individuals with HNAP and those with hypertension, a decrease in SDNN (the most important periodic parameter) and an increase in the LF/HF index (characterizing sympatho-vagal balance) were observed, indicating a shift towards sympathetic dominance in autonomic regulation. Moreover, the tendency toward a decrease in pNN50 in both groups suggests reduced intensity of parasympathetic modulation.

Conclusion. Our results show a positive correlation between blood pressure levels and HRV, reflecting inadequate sympatho-vagal activity and impaired neurohumoral regulation of cardiac function, serving as predictors for ventricular tachyarrhythmias and sudden cardiac death.

Thus, the use of a non-invasive, simple, and accessible method like short-term ECG recording allows for early detection and monitoring of individuals with high cardiovascular risk based on HRV analysis among those with elevated blood pressure levels.

Keywords: heart rate variability, blood pressure, autonomic regulation

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ENDOTHELIN-1 DYSREGULATION AND ITS ASSOCIATION WITH ENDOTHELIAL DYSFUNCTION: A CROSS-SECTIONAL PHYSIOLOGICAL ANALYSIS

ABSTRACT

Background: Endothelin-1 (ET-1), a potent vasoconstrictor peptide, plays a critical role in vascular homeostasis. Dysregulation of ET-1 is implicated in endothelial dysfunction, which contributes to various cardiovascular and renal pathologies. This study aimed to evaluate the relationship between circulating ET-1 levels and endothelial function in a healthy and pre-hypertensive adult population.

Methods: A total of 120 participants (mean age: 44.6 ± 11.2 years; 60 men and 60 women) were enrolled in this cross-sectional study. Plasma ET-1 levels were measured via ELISA. Endothelial function was assessed using flow-mediated dilation (FMD) of the brachial artery. Correlation and regression analyses were conducted to evaluate associations. Statistical significance was set at $p < 0.05$.

Results: ET-1 levels were significantly higher in the pre-hypertensive group (n=60) compared to normotensive controls (4.12 ± 0.63 pg/mL vs. 2.86 ± 0.49 pg/mL; $p < 0.001$). FMD values were inversely correlated with ET-1 levels ($r = –0.61$, $p < 0.001$). Multivariate regression analysis showed that ET-1 was an independent predictor of impaired endothelial function ($\beta = –0.52$, 95% CI: –0.67 to –0.38, $p< 0.001$), even after adjusting for age, BMI, and lipid profile.

Conclusion: Elevated plasma ET-1 levels are strongly associated with reduced endothelial function, suggesting that endothelin dysregulation may serve as an early biomarker and potential therapeutic target in pre-hypertensive individuals. Further interventional studies are warranted to evaluate ET-1 modulation strategies in preserving vascular health.

Keywords: endothelin-1, flow-mediated dilation, endothelial dysfunction

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INFECTIONS AROUND THE PROSTHESIS

ABSTRACT

Osteoarthritis and arthroplasties are increasing worldwide. The average lifetime risk of revision surgery after arthroplasty is 5%. Periprosthetic infections are an important cause of revision surgery and their diagnosis is critical in treatment planning. Magnetic resonance imaging (MRI) is the most sensitive radiological imaging method for showing both joint and bone infection; however, radiographs can be used at the beginning and follow-up, and computed tomography and ultrasonography can also be used in cases where MRI is not available.

Introduction. Osteoarthritis (OA) is among the top ten disabling diseases worldwide. According to the World Health Organization's 2024 estimates, 10% of men and 18% of women over the age of 60 will report moderate or severe symptomatic OA. The most affected large joints are the hip, knee, and shoulder [1,2]. Hip, knee, and shoulder arthroplasties are effective surgical methods frequently used to correct joint function and quality of life loss due to primary or secondary OA. According to the data of the member countries of the Organization for Economic Co-operation and Development (OECD), the rate of hip arthroplasty increased by 22% and the rate of knee arthroplasty increased by 35% between 2009-2019; shoulder arthroplasties, although performed less frequently than hip and knee, increased at least 5-fold between 2017-2024 in the USA [2,3]. These data are an indirect indication that the number of patients screened for arthroplasty complications will increase.

Although pain reduction and function recovery are achieved after arthroplasty, the average lifetime risk of revision surgery is 5% for all patients. This risk can be as high as 35% in male patients under the age of 50. Although the reasons for revision surgery vary, the main ones are aseptic loosening (55%) and periprosthetic infections (8%) [4,5]. The European Association of Radiology, the European Association of Nuclear Medicine, the European Association of Bone and Joint Infections, and the European Society of Clinical Microbiology and Infectious Diseases have reported an algorithmic approach to the diagnosis of periprosthetic bone and joint infections with consensus [6, 7]. The distinction between aseptic loosening and periprosthetic infection is important due to the difference in surgical approaches. Periprosthetic infection should be suspected if one or more of the following signs are persistent local pain, erythema, swelling, impaired wound healing, and fever. In chronic infections that develop years after arthroplasty, none of the clinical findings may be present, or the only findings may be ongoing or increasing pain and loosening of the prosthesis. In the suspected periprosthetic infection, the examination flow chart primarily includes blood culture, C-reactive protein, erythrocyte sedimentation rate, white blood cell count, radiography, and analysis of the discharge from the sinus tract. If the suspicion

persists as a result of these (some tests may need to be repeated several times), bone or soft tissue biopsy or imaging-guided aspiration or advanced radiologic and nuclear medicine imaging should be used. Both magnetic resonance imaging (MRI) and leukocyte-labeled scintigraphy are the imaging methods with the highest diagnostic performance in the diagnosis of periprosthetic infections (nuclear medicine examinations are not within the scope of this review). The most appropriate imaging method depends on many variables, such as patient benefit, local experience, cost, and accessibility. In this review, we will focus on the findings that can be detected in radiographs, ultrasonography, computed tomography (CT) and MRI used in imaging periprosthetic infections and the advantages and limitations of these methods.

Conclusion. The most sensitive radiological method for diagnosing periprosthetic bone and joint infections is MRI, which uses techniques to reduce metal artifacts. Periprosthetic osteomyelitis or complex effusion in the joint, capsular edema (edematous synovitis or lamellar hyperintense synovitis), pericapsular edema, fluid loculations in soft tissues and periosteal reaction, as well as increased number and size of regional lymphadenopathies (maximum lymph node diameter ≥17 mm) and, although rare, sinus tracts between the skin and pseudocapsule or implant are findings with high specificity in diagnosing periprosthetic infection.

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COMPLICATIONS ASSOCIATED TO REMOVABLE DENTURES WITH IMPROPER USE AND POOR ORAL HYGIENE

ABSTRACT

Introduction. The importance of oral care and its relationship with an individual's well-being has been identified over the past few decades. As there is a drastic increase in the aging population, so did the use of removable dentures more than ever before. The use of dentures among the elderly provides functional advantages and esthetic benefits. However, improper use and poor oral hygiene with removable dentures come with complications, including denture stomatitis, ulcerations, pneumonia, and many more. The study aims to determine the complications associated with inappropriate use and poor oral care and bring forth evidence-based dentist-recommended guidelines for denture maintenance.

In this study, we have seen pathological biofilm formation on dentures, life-threatening pneumonia, denture stomatitis, and accidental ingestion/aspiration of dentures amongst the elderly population. The study also identified members with low literacy rates, minorities, and low-income families seem to be at higher risk of poor oral care and denture hygiene. We identified that most of these complications could be prevented with proper guidance and education. In the future, a further detailed study is important as no clear consensus exists in terms of best practices of denture cleaning methods. In addition, measures should be initiated to encourage regular dentist appointments and increase accessibility among members of low socioeconomic status and minorities.

In the elderly population, dentures provide functional and cosmetic benefits. However, wearing dentures comes with some risks: ill-fitting dentures, incorrect use, and poor oral hygiene can result in irritation of the gums and oral mucosa, ulcerations, and denture stomatitis [1]. Denture surfaces have also been identified as a reservoir for various pathogenic organisms. Aspiration pneumonia, halitosis, infective endocarditis, septic meningitis, and other complications can result from biofilm formation. In addition, accidental aspiration and ingestion of dentures are also more common in the elderly; potential risk factors include alcoholic intoxication, advancing dementia, stroke, and epilepsy [2,3,4]. Necrosis, perforation, ulceration, fistula formation, penetration of neighboring organs, bleeding, and obstruction are risks associated with ingesting dentures [5].

Method. These clinical situations and life-threatening complications may be merely prevented with proper guidance from medical professionals, including primary care providers, dentists, and dental hygienists. Even though more education is required, relatively little information is accessible about appropriate, evidence-based techniques for cleaning

dentures and their optimal use [6]. According to studies, at least 40% of senior patients do not disinfect properly or remove their dentures at night, and serious pneumonia occurrences are twice as frequent in these individuals. Hence, professional advice on proper denture use and cleaning is essential for all users, particularly the elderly and their caregivers [6].

The lack of proper education among denture users and the lack of routine dental care services among the underserved and elderly worsen the problem further. Many older individuals cannot pay for the preventive and rehabilitative care they require. Improving patients' oral health literacy personally may also be necessary to avoid and prevent future issues.

Oral health is crucial for various aspects of life, including eating, talking, self-esteem, social interaction, and freedom from pain. Poor oral care can result in plaque formation, gingival irritation, halitosis, dental caries, periodontal diseases, tooth loss, and systemic illnesses such as pneumonia, complications from diabetes, and even death.

Many pathogens were identified in removal dentures, such as *Escherichia coli*, *Klebsiella pneumoniae*, *Enterobacter cloacae*, and Gram-negative bacilli (Enterobacteriaceae and nonfermenting) were significantly more in denture wearers compared to the control group without denture usage. These pathogenic species may cause infections that can disseminate to other body parts. Oral health measures should be implemented to reduce the risk of cross-infection in individuals with removable dentures.

The relationship between the aspiration of oral bacteria and pneumonia is very heavily supported; the increased incidence of stroke, cognitive decline, and dysphagia further increase the risk of aspiration pneumonia among the aging population. Three studies in our systemic review discussed the use of dentures and their subsequent increase in pneumonia risk.

Conclusions. This systematic review analyzed inappropriate denture use and poor oral hygiene in the elderly population using removable dentures. Our study highlighted the complications associated with improper use of dentures. Through our review, we have seen pathological biofilm formation on dentures, life-threatening cases of pneumonia, denture-related stomatitis, and accidental ingestion/aspiration of dentures amongst elderly populations. Most of these complications can be easily prevented with proper guidance and education. However, it is unfortunate that the majority of the elderly population and their caregivers are not adequately educated about proper cleaning techniques by their dental providers. In addition, there is also a wide inequality of access to dental care by patients on Medicaid or individuals of minority groups, complicating care even further. Oral hygiene and well-being significantly impact an individual’s social, physical, and psychological status. Therefore, addressing these issues is important to society more than ever before. In the future, a further detailed study should be conducted as no clear consensus exists in terms of the best practice of denture cleaning methods. In addition, measures should be initiated to encourage regular dentist appointments and increase accessibility among members of low socioeconomic status, low literacy rate, and minorities.

Keywords: oral diseases, oral health care, removable denture, poor oral hygiene.

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BIOPHYSICAL PROPERTIES OF THE CELL MEMBRANE AND DRUG TRANSPORT

ABSTRACT

Introduction

The cell membrane is one of the fundamental structural units of life. Its biophysical properties play a crucial role not only in maintaining the internal stability of the cell but also in regulating interactions with the external environment. The structure and physical characteristics of the cell membrane directly affect the processes of drug entry into and exit from the cell. This article systematically explains the biophysical properties of the cell membrane and the mechanisms of drug transport.

Structure of the Cell Membrane

The cell membrane primarily consists of a lipid bilayer, proteins, and carbohydrate components. The main structural elements are phospholipids. These molecules are arranged with their hydrophobic tails facing inward and their hydrophilic heads oriented toward the extracellular and intracellular environments.

From a biophysical perspective, the membrane is: selectively permeable, highly fluid, asymmetric in structure

These features directly influence the membrane's ability to interact with and allow the passage of drug molecules.

Biophysical Properties of the Cell Membrane

1. Membrane Fluidity. Membrane fluidity depends on lipid composition, the ratio of saturated to unsaturated fatty acids, and cholesterol content. Higher fluidity facilitates the diffusion and absorption of drugs across the membrane.

2. Selective Permeability, the membrane controls the passage of ions, nutrients, and drug molecules. Small, nonpolar molecules (e.g., oxygen, carbon dioxide) can pass freely, while larger and polar substances require specific carrier proteins or channels.

3. Electrical Potential and Polarization, the difference in ion distribution across the membrane generates an electrical potential. This potential influences drug transport, especially for charged molecules.

4. Membrane Proteins, integral and peripheral proteins participate in substance recognition, transport, and signal transduction. These proteins serve as specific targets for many drug molecules.

Mechanisms of Drug Transport

Drug molecules cross the cell membrane through several key mechanisms:

1. Passive Diffusion, the movement of molecules from a region of higher concentration to one of lower concentration. Lipophilic drugs can easily diffuse across the membrane by this method.

2. Facilitated Diffusion, transport across the membrane aided by carrier proteins. It does not require energy expenditure. For example: Glucose transport.

3. Active Transport. The movement of substances against their concentration gradient, requiring energy (ATP). It is essential for transporting large or charged drug molecules.

4. Endocytosis and Exocytosis

Large drug complexes are internalized into the cell via membrane invagination (endocytosis) or expelled from the cell (exocytosis).

Impact of the Cell Membrane on Drug Effectiveness

For a drug molecule to achieve its intended therapeutic effect, it must cross the cell membrane efficiently, reemain stable inside the cell, reach and interact with its intracellular targets without premature degradation.

Thus, drug design must account for membrane interactions. Nanoparticle delivery systems, liposomes, and dendrimers have been developed to efficiently carry drugs across biological membranes and overcome membrane barriers.

Conclusion

The biophysical properties of the cell membrane are critical in determining how drugs are absorbed and transported within the body. Membrane fluidity, permeability, electrical potential, and the activity of membrane proteins directly influence drug uptake and efficacy. Modern drug design increasingly relies on these biophysical principles to develop more targeted and effective therapies.

A deeper understanding of drug transport mechanisms across cell membranes will continue to advance the development of more specific and less toxic therapeutic strategies in the future.

Keywords: electrical potential, polarization, drug transport mechanism

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MOLECULAR BASIS AND DIAGNOSIS OF INHERITED DISEASES

ABSTRACT

Introduction

Inherited diseases, also known as genetic disorders, are conditions caused by abnormalities in an individual's DNA sequence. These diseases can result from mutations in a single gene, multiple genes, or chromosomal alterations. Understanding the molecular basis of inherited diseases has profound implications for early diagnosis, effective treatment, and potential prevention. Advances in molecular biology and genomics have significantly enhanced our ability to detect and characterize these genetic abnormalities.

Molecular Basis of Inherited Diseases. The molecular foundations of inherited diseases are diverse, encompassing a wide array of genetic mutations and structural DNA changes.

1. Single-Gene (Monogenic) Disorders. Single-gene disorders result from mutations in one specific gene. Depending on the nature of the mutation and the mode of inheritance, they can be classified into:

Autosomal Dominant Disorders: Only one copy of the mutated gene is sufficient to cause the disease (e.g., Huntington’s disease, Marfan syndrome). Autosomal Recessive Disorders: Two copies of the mutated gene are necessary for disease manifestation (e.g., cystic fibrosis, sickle cell anemia). X-linked Disorders: Mutations in genes located on the X chromosome primarily affect males (e.g., Duchenne muscular dystrophy, hemophilia A).

2. Polygenic and Multifactorial Disorders. These disorders result from the combined effect of multiple genes often interacting with environmental factors. Examples include diabetes mellitus, hypertension, and many psychiatric disorders.

3. Chromosomal Disorders. Structural or numerical abnormalities in chromosomes can cause inherited diseases. Examples include: Down syndrome (trisomy 21), Turner syndrome (monosomy X), Klinefelter syndrome (XXY karyotype), Chromosomal disorders may involve deletions, duplications, inversions, or translocations of chromosomal segments.

4. Mitochondrial Disorders, Mitochondrial DNA mutations, which are inherited maternally, can lead to diseases affecting organs with high energy demands, such as the brain, muscles, and heart. Examples include Leber's hereditary optic neuropathy and mitochondrial myopathy.

Mechanisms of Genetic Mutations. Genetic mutations underlying inherited diseases may include: Point mutations: Single nucleotide substitutions (e.g., sickle cell anemia). Insertions and deletions (indels): Addition or loss of small DNA segments. Splice site mutations: Disruptions in RNA splicing leading to abnormal protein products. Expansion of trinucleotide repeats: Repeats that expand during DNA replication and cause diseases like Huntington's disease and fragile X syndrome.

Each type of mutation can lead to loss-of-function, gain-of-function, or dominant-negative effects on the protein encoded by the gene.

Diagnosis of Inherited Diseases. Accurate and early diagnosis of inherited diseases relies heavily on molecular genetic techniques, which have evolved considerably over recent decades.

1. Genetic Testing. Polymerase Chain Reaction (PCR): Amplifies specific DNA sequences for mutation analysis. Sanger Sequencing: Gold standard for identifying single nucleotide changes. Next-Generation Sequencing (NGS): High-throughput sequencing that enables the analysis of multiple genes simultaneously. Whole Exome Sequencing (WES) and Whole Genome Sequencing (WGS): Comprehensive approaches to detect mutations across all coding or non-coding regions of the genome.

2. Cytogenetic Analysis. Karyotyping: Visual examination of chromosomes to detect large-scale abnormalities. Fluorescence In Situ Hybridization (FISH): Targets specific DNA sequences on chromosomes, useful for detecting microdeletions or duplications. Comparative Genomic Hybridization (CGH): Detects submicroscopic chromosomal changes.

3. Biochemical Testing. For some inherited metabolic disorders, measuring enzyme activity or metabolite levels can aid in diagnosis (e.g., phenylketonuria).

4. Prenatal and Newborn Screening. Prenatal diagnostic techniques include:

Chorionic villus sampling (CVS). Amniocentesis. Newborn screening programs routinely test for several inherited metabolic and genetic disorders, enabling early intervention.

Advances and Future Directions. The emergence of gene-editing technologies, particularly CRISPR-Cas9, holds promise for correcting pathogenic mutations at the molecular level. Furthermore, the integration of genomics with artificial intelligence is facilitating more precise interpretation of genetic variants, leading to improved diagnostic accuracy.

Ethical considerations remain paramount, particularly regarding genetic privacy, informed consent, and the implications of predictive testing in asymptomatic individuals.

Conclusion

Understanding the molecular basis of inherited diseases has revolutionized the field of medical genetics. The development of sophisticated diagnostic tools has enabled earlier and more accurate detection of genetic disorders, ultimately leading to better management and therapeutic strategies. Continued research in genomics and molecular medicine promises to further refine our ability to diagnose, treat, and perhaps one day cure inherited diseases.

Keywords: inherited diseases, genetic mutations, chromosomal disorders

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RUBINSTEIN-TAYBI SYNDROME IN A CHILD WITH FLOATING HARBOR SYNDROME

ABSTRACT

Floating Harbor syndrome is manifested by multiple congenital anomalies, facial dysmorphism, mental retardation, neck underdevelopment, and expressive speech disorders. The incidence of the disease is 1/100,000 -1/125,000 in live births.

Clinical observation. In the patient we present, as a result of clinical symptoms and genetic examination, the diagnosis of "Floating Harbor syndrome. Rubinstein-Taybi syndrome. Pneumonia. Anemia. Post-heart surgery condition" was made.

Patient Z.F. Born on 16.07.2022, he was admitted with a diagnosis of "Pneumonia". On admission, his condition was serious, his skin was pale, his head was microcephalic, his forehead hair was increased, his nose was short, his eyebrows were dense, his eyelids were long, his upper palate was narrow, high, the distance between the fingers was wide, especially on the foot, the nail covers of both toes were split in two. He did not suck or swallow.

During bacteriological examination of the blood, Klebsiella pneumoniae was detected.

Pneumonic shadows were observed on chest X-ray examination. Full Abdomen USM: During the examination, the exogeneity of both renal pyramids was increased. Neurosonography: vascular sheath cysts, mineralizing vasculopathy were observed in normal areas. EEG examination: Disorganization of the bioelectric activity of the brain with the participation of the central lobes going to the residual background. The child was examined by a geneticist and diagnosed with Rubinstein-Taybi syndrome?, and genetic analysis was recommended.

Taking into account the above, a genetic examination was performed on the patient and "Floating Harbor syndrome. Gene mutation causing Rubinstein-Taybi syndrome" was detected. The patient was prescribed antibacterial, infusion, physiotherapy treatment and was discharged home in good condition.

If there has been a baby born with Rubinstein-Taybi or other syndromes or multiple defects in the family, as well as in consanguineous marriages, they should definitely be examined by a geneticist before planning their next pregnancy.

Keywords: Floating Harbor syndrome, Rubinstein-Taybi syndrome, congenital anomalies

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EFFECT OF VITAMIN D DEFICIENCY ON CYTOKINE SECRETION IN BACTERIAL VAGINOSIS AND AEROBIC VAGINITIS

ABSTRACT

Disruption of the ecosystem is common among all women of reproductive age. Some authors believe that non-specific vaginitis (aerobic) is a consequence of ineffective treatment of bacterial vaginosis and can cause very serious complications such as endometrit, salpingooforit, after invaziv procedures and operations inflamma complications, colpit and neoplasty processes of vaginal neck, increase the risk of abortions, overduct conglutination cause infertility, xorioamnionit, intra-amnional infection, premature. Both of patologies are polyetiological in nature and can cause quantitative and qualitative disturbances of vaginal microbial associations, leading to various complications and relapses that are always relevant in obstetrics and gynecology.

Considering the role of vitamin D in modulating immune responses and regulating adaptive immunity, in order to study the interaction between vaginal pathology and local defense factors, we determined the concentration of some proinflammatory cytokines (TNFα, IL-1β, IL-6) in blood serum and vaginal secretions in the relevant pathologies depending on the amount of vitamin D.

In the Surgical Training Clinic of AMU, maternity hospital N5 named after Sh.Aleskerova, “Referans” clinic 132 reproductive aged patients were examined and taken examinational material. 26 of examined women were healthy, 54 bacterial vagina patients (26 women had vitamin D concentration-normal, less 28), 52 vaginits patients (25 women had vitamin D concentration-normal, less 27).

Examination of the pathological materials taken was carried out in the laboratories of the Department of Clinical Biochemistry, Medical Microbiology and Immunology, Teaching Surgery Clinics of ATU and the “Referens” Clinics laboratori.

A complex of microbiological, biochemical, molecular-genetic methods was used to study the blood and vaginal smear samples taken as research material.

The amount of some proinflammatory cytokines in the blood serum of 108 patients was studied. The concentration of cytokines in the blood serum of patients belonging to group III was slightly increased, and in groups IV and V it was significantly increased compared to other groups. So, the concentration of cytokines in the blood serumwas at its maximum level in group V.

In the cervical secretin examination taken from 98 patients, the concentration of cytokines increased slightly in group II, and significantly in groups III and IV. The concentration of cytokines was at its maximum level in group V.

Thus, the increase in the concentration of proinflammatory cytokines was observed in patients with vitamin D deficiency in the relevant pathologies. In general, the highest concentration of cytokines was observed in patients with aerobic vaginitis with vitamin D deficiency.

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THE DRUG BUDESONIDE (Budenofalk®) IN THE TREATMENT OF PATIENTS WITH AN IMMUNOLOGICAL COMPONENT IN CROHN'S DISEASE AND BECHTEREW'S DISEASE

ABSTRACT

Introduction. Chronic inflammatory disease of the gastrointestinal tract known as Crohn's disease (CD) can be accompanied by damage to the peripheral joints, spine or joints and spine (Bechterew's disease) (BD). At the same time, considerable factual material has been accumulated regarding the immune status of patients with Crohn's disease (CD) with manifestations Bechterew's disease (BD), unfortunately, does not allow to answer a number of important questions and, first of all, whether the immune disorders are primary or secondary in response to chronic inflammation.

The clinical manifestations of joint syndrome are the same in both processes.

Methods. The pathogenesis of the intestinal process and damage to the joints has not been fully established, but it is believed that many mechanisms are involved, in particular, toxic, immune, autoimmune. Budesonide (Budenofalk®) is successfully used to eliminate these manifestations.

In Bechterew's disease, joint manifestations usually occur in childhood and adolescence. The development of peripheral arthritis in Crohn's disease is usually not associated with the carrier of histocompatibility antigen B27. Bechterew's disease is more common in men than in women (3:1). This disease usually develops in people who have HLA B27.

Results. Chronic inflammatory arthritis, a hallmark of several inflammatory rheumatic diseases, and inflammatory bowel disease are lifelong conditions with significant morbidity and even mortality. It is interesting that the coexistence of inflammation of the intestines and joints was found to be noticeable in spondyloarthritis, a group of interrelated rheumatological diseases and is amenable to successful complex treatment with the use of the drug Budesonide (Budenofalk®).

Discussion/Conclusion. In the absence of a positive response in the treatment of refractory forms of Crohn's disease with articular manifestations with drugs of 5-aminosalicylic acid (5-ASA) and steroids, reserve drugs are prescribed - immunosuppressants, which in some cases do not solve the problem. In the complex treatment of this category of patients, biological drugs continue to be used and the use of Budesonide (Budenofalk®) is mandatory.

Keywords: Crohn's disease, Bechterew's disease, treatment, Budenofalk®.

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AMELIORATIVE EFFECTS OF *Solanum nigrum* Methanolic LEAF EXTRACT ON SUB-LETHAL TOXICITY OF CARBON NANOTUBES IN THE BRAIN, GILLS, AND HEART OF *Cirrhinus mrigala*

ABSTRACT

This research explores the therapeutic effects of *Solanum nigrum* in treating the sub-lethal toxicity caused by carbon nanotubes in *Cirrhinus mrigala*. Carbon nanotubes used in the study were characterized using FE-SEM to confirm their size. The fish's LC_{50} was determined to be 327.65 mg/L, and then divided into three experimental doses the 10th, 20th, and 30th parts. Test groups G1, G2, and G3 were exposed to the same dosage (30th fraction) of 32.76 mg/kg of CNTs, while the Solanum nigrum extract for these groups was 30, 40, and 50 mg/L, respectively. The biochemical analysis of the plant indicated the presence of quercetin, caffeic acid, chlorogenic acid, ferulic acid, kaempferol, oxalic acid, malic acid, methyl malonic acid, malonic acid, citric acid, fumaric acid, vanillic acid, syringic acid, and cinnamic acid. The brain, gills, and heart showed various histological abnormalities, which were restored to the original histoarchitecture comparable to the control group (C), while the positive control group (T*) exhibited the most significant histological abnormalities. Solanum nigrum proved to be effective in alleviating the histological abnormalities caused by carbon nanotubes in Cirrhinus mrigala.

Keywords: Cirrhinus mrigala, Solanum nigrum, Carbon Nanotubes.

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LEAF STRUCTURAL AND FUNCTIONAL MODIFICATION OF *Ipomoea carnea* Jacq. AN INVASIVE PLANT SPECIES, UNDER DIVERSE SALINITY GRADIENT

ABSTRACT

The role of structural and functional plasticity of *Ipomoea carnea* for invasion in diverse saline environments was investigated. The populations were collected from 30 different habitats of Pakistan. The populations were divided into 3 groups based on the extent of salinity in their natural habitat. The non-saline habitats (ECe>4 dS m^{-1}) were Kohala, Islamabad, Pahari Nala, Pir Kot, Nerian Sharif, Daska, Dhir Kot, Namal, Lower Jhelum and Majuhan. Moderately saline habitats (ECe 4-8 dS m^{-1}) were Mong Depo, Pasrur, Layyah, Mana Wala, Phularwan Roadside, Kharian Wala, Phulrwan canal, Rasool, Puran and Shah Kot. Highly saline habitats (<8 dS m^{-1}) included Gunjal, Gutwala, Skindar Pura, Choa Sadien Shah, Phid, Buchal, Kallar Kahar, Cholistan Desert, Sangla Hills and Sahian Wala. The hyper-saline population accumulated more compatible solutes like total soluble sugars, phenolics and flavonoids linked to osmoprotection. Increased sclerifcation and phloem thickness in hyper-saline and moderately saline populations. Increased density of trichomes and salt excretory glands prevented water loss and excreted toxic ions through leaf surface. In conclusion, *I. carnea* populations adopted different strategies like water conservation via water storage in parenchymatous tissues, accumulation of compatible solutes (total soluble sugars) and allelochemicals (flavonoids and phenolics) for chemical defense. All these aspects were key factors for survival and invasive success in a variety of habitat types and environmental conditions.

Keywords: Environmental heterogeneity, Invasive species, *Ipomoea carnea*, Sclerifcation, Trichomes.

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Murraya koengii: AN ALTERNATIVE TO TREAT BURN INFECTION

ABSTRACT

Utilization of medicinal plants in medications has tremendous history. Curry leaves *(Murraya koenigii*) indigenous to our country are known for their vast nutraceutical attributes and can be used for formulation of medicament and food supplements because of their easy availability, no side effects and economical effectiveness. These benefits of medicinal plants have been widely used method to cure a various kind of disease as compared to traditional method. The main objective of current research work was synthesis of bandage from *Murraya koenigii* leaves to treat burn infections. The green biomolecules extracted from curry leaves by decoction and bio binder hydrogel was used to synthesize silver nanoparticles. Extract and hydrogel were analysed by HPLC to identify different bio actives extracted from leaves. The phenolic compounds present in curry leaves extract were Quercetin, Gallic acid, Caffeic acid, Vanillic acid and Syringic acid whereas xanthan hydrogel displayed the existence of number of antioxidants. The different functional groups were identified by FTIR in synthesized silver nanoparticles and hydrogel. The morphological pattern of silver nanoparticles and hydrogel were determined by SEM analysis which have shown the spherical shape in AgNPs and elongated shape in hydrogel. Maximum DPPH was shown by silver nanoparticles as compared to aqueous extract and hydrogel. The haemolytic activity was found maximum in aqueous extract followed by AgNPs and hydrogel. The maximum biofilm inhibition was shown by hydrogel followed by aqueous extract and AgNPs in *staphylococcus aureus* whereas in *E.coli* maximum biofilm inhibition was shown in hydrogel followed by aqueous extract and hydrogel. The maximum antibacterial activity of silver nanoparticles, hydrogel and aqueous extract was shown against *Staphylococcus aureus as* compared to *E.coli*. The maximum efficacy of prepared AgNPs dressing was against *staphylococcus aureus* followed by *E.coli*. Thus the results showed that the green synthesized silver nanoparticles had a potential applications in medical field and safe to use.

Keywords: Healing agent, *Murraya koengii*, HPLC, FTIR, TPC, DPPH, antimicrobial.

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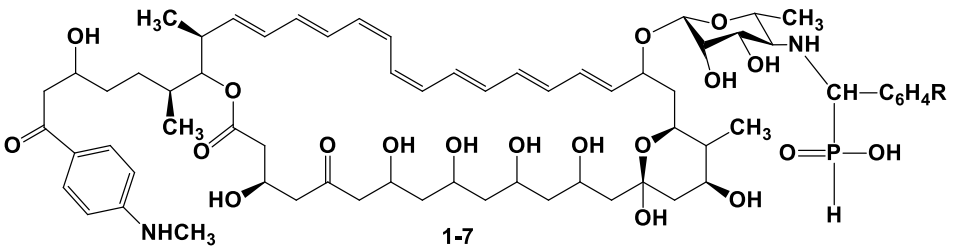
HYDROPHOSPHORYL DERIVATIVES OF PERIMYCIN: PREPARATION, PHARMACOLOGICAL PROPERTIES AND ANTIFUNGAL ACTIVITY

ABSTRACT

The antifungal antibiotic perimycin, obtained by biosynthesis using the producer *Streptomyces coelicolor* var. *Aminophilis*, belongs to the group of heptaene macrolide antibiotics. However, due to unacceptable medical and biological properties associated with high toxicity, poor tolerability when used systemically and a relatively narrow spectrum of antifungal activity, perimycin has not found application in medical mycology, unlike other heptaene macrolide antibiotics such as amphotericin B and candicidin.

It is known that chemical modification of polyene macrolide antibiotics leads to the creation of less toxic derivatives with improved medical and biological properties. Semisynthetic derivatives of perimycin of various structures obtained by chemical modification have high antifungal activity and lower toxicity. Organophosphorus derivatives of perimycin have not been described in the literature.

We have shown that reactions of perimycin with aromatic aldehydes and hypophosphorous acid result in the formation of its hydrophosphoryl derivatives **1-7** (Scheme 1). The studied reaction can be considered as a variation of the Kabachnik-Fields synthetic method.



Scheme 1. Structure of hydrophosphoryl derivatives of perimycin **1-7**.

Pharmacological studies have found that the acute toxicity (LD_{50}) of hydrophosphoryl derivatives of perimycin **1-7** was 2.5-3.0 times less than that of the original antibiotic and ranged from 675 to 750 mg/kg (mice, intravenously).

Compounds **3-7** possessed high antifungal activity against aspergillosis pathogens *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus clavatus*, *Aspergillus niger*, *Aspergillus nidulans* and *Aspergillus terreus* (the minimum fungistatic concentration ranged from 0.8 to 12.5 μg/mL) unlike perimycin (the minimum fungistatic concentration ranged

from 3.12 to 25.0 μg/mL), and only compounds **1** and **2** were inferior to the original antibiotic.

Keywords: Perimycin, Chemical Modification, Hydrophosphoryl Derivatives, Toxicity, Antifungal Activity, Aspergillosis Pathogens

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STRUCTURAL DEPENDENCE OF ANTIMICROBIAL ACTIVITY IN DICHLORODIAZADIENE DERIVATIVES

ABSTRACT

In this study, five newly synthesized dichlorodiazadiene derivatives were evaluated for their antimicrobial and antifungal activities against selected reference strains: *Staphylococcus aureus*, *Escherichia coli*, *Salmonella enteritidis*, and *Candida albicans*. Using the standard agar disk diffusion assay, each compound demonstrated a distinct inhibition profile. Notably, compound IV exhibited the highest antibacterial activity (36 mm) against *S. aureus*, a Gram-positive organism. Compound II showed selective potency against *S. enteritidis*, with a 30 mm inhibition zone, indicating targeted activity against Gram-negative bacteria. In contrast, compound V showed pronounced antifungal activity with a 22 mm zone of inhibition against *C. albicans*. Structure–activity relationship (SAR) analysis highlighted that the nature and position of functional groups, particularly nitro and methyl substituents on aromatic rings, critically influenced biological performance. Specifically, meta-substituted nitro groups appeared to avoid resonance delocalization, which may enhance reactivity and microbial interaction. These findings underscore the structural sensitivity of dichlorodiazadienes,

suggesting their potential for structure-guided optimization. Overall, the study supports the development of selective antimicrobial agents based on rational design and functional group manipulation.

Keywords dichlorodiazadiene, antimicrobial, structure–activity relationship

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HONEY EFFICACY AS ANTIMICROBIAL AGENT AGAINST MULTISPECIES BACTERIAL BIOFILMS

ABSTRACT

Bacterial biofilms are a major worldwide healthcare problem (urinary tract infections) and are associated with decreasing quality of life and significant patient morbidity. This study is first to test Pakistani honey bess, *Apis dorsata* and *A. cerana* honey samples as anti biofilm, anti quorum sensing (QS) and biofilm dispersal agents honey against multispecies biofilm of bacteria (obtained from obese patients). Briefly, five previously identified isolates *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, *Morganella morganii* and *Klebsiella pneumoniae* (MT448672-MT448676) were selected. Antibiogram study of all five isolates was tested against three antibiotics *viz*., erythromycin (20 µg/mL), lincomycin (100 µg/mL) and rifampicin (100 µg/mL). In order to form multispecies biofilm, identified bacteria were grown in batch culture by mixing equal volumes (OD_{590nm}= 0.1) of 2, 3 and 5 bacterial isolates. In total 11 groups (g1-g11) were made. Crystal violet (CV) staining method was used to evaluate the antibiofilm potential and biofilm dispersal potential of both honey samples. QS inhibition in *P. aeruginosa* was measured following culture supernatant method. Antibiogram study showed significant ($p < 0.05$) resistance by *P. aeruginosa* against tested antibiotics. *E. coli*, *M. morganii* and *K. pneumoniae* were significantly susceptible to erythromycin and *S. aureus* to lincomycin. Minimum inhibitory concentrations (MIC) values of both honey samples showed 2 and 5% concentrations as having significant ($p < 0.05$) inhibition potential of multispecies biofilm by all test groups (g1-g11). Though *A. dorsata* honey significantly inhibited biofilm formation at 2 and 5% against all groups but 2% concentration was highly significant against g2-g4 groups. Regarding *A. cerana* honey, 2% concentration was significantly effective against g1, g4-g7 and g9-g11 groups. Both honey samples significantly inhibited QS at 2 and 5%. The 5% concentration of *A. dorsata* honey significantly dispersed biofilm by all groups compared to 2% which showed dispersal potential only by g2 and g3 groups. Collectively, honey samples showed significant antibiofilm, anti-QS and biofilm dispersal potentials thus can be considered as good alternative to antibiotics.

Keywords: Honey potential as antibiofilm, quorum sensing, antibiotic resistance, resistant isolates

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QUORUM SENSING INHIBITION BY ALGAL COMPOUNDS AGAINST MARINE BIOFILMS

ABSTRACT

We examined that whether patulin and penicillic acid, two well-known quorum sensing inhibitors (QSI) for human pathogen *Pseudomonas aeruginosa* PAO1, can prevent biofilm formation. The study aims for amplification of a putative *luxS* gene homologue in the marine microorganism *H. pacifica* ATCC 27122, as well as monitoring AI-2 QS in marine organisms. Degenerated primers were designed based on the *luxS* protein sequence of ten gram-negative, □-, □- and □- proteobacteria, and used for *luxS* gene amplification in *H. pacifica*. AI-2 assays were carried out using the well-established *Vibrio harveyi* BB170 AI-2 bioluminescence assay. Effect of penicillic acid on AI-2 induction of *H. pacifica* showed strong inhibitory effect at non-growth inhibitory concentrations compared to patulin having adverse effect at the highest concentration (25 µM) tested in our study. QSIs effect on biofilm forming capability of marine isolates was isolate specific. Detection of bioluminescence in the autoinducer bioassay and the presence of a putative *luxS* gene orthologue are biochemical and genetic evidence for the production of a signalling molecule(s) and provide a first step in characterizing *H. pacifica* quorum sensing. Our study emphasize that QSI compounds must be selected in the specific system in which they are to function and they cannot easily be transferred from one QS system to another.

Keywords: Biofilm formation, *H. pacifica*, AI-2 assay, *LuxS* gene, Patulin, Penicillic acid

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THE EFFECT OF REPERFUSION ON LIVER TISSUE STRUCTURE AFTER MEDIUM-TERM ISCHEMIA

ABSTRACT

Introduction. One of the urgent problems of modern medicine is to improve the treatment and diagnostics of liver diseases using modern technological means and to increase the rehabilitation rate of patients suffering from this pathology. Along with all this, reperfusion syndrome still remains a problem awaiting a solution. One of the necessary links in the study of this problem is the clarification of the mutual relationships between the structural changes occurring in the organs during reperfusion and the biochemical and biophysical processes.

Materials and methods. The research work was carried out at the Scientific Research Center of Azerbaijan Medical University and the Department of Pathological Anatomy. After creating ischemia in the liver for 15 minutes, reperfusion was performed in 25 experimental animals and these animals were divided into 5 subgroups (5 animals in each). All manipulations performed, including the creation of ischemia and reperfusion models in the liver, decapitation were performed under pain relief conditions created by intramuscular injection of 1 ml of calypsol solution. Slices were taken from the parts of the liver exposed to ischemia and reperfusion and used to prepare histological preparations. In order to study the changes in the structure of the liver, slices taken from the liver were stored in formalin and, after appropriate processing, were embedded in paraffin blocks. The obtained preparations were stained with hemotoxylin and eosin, carmine dyes (Best method). When examining the preparations, attention was paid to the following issues: the level of dystrophic and necrobiotic changes in hepatocytes, the state of the portal triad and v. centralis, the level of inflammatory cell infiltration of the portal tract, the degree of damage to reticular fibers, the state of sinusoidal and Disse spaces, the degree of glycogen distribution in the liver.

Conclusion. In the examination of microscopic sections taken from the liver tissue of experimental animals included in this group 15 minutes after reperfusion, the sinusoids of the lobes were slightly enlarged, the central vein was distinguished from 5-minute ischemia by its low blood saturation. Hydropic dystrophy was noted in hepatocytes, leukocytic infiltration around the portal tract, and membrane permeability was slightly increased. 30 minutes after reperfusion, the sinusoids of the lobes that make up the liver tissue were enlarged, and the central vein attracted attention with its low blood saturation. The presence of granular inclusions in the cytoplasm of hepatocytes located around the central vein, interstitial edema around the portal tract, and hydropic dystrophy in some of the hepatocytes in the peripheral part of the segments were detected. Glycogen granules were unevenly distributed in the cytoplasm of hepatocytes. The central vein was distinguished by its fullness. During microscopy of preparations prepared from liver tissue 1 hour after reperfusion, it was revealed that the sinusoids of the liver segments continued to expand. The central vein was distinguished by its more pronounced fullness from previous

observation days. At the 3rd hour of reperfusion, the sinusoids in the liver were expanded and full of blood. During the examination of preparations prepared from the parietal tissue 24 hours after reperfusion after staining with hematoxylin and eosin, the following picture appeared in the preparations.

Thus, as the reperfusion period increases after the 15th minute of ischemia, the regenerative ability of hepatocytes increases. Liver tissue acquires characteristics characteristic of a healthy tissue structure.

Keywords: Reperfusion, Liver tissue, Disse.

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TRANSLATION, CULTURAL ADAPTATION AND VALIDATION OF THE GENERAL MEDICATION ADHERENCE SCALE (GMAS) IN MOROCCAN PATIENTS WITH TYPE-2 DIABETES

ABSTRACT

Background: The objective of the study was to cross-culturally adapt and validate the General Medication Adherence Scale (GMAS) in patients with type-2 diabetes in Morocco.

Methods: The study was a cross-sectional study conducted between September 12 and October 12, 2022, and included patients with type-2 diabetes from a primary health care network. To measure the different psychometric parameters of the construct, data analysis was performed using SPSS v20. The study was approved by the Moroccan Association for Research and Ethics.

Results: A total of 284 patients were included in the study; the results of the different psychometric parameters were largely acceptable. Indeed, the improvement of the goodness-of-fit of the model in relation to the independence model was evaluated by the comparative fit index (CFI), which was higher than 0.95, as well as the normalized fit index (NFI), which expresses the percentage of the general covariance between the variable demonstrated via the tested model when the null model is taken as reference and was also higher than 0.95 in this study. Additionally, the Tucker Louis Index (TLI) or Unstandardized Fit Index, which measures the increase in goodness of fit when moving from the reference model to the model under study, had a value of > 0.95. The correlations between the items were good; indeed, the Kaiser-Meyer-Olkin (KMO) index was > 0.7. The translated tool presents good internal consistency; thus, Cronbach's α had a value of approximately 0.804 (> 0.7).

Conclusions: The version of the GMAS tool adapted to the Moroccan context has very acceptable psychometric values. This means that Moroccan researchers and health professionals can use it as an instrument to measure adherence among individuals with type-2 diabetes.

Keywords: GMAS, Adherence, Type-2 diabetes, Validation study, Morocco

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CRITICALLY ANALYZING GLOBAL LEGAL RESPONSE TO THE EFFECT OF THAWING OF PERMAFROST ON HUMAN HEALTH

ABSTRACT

From the time Homo sapiens were born on the earth and their evolution began, so did the threat to their survival evolved constantly. Homo sapiens are intelligent enough to gauge these problems and respond appropriately to prolong their survival. In second half of the 20th century leaders of the world understood the importance of nature and began the long journey to protect environment with little steps. Incremental but meaningful steps were taken, leading to notable progress by the end of the second decade of the 21st century in areas such as ozone layer protection, greenhouse gas reduction, and climate change mitigation—largely enabled by an evolving global legal framework. However, several aspects of environmental degradation continue to be overlooked or insufficiently quantified. One such neglected but essential component of nature is, Permafrost thawing. Permafrost thawing is probably at the bottom in the list of concerned topics for global leaders who are equipped with duty to protect the environment. According to the small pool of dedicated scientist community the permafrost thawing can be the ignition to next mass extinction. This research paper analyses the far-reaching detrimental impact of thawing of permafrost on human health and its co-relationship with pandemics. The researcher also analyses the contemporary global legal responses to combat thawing of permafrost and limit its lethal impact on human health and to arrest its potential to amplify pandemics. The researcher attempts to critically examine if there is need of shift in contemporary global legal paradigm to address this escalating threat effectively. Ultimately this study aims to lay a foundational framework for incorporating permafrost preservation into global environmental law and calls for urgent attention from policymakers to recognize its ecological and public health significance.

Keywords: Permafrost, Pandemic, International Enviro Legal Paradigm.

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CORRELATION STUDY ON ETIOLOGICAL FACTORS OF HEART DISEASE IN DIABETIC PATIENTS IN LAHORE, PAKISTAN

ABSTRACT

Diabetes is a chronic disorder and inability to process and regulate blood glucose levels. This disorder may arise from excessive secretion of insulin by pancreas in our body. Type I diabetes is a chronic autoimmune disease characterized by deficiency of insulin, resulting in an increase in blood glucose level in body. This dysfunction includes autoimmune destruction of beta cells in pancreas leads to complete lack of insulin production. Type 2 diabetes is most prevalent metabolic disorder characterized by inadequate insulin production and impaired response of tissues to insulin. Global burden of diabetes mellitus represents a significant public health challenge. Heart disease is a serious health condition that affects millions of people. Heart diseases includes coronary artery disease (CAD), myocardial infarction, angina, heart failure, congenital heart disease, atrial fibrillation and heart valve disorder. Etiological factors of heart disease are modifiable factors, conventional factors, environmental factors, non- traditional factors and psychological factors that collectively contribute to diabetes prevalence. Modifiable factors include high blood pressure, obesity and metabolic syndrome while conventional factors include age, gender and family history. Complications related to diabetes like liver cirrhosis, alcohol related liver disease and renal disease also promote cardiovascular disorders. Different risk factors show different level of correlation with each other. Age limit, duration of diabetes and high level of cholesterol has significant level of positive correlation. Moreover, high level of cholesterol in diabetic patients correlate with normal systolic blood pressure which is also an indication of prevalence of heart disease in diabetic patients. Treatment and preventions focus on stress management, lifestyle interventions and balanced diet.

Keywords: Diabetic Heart Disease, cardiovascular complications, Etiological Factors , Correlation Study

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OVERPROTECTION, SELF-DOUBT AND CINDERELLA SYNDROME IN FEMALE UNIVERSITY STUDENTS

ABSTRACT

The aim of this study was to explore the relationship between overprotective parenting, self-doubt, and Cinderella Syndrome in female university students. It was hypothesized that overprotective parenting and self-doubt would have a significant relationship with Cinderella Syndrome. Data was collected from 200 students within the range of 18 to 26 years using standardized scales that measured overprotective parenting, self-doubt, and Cinderella Syndrome. The findings revealed that students who experienced overprotective parenting especially forms like anxious rearing and privacy invasion were more likely to develop Cinderella Syndrome traits such as helplessness, emotional dependency, and a desire to be rescued. Self-doubt also showed a strong positive relationship with Cinderella Syndrome, indicating that students who doubt themselves are more likely to rely on others for emotional support and life decisions. Interestingly, not all types of overprotection had the same effect; anxious rearing showed a stronger influence compared to other forms. This study highlights how parenting styles and internal beliefs formed during early life can shape personality and coping patterns in adulthood. The results can help parents, psychologists, and educators understand how overprotection and low self-confidence can lead to long-term psychological struggles. Creating awareness about balanced parenting and building confidence in children may help reduce the chances of developing such dependency-based patterns.

Keywords: Cinderella Syndrome; Overprotective parenting; self-doubt: female university students; emotional dependency

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THE ROLE OF HIGH FAST FOOD, SUGARY BEVERAGE, AND SUGAR INTAKE IN THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE: A CLINICAL AND LITERATURE-BASED ANALYSIS

ABSTRACT

Chronic Kidney Disease (CKD) represents a rapidly growing global health concern, contributing significantly to morbidity, mortality, and healthcare costs. The increasing prevalence of CKD has been closely associated with modifiable lifestyle and dietary factors, especially the widespread consumption of fast foods, sugary beverages, and refined sugars. These dietary habits, now prevalent across all age groups and socioeconomic backgrounds, are known to contribute to key risk factors for CKD, including obesity, hypertension, diabetes mellitus, and metabolic syndrome. Despite growing awareness, limited clinical research incorporates real-time patient data to substantiate these associations.

This study aims to bridge this gap by combining an extensive literature review with analysis of real-time clinical data from patients diagnosed with CKD who have a documented history of high intake of processed foods and sugary beverages. The review explores the pathophysiological mechanisms—including increased oxidative stress, chronic low-grade inflammation, insulin resistance, and glomerular hyperfiltration—that underlie diet-induced renal damage. The clinical data, drawn from primary care settings and nephrology clinics, include laboratory parameters, lifestyle questionnaires, and progression patterns in CKD staging, offering direct insight into how dietary excesses translate into kidney dysfunction.

Through in-depth case studies, the research highlights variations in disease progression based on dietary patterns, demonstrating that early dietary interventions—especially reduced sugar and sodium intake—may decelerate kidney function decline. Moreover, patient outcomes reflect how education, counseling, and diet modification can impact long-term renal health, even in early-stage CKD.

This integrative approach strengthens the evidence that fast food and sugary beverage consumption are not merely associated with but are likely contributing to renal deterioration. Public health implications are substantial: this study underscores the necessity for early lifestyle interventions, tailored dietary counseling, and public health policies that limit the availability and marketing of nephrotoxic food products.

By presenting both theoretical foundations and real-world data, this paper offers a holistic perspective on the role of nutrition in CKD and calls for the urgent implementation of preventive strategies in both clinical and community settings. It lays the groundwork for more targeted future research that combines nutritional epidemiology, clinical nephrology, and health policy**.**

Keywords: Chronic Kidney Disease (CKD), Early-stage CKD, Kidney Disease Prevention, Dietary Habits, Obesity, Hypertension, Kidney Disease Progression Fast Food Consumption, Sugary Beverages, Nutritional Modifications, Lifestyle Changes.

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IN SILICO PREDICTION OF BACTERICIDAL POTENTIAL USING ANTIBAC-PRED FOR DICHLORODIAZADIENE DERIVATIVES

ABSTRACT

This work focuses on evaluating the antibacterial potential of five dichlorodiazadiene derivatives through computational prediction models. Using the AntiBac-Pred platform, activity probability (Pa) values were determined for each compound against a wide panel of clinically relevant bacterial pathogens. Compound V stood out with the highest predicted activity against *Yersinia pestis* (Pa = 0.7181), followed by compound III (Pa = 0.6694) and compound IV (Pa = 0.6141). Additionally, moderate activity was forecasted against *Mycobacterium spp.* and *Bacillus subtilis* for these compounds. The observed activity was associated with the presence of electron-withdrawing groups (chlorine, nitro) and electron-donating groups (methoxy, methyl), influencing molecular polarity and membrane permeability. These electronic and steric parameters were found to modulate the predicted bioactivity spectrum. Importantly, the computational data aligned with experimental inhibition zones, validating the reliability of AntiBac-Pred for early drug screening. Such predictive approaches accelerate lead compound identification and reduce reliance on

extensive wet-lab screening. This study presents compelling evidence for integrating in silico tools in antibacterial drug design and prioritizing structurally optimized compounds for further biological testing.

Keywords AntiBac-Pred, Yersinia pestis, dichlorodiazadiene, computational prediction, bacterial inhibition, drug screening

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IN SILICO PREDICTION OF CYP450 INHIBITION PROFILES AND METABOLIC STABILITY OF HYDRAZONE ESTER DERIVATIVES

ABSTRACT

Metabolic stability and drug–drug interaction potential are strongly influenced by a compound's interaction with cytochrome P450 (CYP450) enzymes. In this study, four hydrazone ester derivatives were analyzed in silico to evaluate their predicted inhibition profiles against key CYP450 isoforms. All compounds were found to inhibit **CYP1A2** and **CYP2C19**, while showing **no predicted inhibition** of **CYP2C9**, **CYP2D6**, or **CYP3A4**. The consistent inhibition of CYP1A2 and CYP2C19 across all derivatives suggests a possible shared binding mechanism, likely influenced by the aromatic and hydrazone functionalities. Notably, none of the compounds are predicted to interact with **CYP3A4**, the most clinically significant isoform in hepatic metabolism, which may reduce the risk of broad metabolic interference. Additionally, none of the molecules were identified as **P-glycoprotein substrates**, lowering the likelihood of efflux-related metabolic resistance. These results provide a valuable initial profile of metabolic liabilities and suggest that while further in vitro metabolic studies are warranted, these compounds may offer **selective metabolic pathways** with reduced risk for severe drug–drug interactions.

The table below summarizes the key findings:

Molecule	CYP1A2 Inhibitor	CYP2C19 Inhibitor	CYP2C9 Inhibitor	CYP2D6 Inhibitor	CYP3A4 Inhibitor
Mol 1	Yes	Yes	No	No	No
Mol 2	Yes	Yes	No	No	No
Mol 3	Yes	Yes	No	No	No
Mol 4	Yes	Yes	No	No	No

Keywords- CYP450 inhibition, cytochrome P450, CYP1A2, CYP2C19, drug–drug interaction, metabolic stability, hydrazone esters, in silico metabolism, SwissADME

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EVALUATION OF THE EFFECT OF METHIMAZOLE ON UREASE ACTIVITY WITH DIFFERENT KINETIC EQUATIONS

ABSTRACT

Introduction: Urease (urea amidohydrolase, EC 3.5.1.5) is a nickel-dependent metalloenzyme found in plants, bacteria, and fungi. It catalyzes the hydrolysis of urea into ammonia and carbamate. Urease plays a critical role in the survival and colonization of certain pathogenic bacteria, particularly *Helicobacter pylori*, by facilitating their adaptation to the acidic environment of the stomach[1].

Aim: In this study, the effect of methimazole, which is chemically similar to thiourea derivatives and is also used in the treatment of hyperthyroidism, on urease activity is investigated, and the results are evaluated with different kinetic equations.

Material and Method: Jack bean urease was used. The activity of urease was measured spectrophotometrically [2]. Specific activity for urease is defined as the amount of enzyme that releases 1 μmol NH_4^+ per minute. Activity measurements of urease were made at least 3 times at pH 7 and 37 °C in urea concentrations ranging from 0.25 to 15 mM. Enzyme activities were measured in the presence of 0.5 mM and 1.0 mM Methimazole under the same reaction conditions. K_m, V_{max}, k_{cat}, k_{cat}/K_m values of the urease was calculated using the Lineweaver-Burk (LWB), Hanes-Woolf (HW) and Eadie-Hofstee (EH) equations in the presence and absence of methimazole. Microsoft® Excel was used to analyze the kinetic data [3].

Results: The kinetic parameters calculated as a result of the experiment are given in Table.

Table. Kinetic Parameters of Urease

	Methimazole Concentration	V_{max} (µmol NH_4^+/min.mg prot.)	K_m (mM)	k_{cat} s^{-1}	k_{cat}/K_m ($s^{-1}M^{-1}$)
LWB	Free Urease	94.3	2.6	125.7	$4.9x10^4$
	0.5 mM Methimazole	54.1	0.3	72.1	$25.4x10^4$
	1.0 mM Methimazole	35.6	0.32	47.4	$14.5x10^4$
EH	Free Urease	104.9	2.90	140.0	$4.9x10^4$
	0.5 mM Methimazole	0.28	3.60	70,80	$25.3x10^4$
	1.0 mM Methimazole	53.10	0.28	43.4	$15.5x10^4$
HW	Free Urease	115.9	3.98	154.5	$3.9x10^4$
	0.5 mM Methimazole	52.63	0.246	70.2	$28.5x10^4$
	1.0 mM Methimazole	46.5	1.12	62	$5.5x10^4$

As the concentration of methimazole increased, the urease's catalytic efficiency (kcat/Km) decreased. However, these values are also higher than that of free urease catalytic efficiency. In addition, when different kinetic equations were used, the kinetic parameters of urease were found to be different from each other.

Keywords: Urease, Enzyme inhibition, Methimazole, Lineweaver-Burk, Hanes-Woolf, Eadie-Hofstee

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IMMOBILIZATION OF LIPASE ON MODIFIED ZrO_2 AND INVESTIGATION OF ITS HYDROLYTIC ACTIVITY

ABSTRACT

Introduction: Lipases (triacylglycerol acyl hydrolase, EC 3.1.1.3) are enzymes that catalyze the hydrolysis of ester bonds in triacylglycerols (TAGs), producing free fatty acids and glycerol [1]. In addition to hydrolysis, lipases can catalyze esterification, acidolysis, alcoholysis, interesterification, and aminolysis reactions in both aqueous and non-aqueous environments [2]. Microbial lipases are utilized in fields such as food processing, medicine, detergents, biodiesel production, cosmetics, textiles, and environmental protection. They are also widely studied in laboratory-scale research. The use of free and immobilized lipases is gaining prominence in green and sustainable chemistry [3].

Aim: This study aims to determine the hydrolytic activity and kinetic parameters (V_{max}, K_m, k_{cat}, k_{cat}/K_m) of immobilized *Candida rugosa* lipase.

Material and Method: The support material, ZrO_2, was chemically modified using glutaraldehyde (GA), bis(3-aminopropyl)amine (BIS), and 1,2-bis(3-aminopropylamino) ethane (1,2-BIS) [4]. Lipase was immobilized on the modified supports, and both the amount of enzyme bound and the immobilization efficiency were determined. The hydrolytic activities of free and immobilized lipase were measured at 37 °C using various concentrations of olive oil (1.25–15% w/v) as the substrate [5]. Kinetic parameters were calculated using the Lineweaver–Burk equation.

Results: The amount of lipase bound to the modified supports was found to be 23.4 mg/g for ZrO_2–GA, 19.8 mg/g for ZrO_2–GA–BIS, and 16.2 mg/g for ZrO_2–GA–1,2-BIS. The corresponding immobilization efficiencies were 33.8%, 28.6%, and 23.4%, respectively. The kinetic parameters determined for both free and immobilized lipases are summarized in

the table below. Among the tested supports, lipase immobilized on glutaraldehyde-modified ZrO_2 (ZrO_2–GA) exhibited the highest catalytic activity.

Table. Kinetic parameters of free and immobilized lipases.

Types of Lipase	Kinetic Parameters			
	V_{max} (µmol FA/ min.mg prot.)	K_m (%(w/v))	k_{cat} (s^{-1})	k_{cat}/K_m
Free Lipase	17.8	10.1	35.6	3.5
Imm. (ZrO_2-GA) Lipase	1.7	0.75	3.3	4.4
Imm. (ZrO_2-GA-BIS) Lipase	2.6	2.7	5.2	1.9
Imm. (ZrO_2-GA-1,2 BIS) Lipase	1.2	1.1	2.4	2.2

*FA:Fatty Acid, Imm.: Immobilized, prot: protein

Keywords: Lipase, Zirconium (IV) Oxide, Immobilization, Hydrolytic Activity

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MOLECULAR DETECTION OF *COXIELLA BURNETII* IN VAGINAL SWAB SAMPLES FROM NOMADIC SHEEP THAT ABORTED IN SİİRT PROVINCE

ABSTRACT

Coxiella burnetii, the causative agent of coxiellosis, is an obligate intracellular bacterium that causes significant infections in humans and animals. *C. burnetii* has a wide reservoir, ranging from ticks to mammals. The agent, which stands out as an important abortive zoonotic pathogen in livestock, is difficult to detect using classical microbiological techniques and poses a risk to laboratory personnel. Polymerase Chain Reaction (PCR) is a molecular diagnostic test that stands out for its speed, reliability, and high specificity in detecting *C. burnetii* DNA. In this study, it was aimed to molecularly investigate the presence of *C. burnetii* by PCR method in vaginal swab samples taken from nomadic sheep that had aborted in the province of Siirt. To this end, vaginal swab samples were collected from 26 sheep within the first 30 days post-abortion, and genomic DNA was obtained using a commercial DNA extraction kit. PCR analysis was performed using primers specific to the IS1111a insertion element unique to *C. burnetii*. Four (15.38%) of the vaginal swab samples taken from nomadic sheep that aborted in the Siirt region tested positive by PCR. As a result, it was determined that there is a considerable rate of coxiellosis infection in the region. It was concluded that *C. burnetii* should be considered a significant risk factor in the control and prevention programs to be developed for combating sheep abortions.

Keywords: *C. burnetii*, abortion, nomadic sheep, PCR, Siirt

SİİRT İLİNDE ABORT YAPAN GÖÇER KOYUNLARDAN ALINAN VAJİNAL SÜRÜNTÜ ÖRNEKLERİNDE *COXİELLA BURNETİİ*'NİN MOLEKÜLER OLARAK TESPİTİ

ÖZET

Coxiellosisin etkeni olan *Coxiella burnetii*, insan ve hayvanlarda önemli infeksiyonlara neden olan zorunlu hücreiçi bir bakteridir. *C. burnetii* kenelerden memeli canlılara kadar geniş bir rezervuara sahiptir. Çiftlik hayvanlarında önemli bir abortif zoonotik ajan olarak öne çıkan etkenin klasik mikrobiyolojik tekniklerle tespiti zor ve laboratuvar personeli için tehlikelidir. Polimeraz zincir reaksiyonu (PCR) *C. burnetii* DNA'sının tespitinde hız, güvenilirlik ve yüksek özgüllüğü ile öne çıkan bir moleküler tanı testidir. Bu çalışmada, Siirt ilinde abort yapan göçer koyunlardan alınan vaginal sürüntü (swap) örneklerinde *C. burnetii* varlığının PCR yöntemi ile moleküler olarak araştırılması amaçlanmıştır. Bu amaçla abort sonrası ilk 30 gün içinde 26 adet koyundan vajinal swap örnekleri alınarak ticari bir DNA ektraksiyon kiti ile genomik DNA elde edildi. *C. burnetii*'ye özgü IS1111a ekleme elementine spesifik primerler kullanılarak PCR analizi gerçekleştirildi. Siirt bölgesindeki göçer koyun abortlarında alınan vajinal swap örneğinin 4 adedi (% 15,38) PCR sonucunda pozitif olduğu tespit edildi. Sonuç olarak bölgede kayda değer bir oranda coxiellosis enfeksiyonunun olduğu tespit edildi. Koyun abortlarıyla mücadelede oluşturulacak kontrol ve mücadele programlarında *C. burnetii* önemli bir risk faktörü olarak dikkate alınması gerektiği kanısına varıldı.

Anahtar Kelimeler: *C. burnetii*, abort, göçer koyun, PCR, Siirt

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PHARMACOKINETICS OF ENROFLOXACIN AND CIPROFLOXACIN AFTER SINGLE AND REPEATED ADMINISTRATION OF ENROFLOXACIN IN CHUKAR PARTRIDGE

ABSTRACT

This study aimed to determine the pharmacokinetics of enrofloxacin and its active metabolite, ciprofloxacin, after single and repeated administration of enrofloxacin in chukar partridges. The research was carried out in two stages, single and repeated pharmacokinetics,

on 18 chukar partridges (*Alectoris chukar*). Enrofloxacin was administered orally at 10 mg/kg in both phases. In the first phase of the study, a single dose of enrofloxacin was administered to the partridges, and in the second phase, enrofloxacin was administered once a day for 5 days. Analysis of enrofloxacin and ciprofloxacin from the blood samples taken was carried out with the help of high pressure liquid chromatography. Pharmacokinetic parameters were calculated by non-compartmental analysis. After a single dose administration of enrofloxacin, the elimination half-life ($t_{1/2\lambda z}$), area under the plasma concentration-time curve ($AUC_{0\text{-last}}$), peak plasma concentration (C_{max}) and time to reach C_{max} (T_{max}) were 3.99 hours, 14.17 hours*µg/mL, 1.60 µg/mL and 3.17 hours, respectively. The $AUC_{0–last\ ciprofloxacin}/AUC_{0–last\ enrofloxacin}$ ratio was 19.97%. After repeated administration, $t_{1/2\lambda z}$ (from 3.99 to 7.44 hours), $AUC_{0\text{-last}}$ (from 14.17 to 20.45 hours*µg/mL), C_{max} (from 1.60 to 2.03 µg/mL) and T_{max} (from 3.17 to 4.00 hours) values increased. When the first day and last day values were compared, it was determined that the $AUC_{0–last}$ value increased from 13.98 to 19.14 h*µg/mL and the C_{max} value increased from 1.55 to 2.03 µg/mL. The body accumulation of ratio was determined as 1.37-2.59. These results show that the pharmacokinetic parameters changed significantly after repeated application of enrofloxacin in partridges.

Keywords: Ciprofloxacin, Enrofloxacin, Partridges, Pharmacokinetics.

KEKLİKLERDE ENROFLOKSASİNİN TEK VE TEKRARLI UYGULANMASI SONRASI ENROFLOKSASİN VE SİPROFLOKSASİNİN FARMAKOKİNETİĞİ

ÖZET

Bu araştırmanın amacı kınalı kekliklerde enrofloksasinin tek ve tekrarlı uygulaması sonrası enrofloksasin ve aktif metaboliti olan siprofloksasinin farmakokinetiğini belirlemektir. Araştırma 18 adet kınalı keklik (*Alectoris chukar*) üzerinde tek ve tekrarlayan farmakokinetik olmak üzere iki aşamada gerçekleştirildi. Enrofloksasin her iki aşamada da 10 mg/kg dozda oral yolla uygulandı. Çalışmanın ilk aşamasında kekliklere tek doz, ikinci aşamasında ise günde bir defa 5 gün boyunca enrofloksasin uygulandı. Alınan kan örneklerinden enrofloksasin ve siprofloksasinin analizi yüksek basınçlı sıvı kromotografisi yardımıyla gerçekleştirildi. Farmakokinetik parametreler non-kompartmental analiz ile hesaplandı. Enrofloksasinin tek doz uygulaması sonrası eliminasyon yarılanma ömrü ($t_{1/2\lambda z}$), plazma konsantrasyon zaman eğrisi altında kalan alan ($AUC_{0\text{-last}}$), maksimum plazma konsantrasyonu (C_{max}) ve C_{max}'a ulaşma zamanı (T_{max}) sırasıyla 3.99 saat, 14.17 saat*µg/mL, 1.60 µg/mL ve 3.17 saat idi. $AUC_{0\text{–last siprofloksasin}}/AUC_{0\text{–last enrofloksasin}}$ oranı %19.97 olarak belirlendi. Tekrarlı uygulama sonrası $t_{1/2\lambda z}$ (3.99'den 7.44 saate), $AUC_{0\text{-last}}$ (14.17'den 20.45 saat*µg/mL'ye), C_{max} (1.60'den 2.03 µg/mL'ye) ve T_{max} değerinin (3.17'den 4.00 saate) arttığı belirlendi. İlk gün ve son gün değerleri karşılaştırıldığında $AUC_{0\text{–last}}$ değerinin 13.98'den 19.14 saat*µg/mL'e ve C_{max} değerinin 1.55'den 2.03'e µg/mL'ye arttığı belirlendi. Enrofloksasinin vücut birikim oranı 1.37-2.59 olarak belirlendi. Bu sonuçlar kekliklerde enrofloksasinin tekrarlı uygulaması sonrası farmakokinetik parametrelerin önemli oranda değiştiğini göstermektedir.

Anahtar kelimeler: Enrofloksasin, Farmakokinetik, Keklik, Siprofloksasin.

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SPORTS PHYSIOLOGY FOR PERFORMANCE OPTIMIZATION

ABSTRACT

The optimization of athletic performance plays a pivotal role in surpassing records, securing medals, and acquiring trophies; to meet these demands, the performance of athletes can be refined through tailored and systematic training methodologies. A comprehensive understanding of the physiological requirements of athletes is essential for the selection of specific and effective individualized training programs. This investigation will be conducted through a thorough analysis of the most prevalent literature in the field. The findings have demonstrated the impact of physiological factors on physical performance during training sessions and competitive matches. The discipline of exercise physiology is integral to the enhancement of performance, as it equips coaches with an understanding of the functions and adaptations of bodily systems during physical exertion. This expertise facilitates the development of precise fitness assessments and exercise regimens that cater to the unique needs of athletes, alongside nutritional strategies that can augment endurance, strength, and recovery. By comprehending the effects of nutrition on physiological responses, athletes can design personalized programs that not only elevate performance levels but also contribute to injury prevention and recovery processes.

Keywords : physiology,sport,optimization,adaptation

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THE INFLUENCE OF WATER INTAKE ON BODY COMPOSITION ASSESSMENT IN YOUNG MALES: ACCURACY, VARIABILITY, AND IMPLICATIONS

ABSTRACT

Aim: Bioelectrical Impedance Analysis (BIA) is a widely used, non-invasive technique for assessing body composition, particularly fat mass percentage, and hydration status, making it a valuable tool in evaluating overall health conditions. BIA estimates body composition by measuring the varying resistance of different body tissues to a low-level electrical current, offering insights into fat, muscle, and fluid distribution.

In this study, we aimed to evaluate the efficacy of the BIA method in assessing fat mass and body water status, specifically in relation to the impact of increased body water levels on body composition.

Material and Methods: A total of 100 healthy young males (age: 21.2±1.7 years, height: 176.9±6.1 cm, and body mass index (BMI): 22.36±2.8 kg/m2) participated, and body composition measurements were performed using BIA method. Each subject body composition was measured before and 30 min after 1 liter of water intake using body composition analyser. A paired t-test was used to evaluate the data for statistical significance.

Results: The body weight increased from 70.06±9.84 kg to 71.06±9.82 kg. After 1 lt of water intake body fat mass percent increased from 13.306±5.16 to 13.99±5.45 ($p<0.01$); fat mass increased from 9.62±5.16 kg to 10.24±5.34 kg ($p<0.0001$) and fat-free mass increased from 60.44±6.27 kg to 60.81±6.56 kg ($p=0.04$). However, total body water did not change significantly before (42.43±3.80 kg) and after water intake (42.64 ±4.05 kg) ($p=0.1$)

Conclusion: In conclusion, while the intake of 1 liter of water significantly altered measurements of body fat percentage, fat mass, and fat-free mass, it did not produce a statistically significant change in total body water, highlighting potential limitations in BIA accuracy under acute hydration shifts. Given its sensitivity to fluctuations in hydration, the reliability of BIA measurements should be carefully considered before making critical clinical decisions, particularly in individuals prone to elevated body water levels, such as those with obesity, hypertension, or renal disorders

Keywords: BMI, Fat mass percent, Total body water, Fat free mass, Health

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THE BIRTH PROCESS OF A PATIENT WITH A HISTORY OF UNPLANNED ADVANCED PREGNANCY USING THE TRAVELBEE MODEL OF HUMAN-TO-HUMAN RELATIONSHIPS: CASE REPORT

ABSTRACT

Fear of childbirth is a common emotion experienced by pregnant women and can occur before, during or after childbirth. Intense fear has a negative impact on the physical and psychological state of pregnant women. This fear can range from mild anxiety to severe phobia and can have detrimental effects on both maternal and fetal health. Women who experience high levels of fear of childbirth are more likely to request elective cesarean sections, experience prolonged labor, and report negative birth experiences. In addition, fear of childbirth has been associated with an increased risk of postpartum depression and difficulties in mother-infant bonding. This case was planned to improve the nursing care of a patient with fear of childbirth, advanced age, unplanned pregnancy, using the Travelbee Model of Human-to-Human Relationships. Case A.T. was 43 years old, married, mother of 4 children, primary school graduate, residing with her family in a village in the central district of Konya. The patient, who was 39+5 weeks pregnant, presented to the hospital with the complaint of pain. The patient had no chronic disease. A.T. stated that her pregnancy was not planned and that she did not want pregnancy at the beginning. She stated that the thought of not wanting pregnancy increased her fear of childbirth. Therefore, it was evaluated that the patient needed individual-centered nursing care. Nursing care was applied in the communication process established in this context with the patient based on Travelbee's “Theory of Human-to-Human Relations”. As a result, the patient was able to cope with the fear of childbirth and spend the process more comfortably. It can be recommended to increase the training and counseling given by using Travelbee's “Human Human Relationship Theory” in the nursing care process and to use it in clinical practice.

Keywords: Fear of Childbirth, Case Report, Travelbee

PLANLI OLMAYAN İLERİ YAŞTAKİ GEBELİK ÖYKÜSÜNE SAHİP HASTANIN DOĞUM SÜRECİNİN TRAVELBEE İNSAN İNSANA İLİŞKİLER MODELİ İLE İNCELENMESİ: OLGU SUNUMU

ÖZET

Doğum korkusu, hamile kadınlar tarafından deneyimlenen yaygın bir duygudur ve doğumdan önce, doğum sırasında veya doğumdan sonra ortaya çıkabilmektedir. Yoğun korku, hamile kadınların fiziksel ve psikolojik durumları üzerinde olumsuz bir etkiye sahiptir. Bu korku, hafif kaygıdan şiddetli fobiye kadar değişebilir ve hem anne hem de fetüs sağlığı üzerinde zararlı etkilere sahip olabilir. Yüksek düzeyde doğum korkusu yaşayan kadınların elektif sezaryen talep etme, uzun süreli doğum deneyimi yaşama ve olumsuz doğum deneyimleri bildirme olasılıkları daha yüksektir. Ek olarak, doğum korkusu, doğum sonrası depresyon riskinin artması ve anne-bebek bağında zorluklarla ilişkilendirilmiştir. Bu olgu doğum korkusu olan, ileri yaş, plansız gebeliği olan bir hastanın Travelbee İnsan İnsana İlişkiler Modeli kullanarak, hemşirelik bakımını geliştirmek amacı ile planlamıştır. Olgu A.T 43 yaşında evli, 4 çocuk annesi, ilkokul mezunu, ailesiyle birlikte Konya'nın merkez ilçesine bağlı bir köyde ikamet etmektedir. 39+5 haftalık gebe olan hasta, hastaneye ağrı şikâyeti ile başvurmuştur. Hastanın kronik bir hastalığı yoktur. A.T. gebeliğinin planlı olmadığını ve başlangıçta gebeliği istemediğini belirtmiştir. Gebeliği istememe düşüncenin doğuma yönelik korkusunu arttırdığını ifade etmiştir. Bu nedenle hastanın birey merkezli bir hemşirelik bakımına ihtiyacı olduğu değerlendirilmiştir. Travelbee'nin "İnsan İnsana İlişkiler Teorisi"ne dayalı hasta ile bu bağlamda kurulan iletişim sürecinde hemşirelik bakımı uygulanmıştır. Sonuç olarak hastanın doğum korkusu ile baş etmesi ve süreci daha konforlu geçirmesi sağlanmıştır. Hemşirelik bakım sürecinde Travelbee'nin "İnsan İnsana İlişkiler Teorisi kullanılarak verilen eğitimin ve danışmanlığın artırılması ve klinik uygulamalarda kullanılması önerilebilir.

Anahtar Kelimeler: Doğum Korkusu, Olgu Sunumu, Travelbee

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CT-BASED DIAGNOSTIC INSIGHTS IN A RARE CASE OF LARYNGEAL TUBERCULOSIS

ABSTRACT

INTRODUCTION

In 2023 overall tuberculosis (TB) incidence rate was 134/100,000. Most TB cases reported in regions of South-East Asia (45%), least in Europe (2.1%) (*World Health Organisation*, 2024) disproportionately affecting males (Pape et al., 2024). TB incidence in Lithuania declined from 31.8 to 21.3 per 100,000 in years 2019 - 2023 (*Nacionalinis Visuomenės Sveikatos Centras Prie Sveikatos Apsaugos Ministerijos*, 2023) . A lower proportion of extrapulmonary TB was seen in Eastern Europe (17.4%) and Southern Europe (29.6%) compared with Western (35.7%) and Northern Europe (41.8%) (Hayward et al., 2021).

RESEARCH AND FINDINGS:

A 49 y.o. male presented with cough, unintentional weight loss, fever, difficulty swallowing and throat pain. Patient hospitalized in ENT for suspected laryngeal carcinoma. Enlarged left neck lymph node detected. Laryngoscopy revealed increased mucus, edematous epiglottis, and ulceration on the right laryngeal surface and aryepiglottic fold, suspecting laryngeal carcinoma, risk factors including smoking and alcohol use, unemployment.

Neck CT scan revealed soft tissues thickening and contrast enhanced infiltration of epiglottis, glossoepiglottic, pharyngoepiglottic, and aryepiglottic folds, and the right vestibular fold raised suspicion of granulomatous disease (Fig.1).

Chest X-rays were performed, showing typical TB signs, AFB test was positive, and culture confirmed Mycobacterium tuberculosis. Laryngeal biopsy excluded malignancy and showed granulomatous inflammation due to tuberculosis.

DISCUSSION

CT is superior to laryngoscopy in laryngeal TB diagnostics. CT patterns include diffuse thickening with enhancement, especially pronounced mucosal thickening, polypoid or fungating mass, and fluid collection, also bilateral enhancement with variable paralaryngeal fat infiltration, calcifications in necrotic lymph nodes, smooth or irregular, swollen epiglottis can be present (Alshoabi et al., 2022).Differentiating laryngeal TB from carcinosis, sarcoidosis, granulomatosis can be done by identifying characteristic features in CT as shown in table 1.

CT findings	Our patient	Laryngeal TB	Laryngeal Ca	Laryngeal sarcoidosis	Wegener's granulomatosis
Bilateral and/or diffuse location	+	+	-	+	+
Soft tissues thickening	+	+	-	+	+
Cartilage destruction	-	+	+	-	+
Extra laryngeal invasion	-	-	+	-	+

Table 1. CT Features of Laryngeal Diseases: Tuberculosis, Carcinoma, Sarcoidosis, GPA. (El Kettani et al., 2010) (Reis et al., 2016) (Ladeb & Peh, 2022) (Baba et al., 2022) (D'Anza et al., 2017) (Guzman-Soto et al., 2021)

Keywords : Laryngeal tuberculosis, Extrapulmonary TB, CT imaging of tuberculosis

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EVALUATION OF SERTRALINE-INDUCED CYTOTOXICITY IN C6 GLIOMA CELLS: A PRELIMINARY IN VITRO STUDY

ABSTRACT

Glioblastoma multiforme (GBM) is the most aggressive and lethal primary brain tumor in adults, with limited therapeutic options and poor prognosis. One of the major challenges in GBM treatment is the restricted delivery of chemotherapeutic agents across the blood-brain barrier (BBB). Selective serotonin reuptake inhibitors (SSRIs), such as sertraline, have demonstrated the ability to cross the BBB and have shown potential anticancer properties in various tumor models. This preliminary study aimed to investigate the cytotoxic effects of sertraline on C6 rat glioma cells and assess its potential for repurposing as an adjuvant therapeutic agent in GBM treatment. Sertraline was dissolved in PBS and RPMI medium at a concentration of 2.5 mg/mL, filtered through a 0.22 µm membrane, and added to 96-well plates containing C6 glioma cells to reach a final concentration of 2.92 mM. After 24 h of incubation, morphological changes were documented under 10× and 40× magnification. Cell viability was quantitatively assessed using the MTS assay. Microscopic evaluation revealed pronounced morphological alterations and cell detachment in sertraline-treated groups compared to controls. MTS assay results confirmed a significant reduction in cell viability, indicating a strong cytotoxic effect of sertraline at the tested dose. These findings suggest that sertraline exerts notable cytotoxic effects on glioma cells in vitro. This supports its potential for further investigation, particularly in combination with standard chemotherapeutics like temozolomide, as a novel therapeutic strategy for GBM.

Key words: Sertraline, Glioblastoma, Cytotoxicity, Anticancer effect, Drug repurposing

C6 GLİOMA HÜCRELERİNDE SERTRALİN KAYNAKLI SİTOTOKSİSİTENİN DEĞERLENDİRİLMESİ: BİR İN VİTRO ÖN ÇALIŞMA

ÖZET

Glioblastoma multiforme (GBM), erişkinlerde görülen en agresif ve ölümcül primer beyin tümörüdür. Mevcut tedavi seçenekleri sınırlı olup prognoz oldukça kötüdür. GBM tedavisindeki en önemli zorluklardan biri, kemoterapötik ajanların kan-beyin bariyerini (BBB) geçme yetisinin kısıtlı olmasıdır. Seçici serotonin geri alım inhibitörleri (SSRI'lar) arasında yer alan sertralin, BBB'yi geçebilen ve çeşitli tümör modellerinde antikanser etki potansiyeli gösteren bir ajan olarak dikkat çekmektedir. Bu ön çalışmanın amacı, sertralinin C6 rat glioma hücreleri üzerindeki sitotoksik etkilerini incelemek ve GBM tedavisinde adjuvan bir tedavi ajanı olarak yeniden konumlandırılma potansiyelini değerlendirmektir. Sertralin, PBS ve RPMI ortamında 2.5 mg/mL konsantrasyonunda çözülerek 0.22 µm membran filtreden geçirilmiş ve 96 kuyucuklu plaklarda kültüre edilmiş C6 glioma hücrelerine son konsantrasyonu 2.92 mM olacak şekilde uygulanmıştır. 24 saat inkübasyonun ardından hücresel morfolojik değişiklikler 10× ve 40× büyütmelerde mikroskobik olarak değerlendirilmiştir. Hücre canlılığı MTS testi ile kantitatif olarak analiz edilmiştir. Mikroskobik incelemelerde, sertralin ile muamele edilen gruplarda kontrol gruplarına kıyasla belirgin morfolojik değişiklikler ve hücre tutunmasının azaldığı gözlenmiştir. MTS testi sonuçları, sertralin uygulanan hücrelerde hücre canlılığında anlamlı düzeyde azalma olduğunu göstermiştir. Bu durum, test edilen dozda sertralinin güçlü bir sitotoksik etkiye sahip olduğunu ortaya koymuştur. Elde edilen veriler, sertralinin glioma hücreleri üzerinde in vitro koşullarda belirgin sitotoksik etki gösterdiğini ortaya koymaktadır. Bu bulgular, sertralinin özellikle temozolomid gibi standart kemoterapötik ajanlarla kombinasyon halinde kullanımının değerlendirilmesi açısından önemli olup, GBM tedavisinde yeni bir terapötik strateji olarak araştırılmasını desteklemektedir.

Anahtar Kelimeler: Sertralin, Glioblastoma, Sitotoksisite, Antikanser etki, İlaç yeniden amaçlandırma

FULL TEXTS

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ZERO WASTE PROJECT APPROACH FOR A SAFE ENVIRONMENT

ABSTRACT

Problem of the Study: Today, with the advancement of technology, the development of industry and the increasing number of populations, the increase in wastes and poorly managed wastes are becoming a threat to the environment and human health. The zero-waste project has not yet been able to deliver what is expected of it at the desired level. For this reason, it has become necessary to ensure the dissemination of the zero-waste project and to increase the level of inadequate public awareness.

Purpose of the Study: The aim of this study is to reduce the amount of waste, to separate recycling products correctly and to increase public awareness on this issue, based on zero waste approaches.

Method: Within the scope of the zero-waste project, relevant regulations, directives, agreements, standards, principles, target policies and practices and studies in the literature were examined.

Findings: It is seen that a protocol consisting of prevention, waste minimization, reuse, recycling, recovery hierarchy has been established for the zero-waste project. In addition, within the scope of the zero-waste project, legal regulations have been made for official institutions, local governments, non-governmental organizations, businesses and settlements. As a result of these regulations, the number of facilities reporting the amount of waste, the number of zero waste awareness trainings and the amount of recycling have increased.

Although the legal legislation and implementation principles of the zero-waste project have been determined, it is seen that the project has not been implemented sufficiently due to the lack of public awareness. It is observed that both public administration institutions, local administrations and the society, which undertake the execution task, face the difficulties of zero waste implementation.

Conclusions In order for the zero-waste project to be successful, it is necessary to standardize these studies with the cooperation of individuals, institutions and the state and to ensure the participation of the society. For this reason, it is important to give importance to education and practices at all levels starting from primary school age, in workplaces and local administrations. By periodically emphasizing the importance of the issue in social media and other communication organs, valuable results can be achieved in terms of public awareness and consciousness. In addition to these regulations, it would be appropriate to eliminate the legal deficiencies arising from legislation and practices through legal regulations.

Keywords: Safe Environment, Health, Zero Waste, Project, Approach

GÜVENLİ BİR ÇEVRE İÇİN SIFIR ATIK PROJESİ YAKLAŞIMI

ÖZET

Çalışmanın Problemi: Günümüzde teknolojinin ilerlemesi, endüstrinin gelişmesi ve artan nüfus sayısıyla ilişkili olarak atıkların artması ve iyi yönetilmeyen atıklar, çevre ve insan sağlığını tehdit eder hale gelmektedir. Sıfır atık projesi henüz istenilen düzeyde kendisinden bekleneni verememektedir. Bu nedenle sıfır atık projesinin yayılımını sağlamak ve yetersiz toplum bilinç düzeyini artırmak gerekli hale gelmiştir.

Çalışmanın Amacı: Bu çalışmayla sıfır atık yaklaşımlarından hareketle, atık miktarının azaltılması, geri dönüşüm ürünlerinin doğru ayrıştırılması ve bu konuda toplum bilincinin artırılması amaçlanmaktadır.

Metod: Sıfır atık projesi kapsamında ilgili yönetmelik, yönerge antlaşma standart, ilke, hedef politika ve uygulamalar ile alan yazındaki çalışmalar incelenmiştir.

Bulgular: Sıfır atık projesi konusunda; önleme, atık minimizasyonu, yeniden kullanım, geri dönüşüm, geri kazanım hiyerarşisinden oluşan protokol oluşturulduğu görülmektedir. Ayrıca, sıfır atık projesi kapsamında resmî kurumlara, yerel yönetimlere sivil toplum kuruluşlarına işletmelere, yerleşim yerlerine yönelik hukuki düzenlemeler yapılmıştır. Bu düzenlemeler sonucunda Atık miktarını bildiren tesis sayısında sıfır atık farkındalık eğitim sayısında ve geri dönüşüm miktarında artışlar kaydedilmiştir.

Sıfır atık projesi hukuki mevzuat ve uygulamaya yönelik esasları belirlenmesine rağmen, toplum bilincinin eksik olması nedeniyle projenin yeterince uygulamaya konulamadığı görülmektedir. Yürütme görevini üstlenen gerek kamu yönetimi kurumları, yerel yönetimler gerekse de toplum açısından sıfır atık uygulamasının zorluklarıyla karşılaştıkları gözlenmektedir.

Sonuçlar: Sıfır atık projesinin başarılı olabilmesi için birey, kurum ve devlet işbirliğiyle bu çalışmaların standartlaşması ve toplumun katılımını sağlamak gerekmektedir. Bu nedenle ilkokul çağından başlayarak her kademede, işyerlerinde, mahalli idarelerde eğitime ve uygulamalara önem verilmesi önem arz etmektedir. Sosyal medyada, diğer iletişim organlarında konunun önemini periyodik olarak tekrar tekrar vurgulanarak toplum bilinci ve farkındalığı açısından değerli sonuçlar elde edilebilir. Bu düzenlemelere ilave olarak, yasal düzenlemelerle mevzuat ve uygulamalardan kaynaklanan hukuki eksikliklerin giderilmesi uygun olacaktır.

Anahtar kelimeler: Güvenli Çevre, Sağlık, Sıfır Atık, Proje, Yaklaşım

GİRİŞ

İnsan davranışlarına bağlı olarak küresel iklim değişikliği, doğal kaynakların tükenmesi, denizler, su, hava ve toprak verimliliğinin azalması, ormanların yok edilmesi, çölleşme, buzulların erimesi, biyo-çeşitlilik kaybı, katı atıklar, plastik kirliliği gibi çevresel sorunlar insanlığın geleceğini tehdit etmektedir. Çevresel sorunların en önemli nedenlerinin başında, mevcut al-yap-at odaklı lineer endüstriyel üretim ve tüketim anlayışı ve yapısı gelmektedir. Mevcut lineer endüstriyel üretim ve tüketim yapısının neden olduğu sosyal, ekonomik ve çevresel etkilerin ortadan kaldırılması, sürdürülebilir kalkınmanın odağında yer almaktadır. Döngüsel ekonomi, mevcut lineer üretim yapısına/anlayışına alternatif bir üretim yapısı/anlayışı olarak hem iş dünyasında hem akademi dünyasında hem de politika yapıcıların gündeminde yer edinmiştir. Sürdürülebilirliği sağlamak, çevresel sorumlulukları başarılı bir şekilde üstelenebilmek, kaynak ve enerji verimli temiz ürün ve üretim teknolojileri ile rekabet üstünlüğü elde edebilmek adına önemi giderek artan döngüsel ekonomi, kimi yazarlar tarafından bir paradigma değişimi olarak ifade edilmektedir. Kaynak ve karbon yoğun, sürekli atık üreten bir endüstriyel üretim ve tüketim yapısının, kaynak kullanımı ve çevresel değer kayıplarından koparılmış bir ekonomik büyüme (decoupling) patikasına sevk edilmesi gerçekten de mevcut üretim anlayışının, teknolojik gelişmenin yönünün, yeniliklerin doğasının ve iş örgütlenmelerinin temelden değişimine işaret etmektedir. 1990'lı yıllarla birlikte içeriği belirginleşmeye başlayan döngüsel ekonomi kavramının, 1960'lı yıllara dayanan, biyoloji bilimi ve sistem teorisinin etkisiyle şekillenen bir geçmişinden bahsetmek mümkündür. Doğadaki döngüsellik, döngüsel ekonomi anlayışının doğal (biyo-fiziksel) sistemlerin ekonomik sistemler tarafından taklit edilebileceği argümanının temel dayanağıdır. (Banerjee ve Duflo, 2011)

"Döngüsel bir ekonomi yaklaşımı, "doğal kaynaklar üretilmiş ürünlere dönüştürme diğer endüstriler için kaynak olarak kullanılan imalat yan ürünleri" süreciyle doğal ekosistemleri taklit eden geri bildirim süreçleriyle ekonomik faaliyetlerin organizasyonunu teşvik eder." (Geng ve Doberstein, 2008, s. 232)

"Döngüsel ekonomi, niyet ve tasarım gereği onarıcı veya yenileyici olan ve 'yaşam sonu' kavramını restorasyonla değiştiren, yenilenebilir enerji kullanımına geçiş yapan, yeniden kullanımı bozan zehirli kimyasalların kullanımını ortadan kaldıran, üstün malzeme, ürün, sistem tasarımı ve iş modelleri ile israfın ortadan kaldırılmasını amaçlayan bir endüstriyel sistemdir." (EMF, 2013, s. 7).

"Döngüsel ekonomi, mevcut malzeme ve ürünlerin mümkün olduğunca uzun süre paylaşılmasını, kiralanmasını, yeniden kullanılmasını, onarılmasını, yenilenmesini ve geri dönüştürülmesini içeren bir üretim ve tüketim modelidir." (European Parliament, 2023, s. 1)

"Döngüsel ekonomi, malzemelerin üretimini, tüketimini ve atılmasını en aza indirirken refah yaratmayı amaçlar." (World Bank, 2022, s. 27)

Atık önleme hiyerarşisi: Kurum ve kuruluşlar tarafından kullanılan atık yönetimi hiyerarşisinde 6 sistematik yaklaşım bulunmaktadır. Bunlar:

- Önleme
- Azaltma
- Tekrar kullanım

- Geri Dönüşüm
- Enerji kazanımı
- Bertaraf

1893 yılında, lisans öğrencisi Washington Carver tarafından yayınlanan bir makalede, doğada hiçbir atık materyalin olmadığı, atık hale gelmiş ürünlerin, başka bir ürüne hammadde kaynağı olarak kullanılabileceği belirtilmiştir. Carver "atıkları kılık değiştirmiş bir başka kaynak" olarak tanımlamış, ağaç yapraklarından, çiftlik gübresine kadar birçok atığın tekrar hammadde olarak değerlendirilebileceği konularında sunumlar yapmıştır. Yine 1930'lu yıllarda Henry Ford, ürettikleri otomobillerin bazı parçalarından, soya fasulyesi küspesi elde etmiş, atık şişelerin tekrar kullanılması ve diğer atıkların değerlendirilmesi ile de maddi tasarruf elde etmeyi başarmıştır. Bu girişimleri ile Carver ve Ford, sıfır atık anlayışının öncüleri olarak kabul edilebilmektedir (Yaman ve Olhan, 2010: 53). Tüm Dünyada bütün atıklar atık yönetimi, atıkların önlenmesi, atıkların azaltılması, çevreye saygılı davranma gibi konularda çok sayıda araştırma yapılmaktadır. (Whitmarsh et.al2018) Atık üretimi, insanlık tarihi kadar eskiye dayanmakla birlikte, oluşan atığın yönetimi, son yıllarda üzerine dikkatle durulması gereken bir alan olarak ortaya çıkmaktadır. İnsanların yaşamlarını sürdürebilmek için bazı kaynakları kullanması, varoluşsal bir gereklilik olmakla birlikte, bu kaynakların tüketilmesi, doğanın kendini yenileyebilme gücü sayesinde ilk etapta sorun teşkil etmemiştir. Ancak artan nüfusun tüketme eğilimi ve taleplerde yaşanan artışlar, sadece ekonomik büyümeye odaklanmış ekonomi modelleri ile birleşerek, doğal kaynakların hızla yok olmasına neden olmuştur. Kaynakların tüketilmesi önemli bir sorun olmakla birlikte, üretim ve tüketim faaliyetleri sonrasında yaşanan tahribat, doğal döngünün yenilenebilme kapasitesini aşan bir seviyeye ulaşmıştır (Stainer ve Wiegel, 2009).

ARAŞTIRMA VE BULGULAR

Atık yönetiminin güncel bir yaklaşım biçimi olan sıfır atık kavramı her geçen gün daha çok benimsenmektedir. Atık yönetiminin en önemli maddesi ÖNLEMEDİR. Türkiye'de hızlı nüfus artışı, kentleşme, sanayi, endüstri ve teknolojik alanlarında yaşanan gelişmeler, atık türünün çeşitlenmesine ve miktarının artmasına neden olmaktadır. Bu artış, atıkların oluşumundan, canlılar ve doğa için tehlike oluşturmayacak hale getirilinceye kadar ki süreçte izlenecek yol ve yöntemlerin belirlenmesi gerekliliğini ortaya çıkarmaktadır. Daha az atık üretmeye dayalı üretim ve tüketim faaliyetlerinin hayata geçirilmesi tüm dünyada olduğu gibi Türkiye'de de çevre koruma politikaları arasında önemli bir yere sahiptir. Bu politikalar çerçevesinde Türkiye'de yürürlükte olan ulusal mevzuat aşağıda özetlenmiştir. Alan yazında yapılan araştırmalara bakıldığında, Whitmarsh et. al (2018) İngiltere üniversitelerinde çalışan işçiler üzerinde yaptıkları araştırma sonucunda evde geri dönüştürülen atık oranının (%67), işyerlerine (%39) ve tatil beldelerine (%38) oranla daha yüksek olduğunu bulmuşlardır. Lee & Paik (2011) Kore'deki mevcut ev geri dönüşüm ve atık yönetimi davranışlarını ve bu davranışları etkileyen faktörleri incelemişler ve sonuçta çevresel tutumların, çeşitli demografik değişkenlerle birlikte geri dönüşüm ve atık yönetimi davranışlarını önemli ölçüde etkilediğini belirlemişlerdir. Troschinetz, A. M. & Mihelcic, J. R. (2009) aralarında Türkiye'nin de bulunduğu 23 gelişmekte olan ülkede evsel katı atık üretimi ve geri kazanım oranları üzerine yaptıkları araştırmada ise ortalama evsel katı atık

üretiminin 0,77 kg/kişi/gün ve geri kazanım oranları %5-40 arasında olduğunu belirlemişlerdir. Tadasse (2009) Etyopya'nın Mekelle şehrinde yaptığı araştırmada geri dönüşüm oranlarının çöp konteynerlerinin uzakta olması, ailelerdeki birey sayısı ve atık tutumunun pozitif ilişkili olduğunu göstermiştir.

Türkiye'de Atık Yönetimi ve Sıfır Atık Projesinin Değerlendirilmesi:

T.C. Anayasası Normlar hiyerarşisine göre Türkiye'de en üst norm sayılan, 7 Kasım 1982 tarihli Türkiye Cumhuriyeti Anayasası'nın 56. Maddesinde "Herkes, sağlıklı ve dengeli bir çevrede yaşama hakkına sahiptir. Çevreyi geliştirmek, çevre sağlığını korumak ve çevre kirlenmesini önlemek Devletin ve vatandaşların ödevidir" hükmü bulunmaktadır (T.C. Anayasası, 1982). Söz konusu madde, çok geniş bir alanı kapsamakla birlikte, atık yönetimi bağlamında değerlendirildiğinde; çevre kirliliğine neden olan etmenler içerisinde önemli bir role sahip olan atıkların, bireyler ve devletin müşterek gayretleri ile çevre ve insan sağlığı açısından tehlike arz etmeyecek bir seviyeye getirilmesinin, herkesi bağlayan bir sorumluluk olduğu görülmektedir. 2872 Sayılı Çevre Kanunu 09.08.1983 tarihli 2872 Sayılı Çevre Kanunu "Bütün canlıların ortak varlığı olan çevrenin, sürdürülebilir çevre ve sürdürülebilir kalkınma ilkeleri doğrultusunda korunmasını sağlamak" amacı ile hazırlanmıştır. Bu kanuna göre; devletin ve onu oluşturan bireylerin, gelecek nesillere sağlıklı bir çevre bırakma yükümlülüğü bulunmakla birlikte, sahip oldukları kaynakların kullanması suretiyle de ülke kalkınmasını sağlamaları gerekmektedir. Kanununun temel amacı da bu iki işlevin dengeli bir biçimde yerine getirilmesini sağlamaktır. Her geçen gün artan ve çeşitlenen kirletici türleri nedeniyle tahrip olan çevrenin, idare, vatandaşlar, sivil toplum kuruluşları ve meslek odaları eliyle korunması ve oluşabilecek tehlikelerin de tedbir alınması suretiyle önlenmesi, kanunun genel ilkeleri arasında yer almaktadır. Kanunda yer alan bir diğer husus da kirletme yasağı ve kirleten öder ilkesi olup, kirlenme ihtimalinin bulunduğu hallerde tedbir alınması veya bertaraf edilmesi, kirletenlerin sorumluluğunda bulunmaktadır.

Belediye Kanunu Genel olarak belediyelerin kuruluşu, yönetimi, organları, yetkileri, görev ve sorumlulukları çalışma usul ve esaslarının düzenlendiği 03.07.2005 tarih ve 5393 sayılı Belediye Kanunu, atık yönetimi ile ilgili maddeler içermektedir. Kanununun 15.g maddesinde "Katı atıkların toplanması, taşınması, ayrıştırılması, geri kazanımı, ortadan kaldırılması ve depolanması ile ilgili bütün hizmetleri yapmak ve yaptırmak" (Belediye Kanunu, 2005) belediyelerin görev ve sorumluluğunda olduğu belirtilmiştir. Çevre Kanunu'nun 11. maddesinde "Büyükşehir belediyeleri ve belediyeler evsel katı atık bertaraf tesislerini kurmak, kurdurmak, işletmek veya işlettirmekle yükümlüdürler" hükmü bulunmaktadır.

Büyükşehir Belediyesi Kanunu 5393 sayılı Belediye Kanununda olduğu gibi Büyükşehir Belediyesi Kanununda da, atık yönetimi hususu ele alınmış olup, kanunun 7. maddesinde "…Büyükşehir katı atık yönetim plânını yapmak, yaptırmak; katı atıkların kaynakta toplanması ve aktarma istasyonuna kadar taşınması hariç katı atıkların ve hafriyatın yeniden değerlendirilmesi, depolanması ve bertaraf edilmesine ilişkin hizmetleri yerine getirmek, bu amaçla tesisler kurmak, kurdurmak, işletmek veya işlettirmek; sanayi ve tıbbî atıklara ilişkin hizmetleri yürütmek, bunun için gerekli tesisleri kurmak, kurdurmak, işletmek veya işlettirmek; deniz araçlarının atıklarını toplamak, toplatmak, arıtmak ve bununla ilgili gerekli düzenlemeleri yapmak" (Büyükşehir Belediyesi Kanunu, 2014) hükmü yer almaktadır. Bu madde aynı zamanda il sınırları içerisindeki ilçe belediyelerini de bağlamakta olup,

büyükşehir belediyelerince yapılacak olan yönetim planına uygun olarak katı atıkları toplamak ve aktarma istasyonuna ulaştırmakla sorumludurlar.

Atık Yönetimi Yönetmeliği 02.04.2015 tarihli Atık Yönetimi Yönetmeliği, atık oluşumunun azaltılması, atıkların insan ve çevre sağlığına zarar vermeden bertaraf edilmesi, yeniden kullanım, geri dönüşüm ve doğal kaynak kullanımının azaltılması gibi hususların hangi yöntemlerle ve kimler tarafından yapılacağını belirtmektedir. İlgili yönetmelik, atık üretiminin teknolojik gelişmelerden faydalanılarak, daha az doğal kaynak kullanımı ile üretim, kullanım, geri kazanım ve bertarafının sağlanması, dayanıklı, yeniden kullanılabilen ve geri dönüştürülebilir ürünlerin tasarlanması, atıkların; toplama, taşıma, geri dönüşüm, bertaraf gibi aşamalarında, insan, çevre ve diğer canlılar açısından risk yaratmayacak yöntemlerin kullanılmasını belirlemiştir.

Elektrikli ve Elektronik Araçların Kontrolü Yönetmeliği

22.05.2012 tarihli Atık Elektrikli ve Elektronik Eşyaların Kontrolü Yönetmeliği, elektrikli ve elektronik cihazların üretiminde kullanılan zararlı maddelerin sınırlandırılması, bu sınırlamalardan muaf olacak olanların belirlenmesi, ithalatlarının kontrol altına alınması ve yeniden kullanım, geri kazanım veya geri dönüşüm gibi işlemlerin teknik ve hukuki esaslarının belirlenmesi amacı ile hazırlanmıştır. Yönetmeliğe göre, teknik açıdan uygun olması halinde öncelikle geri dönüşümü sağlanabilen malzemeden imal edilmesi, bir bütün olarak yeniden kullanımının sağlanması, teknik olarak işlendikten sonra geri dönüşüm ve geri kazanımı mümkün olmaması halinde bertarafının sağlanması gerekmektedir (Atık Elektrikli ve Elektronik Araçların Kontrolü Yönetmeliği, 2012).

Ambalaj Atıklarının Kontrolü Yönetmeliği

Ambalajlar, bir ürünün, üreticiden tüketiciye ulaşıncaya kadar, korunması, saklanması, taşınması, gibi amaçlarla üretilmekte olup; yönetmelik, kullanım sonrası oluşacak atıkların önlenmesi, önlemenin mümkün olmaması durumunda, yeniden kullanım, geri dönüşüm veya geri kazanım yöntemleri ile bertaraf edilmesi sürecinde izlenecek yol ve yöntemleri kapsamaktadır. (26 Haziran 2021 tarihinde yürürlüğe giren Ambalaj Atıklarının Kontrolü Yönetmeliği.)

Tıbbi Atıkların Kontrolü Yönetmeliği

Tıbbi atık üreticisi olarak belirtilen hastaneler, toplum sağlığı merkezleri, diyaliz merkezleri, morg ve otopsi merkezleri, laboratuvarlar, kan merkezleri, ambulanslar, akupunktur ve güzellik merkezleri, veterinerler, eczaneler gibi faaliyetleri sonucu tıbbi atık oluşumuna neden olan kişi, kurum ve kuruluşların ürettikleri atıkların, insan ve çevre sağlığına zarar vermeden bertaraf edilmesine ilişkin esasları kapsayan yönetmelik, 25.01.2017 tarihinde yürürlüğe girmiştir. Yönetmeliğe göre tıbbi atık üreticileri tarafından üretilen; kesici, delici, enfeksiyon yapıcı ve patolojik atıkların, oluştukları anda kaynağında ayrıştırılması esas olup, diğer atık türleri ile karıştırılması yasaklanmaktadır. Atıklar, özel eğitimli ve koruyucu giysiye sahip personel tarafından taşıma araçları ile sağlık kuruluşları içerisinde bulunan geçici depolama merkezlerine taşınmakta, burada en fazla 48 saat bekletildikten sonra, ilgili

belediyelerce toplanmakta ve bertaraf tesislerinde işleme tabi tutulmaktadır (Tıbbi Atıkların Kontrolü Yönetmeliği, 2017).

Bitkisel Atık Yağların Kontrolü Yönetmeliği

Yenilebilir katı ve sıvı yağlar ile kullanılmış kızartmalık yağları kapsayan Bitkisel Atık Yağların Kontrolü Yönetmeliği 06.06.2015 tarihinde yayımlanmıştır. Yönetmeliğe göre, bitkisel kökenli yağların, konutlarda, resmi veya özel kuruluşlarda ve yemek hizmeti sunan işletmelerde kullanımı sonrasında, yetkili kişi veya kurumlarca toplanıp, geri kazanım tesislerinde gerekli teknik işlemler yapıldıktan sonra Enerji Piyasası Düzenleme Kurulunca belirlenen standartlarda biyodizel ve biyogaza dönüştürülebilmektedir. Başka herhangi bir şekilde ikincil kullanımı mümkün olmayan atık yağların, yetkisiz kişilerce toplanması veya kanalizasyona boşaltılması yasaklanmakta olup, bitkisel yağ üreticileri, atık yağ üreticileri, belediyeler ve geri dönüşüm tesisleri bu süreçten müteselsil sorumlu bulunmaktadırlar (Bitkisel Atık Yağların Kontrolü Yönetmeliği, 2015).

Atık Pil ve Akümülatörlerin Kontrolü Yönetmeliği

İçeriğinde bulunan kimyasal maddelerin reaksiyona girmesiyle, doğrudan enerji kaynağına dönüşen pil ve akümülatörler, muhteviyatında yer alan cıva, kurşun, nikel, kadmiyum, sülfirik asit gibi tehlikeli maddeler nedeniyle, insan ve çevre sağlığı açısından tehlike yaratabilmektedir. 31.08.2004 tarihli yönetmelik, pil ve akümülatörlerin üretiminden bertarafına kadar ki süreçte, izlenecek teknik ve hukuki esasları düzenlemektedir. Yönetmeliğe göre, üretilen pil ve akümülatörlerin, şarj edilebilir özellikte ve uzun ömürlü olanları öncelikle tercih edilmekte olup, kullanım sonrası geri kazanımları esastır. Üretici ve ithalatçılar, zararlı madde içeren pil ve akümülatörleri üretmemekle veya ithal etmemekle yükümlü bulunmaktadır. Atık pillerin toplanmasında, kota uygulaması bulunmakta olup, her yıl bakanlıkça belirlenen oranlarda, üreticiler tarafından atık pil toplama veya toplatma ve bertaraf yükümlülüğü bulunmaktadır. Atık akümülatörler için de üreticiler tarafından depozito ödeme zorunluluğu bulunmakta olup, bu bedel, akümülatörlerin kapasitesi dikkate alınarak, bakanlık, üreticiler ve geri kazanımcılar tarafından bir yıl geçerli olmak üzere her yıl aralık ayında belirlenmektedir (Atık Pil ve Akümülatörlerin Kontrolü Yönetmeliği, 2004)

SONUÇ

Türkiye'de Sıfır Atık Yönetim Sistemi Türkiye'de 2016 yılında oluşan belediye atığının %65'i düzenli depolama suretiyle bertaraf edilirken, %9 oranında geri kazanım sağlandığı görülmüştür (TÜİK, 2020a). Bu oran gelişmiş ülkelerde farklılık göstermektedir. Bakanlığımız öncülüğünde ve Sayın Emine Erdoğan'ın himayelerinde yürütülen Sıfır Atık Hareketi çalışmaları kapsamında geri dönüşüm oranı 2023 yılında % 34,92'ye yükselerek, hedefe her geçen gün yaklaşılıyor.

Sıfır Atık Hareketi kapsamında yapılan çalışmalar ile:

- 017 yılı haziran ayından bu yana sıfır atık yönetim sistemine geçen bina/yerleşke sayısı yaklaşık **185 bine** ulaşmıştır.

- Sıfır atık konusunda yaklaşık **21 milyon** kişiye eğitim verilmiştir.
- 2017'de % 13 olan geri kazanım oranımız 2021 yılında % 27,2'ye ; 2022 yılında % 30,13'e ; **2023 yılında % 34,92**'ye yükselmiştir.
- Geri kazanım oranımızın **2035 yılında % 60'a** çıkarılması hedeflenmektedir.
- Proje başlangıcından bu yana 29,3 milyon ton kağıt-karton, 7,8 milyon ton plastik, 2,9 milyon ton cam, 3,7 milyon ton metal ve 16,2 milyon ton organik ve diğer geri dönüştürülebilir atıklar olmak üzere toplamda yaklaşık **59,9 milyon ton** geri kazanılabilir atık, Bakanlığımızdan lisans almış işletmelerce işlenerek ekonomiye kazandırılmıştır.
- Toplanan atıklar geri dönüştürülerek **256 milyar TL** ülkemiz ekonomisine kazandırılmış, 2,6 milyar kWh enerji tasarrufu, 819 milyon m^3 su tasarrufu, 104 milyon m^3 depolama alanından tasarruf sağlanmış, 5,9 milyon ton sera gazı salımı önlenmiş, 498 milyon ağaç kurtarılmış, 127 milyon varil petrolden tasarruf edilmiştir.
- Yine ülkemizde sıfır atık projesini destekleyen sürdürülebilirliğine katkı sağlayan Tema vakfı, Diyanet Vakfı, Özel işletmeler, sağlık kuruluşları, Milli Eğitim Bakanlığı'nın teşvik edici uygulamalarını ,eğitim programları düzenlediklerini görmekteyiz.

Türkiye'de sıfır atık mağazacılık konsepti, tüketicilere ambalajsız ürünler sunarak atık oluşumunu en aza indirmeyi hedeflemektedir. Bu mağazalar, özellikle büyük şehirlerde yaygınlaşmakta ve çevre dostu alışveriş alternatifleri sunarak sürdürülebilir tüketim alışkanlıklarını teşvik etmektedir. Ambalajsız ürünler, genellikle yerel üreticilerden temin edilmekte ve bu sayede hem gıda güvenliği sağlanmakta hem de karbon ayak izi azaltılmaktadır. Sıfır atık mağazaları, tüketicilerin kendi kaplarını getirerek ürün satın almasına olanak tanıyarak, tek kullanımlık ambalajların kullanımını azaltmaktadır. Araştırmalar, ambalajsız alışverişin, plastik atıkların %30'a kadar azaltılmasına katkı sağlayabileceğini göstermektedir. Ayrıca, bu mağazalar, toplumsal farkındalığı artırarak çevre bilincini güçlendirmekte ve sürdürülebilir yaşam tarzlarını desteklemektedir. Türkiye'deki sıfır atık mağazaları, bu bağlamda hem ekonomik hem de çevresel sürdürülebilirliğe katkıda bulunarak önemli bir rol oynamaktadır (Küçük, A., & Yıldız, M. 2022 KAYNAK Budak, Y., & Keçeci, M. (2024).

Türkiye'de atık yönetimi ve sıfır atık projesinin işlerliğine bakıldığında bireylerin; sıfır atık projesinde atıkların kaynağında ayrıştırılması gerektiğini, atık değerlendirilmesinin ne şekilde yapıldığı ve Türkiye'de uygulanan sıfır atık projesi hakkında çok az bilgi sahibi olduğu anlaşılmaktadır. Sıfır Atık Projesi kapsamında, konutlarda kâğıt, metal, cam ve plastik atıklara yönelik ayrı toplama işlemi kısmen yapılmakta olup, kişilerin çevrelerinde atıkların türlerine göre ayrı toplanabileceği sıfır atık projesine uygun kumbaralar da kısmen bulunmaktadır. Sıfır Atık Projesi kapsamında kamu kurumlarında kâğıt, metal, cam ve plastik atıklar ayrı olarak biriktirilmekte olup, yine proje kapsamında işyerlerinde de kâğıt, metal, cam ve plastik atıklar ayrı olarak biriktirilmektedir. İfadelere verilen cevaplara göre atıkların ayrı biriktirilme işlemine, çalışma alanlarında konutlara kıyasla daha fazla dikkat edilmektedir. Yapılan araştırmada Ankara'da ikamet eden bireyler de atık kumbaraları kısmen yeterli bulmakta, arttırılması gerekliliği ortaya çıkmaktadır. Araştırmaya katılan bireylerce, sıfır atık projesi ile ilgili yapılan duyurular (dergi, broşür, tanıtıcı reklam, afiş, poster, yazılı ve görsel yayınlar, vb.) yeterli bulunmamaktadır. Kişilerin işyerlerinde yapılan eğitim ve farkındalık oluşturma çalışmaları kısmen yeterli bulunmakta olup, alışveriş poşetlerinin ücretli olmasının da projeye kısmi katkı sağladığı görülmektedir. Özcan (2020)

tarafından yapılan bir çalışmada, sıfır atık yönetim sistemi konusunda işyerlerinde eğitim ve bilinçlendirme çalışmaları yapılıp yapılmadığı araştırılmış, Antalya Konyaaltı Belediyesi'nde %65, Antalya Çevre ve Şehircilik İl Müdürlüğü %88, özel işletmelerde ise %36,3 oranında olumlu yanıt alınmıştır. Bu kapsamda, Sıfır Atık Projesinin icracı kurumları olan belediyeler ve Çevre ve Şehircilik İl Müdürlüklerinde kendi personellerine yönelik eğitim ve bilinçlendirme çalışmalarına önem verildiği yargısı çıkarılabilir. Ancak özel işletmelerde (Ankara'da olduğu gibi) bilinçlendirme çalışmalarına önem verilmesi gerekmektedir. Sıfır Atık Projesi kapsamında, belediyeler veya ilgili kamu kurum ve kuruluşlarının, israfın önlenmesine yönelik bilgilendirme ve farkındalık çalışmaları ile belediyelerin atıklara ilişkin hizmetleri kısmen yeterli bulunmaktadır.

Araştırma sonuçları; bireylerin atık hale gelmiş elektrikli ve elektronik eşyaları, kullanılmış pilleri ve bitkisel atık yağları ayrı biriktirerek toplama noktalarına teslim etmede, asıl kullanım amacını yitirmiş bir ürün veya malzemeyi, mümkün olduğunca geri dönüştürmede, evlerde oluşan katı atıkları sıfır atık projesine uygun olarak ayrıştırmada yeterince özenli davranmadıklarını göstermektedir. Bu bağlamda, atıkların ayrı toplanması için bireylerce yapılan katkının kısmi olduğu tespit edilmiştir. Atıkların ayrı toplanması amacıyla gerekli olan ekipmanların, bireylerin çevrelerinde yeterli miktarda olup olmadığı, konut, işyeri ve kamu kurumu gibi alanlarda, bu ayrı toplama işlemine katılım sağlayıp sağlamadıkları da araştırılmış, bireylerin çevresinde bu ekipmanların çok yaygın olmasa da orta düzeyde bulunduğu ve ayrı toplama işlemine kısmen katıldıkları tespit edilmiştir. Ayrıca, tehlikeli sayılabilecek atıklar ile giysi ve tekstil atıklarının ayrı toplanmasında özenli davrandıkları görülmektedir. Türkiye'de var olan atık yönetim uygulamalarının, mevcut haliyle, atıkların bertaraf edilmesine dönük olduğu, son yıllarda geri kazanım ve geri dönüşüm yöntemlerine ağırlık verildiği, bu kapsamda uygulamaya alınan Sıfır Atık Projesinin önemli olduğu tespit edilmiştir. Alan araştırmasından elde edilen genel kanı ise bireylerin atıklar konusunda yeterince bilgi sahibi olmadığı, kaynağında ayrı biriktirme ile sağlanabilecek faydalar hakkında daha fazla bilinçlenmesi gerektiği, kamu kurum ve kuruluşları, belediyeler ve özel işletmelerce, kişilerin bu konuda bilgi sahibi olması amacıyla bilgilendirme, duyuru ve farkındalık çalışmalarına ağırlık vermesi gerektiği tespit edilmiştir. Her bir birey, kurum, kuruluş veya işletme bir atık üreticisi olarak düşünüldüğünde, atıklar konusunda başarı elde edilebilmesi için topyekûn bir katılım sağlanması gerektiği düşünülmektedir. Atıklar nedeniyle oluşan kirliliğin azaltılmasında bireylerin kendini sorumlu hissetmesi çok olumlu bir yaklaşım olarak tahlil edilmiş, ancak yapılan araştırmada bu yaklaşımın uygulamaya yeteri kadar yansımadığı görülmektedir. Bu birbirine tezat iki durum, farkındalık ve bilgilendirme çalışmaları ile bu konuda verilen hizmetin yeteri kadar olmamasıyla izah edilebilmektedir. Bireylerde görülen sorumluluk hissiyatının, fiili bir kazanıma dönüşmesi için yapılabileceklerin başında, bu konudaki eğitim çalışmalarının arttırılması ve teknik altyapının geliştirilmesi gelmektedir. Araştırma da görüldüğü üzere, yaş kavramı atık konusunda ayrıştırıcı bir neden olmamaktadır. Bu kapsamda, her yaştan her sınıftan bireyin atıklar konusunda bilinçlendirilmesi, vereceği zararların neler olduğu ve bireyin kendine yansımalarının neler olabileceği, geri dönüştürülen her atığın fiili faydaları ve buradan elde edilebilecek kazanımların neler olabileceği gibi hususlarda, her kesime hitap edebilecek farkındalık çalışmalarının yapılması gerektiği görülmektedir. Ayrıca, bireylerin bilinçlenmesi tek başına yeterli bir olmayıp idarelerce teknik altyapının da bu kapsamda geliştirilmesi gerekmektedir. Yayımlanan Yönetmelikte, bina ve yerleşkelerin sisteme dâhil olması gereken süreler açıkça belirtilmiş olup ilgililerin bu kapsamda gereken tedbirleri alarak sürecin takip edilmesi gerekmektedir. Özetle, Sıfır Atık Projesi nedenleri ve sonuçları bağlamında önemli görülmekte, bu yaklaşımın bir tercih değil zorunluluk olduğu düşünülmektedir (Murat GÜL- Kemal YAMAN).

Bütün bu araştırmaların sonucunda Dünya bizim evimizdir. Hangi coğrafya da olursak olalım hangi ırktan hangi dilden olursak olalım tabiat konusunda evrensel ve aynı dili kullanmak zorundayız. Sıfır atık uygulaması proje olmaktan çıkıp her insanın tabiatı korumak, güçlendirmek, sürdürülebilirliğini sağlamak adına görevi olmalıdır. Görüldüğü üzere bu konuyla alakalı yönetmelikler, bu yönetmelikler kapsamında kurumlar, işletmeler, yerleşkeler belirlenmiştir. Ancak bazı uygulamalar gönüllülük esasına dayandırılmıştır. Gönüllük esasına dayandırılması ise uygulamaları kısıtlamakta istenen seviyeye ulaşılamamaktadır. Bu nedenledir ki uygulamaların bir an önce aileler, yaşam mahalleri, binalarda yasal yükümlülüklerle desteklenmeli ve yaşanabilir bir dünya için sorumluluklarımızı yerine getirmeliyiz (Derya, vd.2025).

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FPGA-BASED DATA HANDLING FOR DEEP-SPACE APPLICATIONS UNDER POWER AND COMPUTİNG CONSTRAINTS

ABSTRACT

Deep-space missions demand real-time data processing capabilities under stringent constraints on power, computational resources, and communication bandwidth. Traditional data handling approaches relying on ground-based analysis are becoming increasingly infeasible due to the growing data volumes and significant transmission delays. This paper presents a novel architecture for real-time data handling in deep-space systems using adaptive Field Programmable Gate Array (FPGA) platforms. The proposed framework leverages dynamic partial reconfiguration, low-power processing cores, and custom hardware accelerators to enable in-situ data reduction, compression, and intelligent event detection. By offloading critical tasks such as image preprocessing, anomaly detection, and signal classification to the FPGA, the system minimizes dependency on Earth-based processing and significantly reduces the volume of data requiring transmission. Experimental evaluations demonstrate substantial improvements in throughput and energy efficiency compared to conventional CPU- or GPU-based approaches. The design also incorporates fault-tolerant mechanisms to ensure reliable operation in radiation-prone space environments. This research highlights the potential of adaptive FPGAs to meet the evolving computational demands of autonomous deep-space missions, paving the way for more efficient, intelligent, and responsive exploration systems.

1. Introduction

The exploration of deep-space environments—such as distant planets, moons, asteroids, and interstellar space—has entered a new era marked by increasingly complex missions and scientific instruments. Modern spacecraft are equipped with high-resolution cameras, spectrometers, radar systems, and other advanced sensors that generate massive volumes of data. However, deep-space missions are inherently constrained by limited power availability, harsh radiation conditions, restricted onboard computing capabilities, and long communication delays with Earth. These challenges necessitate a paradigm shift in how data is managed, processed, and utilized in situ. Traditionally, raw or minimally processed data is transmitted back to Earth for detailed analysis. This model, while effective for nearby planetary missions, becomes inefficient and unsustainable for distant or long-duration missions due to several reasons: Bandwidth Limitations: Communication with deep-space probes involves low data rates, often in the range of a few kilobits per second. Latency: Round-trip communication delays can extend to hours or even days, making real-time control or analysis impractical. Energy Constraints: Spacecraft power budgets are limited, especially for missions operating far from the Sun or in shadowed regions where solar energy is minimal. Mission Autonomy Needs: Increasingly, missions require intelligent decision-making onboard to respond to transient phenomena, hazardous terrain, or operational contingencies. In response to these challenges, onboard real-time data handling is emerging as a critical capability. Among various processing platforms, Field Programmable Gate Arrays (FPGAs) offer a compelling balance between performance, reconfigurability, and power efficiency. Modern FPGAs can be tailored for specific applications, support concurrent execution of multiple processing pipelines, and include embedded processors and AI accelerators, making them ideal for resource-constrained, autonomous space missions. This paper explores the application of adaptive FPGA platforms for real-time data handling in deep-space systems. By "adaptive," we refer to systems that can reconfigure themselves dynamically in response to mission demands or environmental conditions. Key contributions of this work include: A power-aware architecture utilizing dynamic partial reconfiguration (DPR) to switch between processing modes and conserve energy. Custom-designed FPGA modules for tasks such as sensor data compression, image preprocessing, machine learning inference, and anomaly detection. Fault mitigation strategies to ensure robustness against single-event upsets (SEUs) and other radiation-induced errors. Experimental validation through hardware-in-the-loop simulations and FPGA prototyping, demonstrating performance gains and energy savings over conventional processors. In the sections that follow, we review the state-of-the-art in deep-space onboard processing, describe the architecture and implementation of our FPGA-based system, present experimental results, and discuss implications for future mission designs.

2. Literature Survey

Recent advancements in deep-space exploration have highlighted the growing need for onboard data processing to overcome the limitations of long-distance communication and resource constraints. Numerous studies have investigated methods for enabling real-time or near-real-time data handling in space systems, with increasing emphasis on the use of reconfigurable hardware such as FPGAs.

2.1 Onboard Processing Challenges in Deep-Space Missions

Traditional spacecraft systems rely on fixed-function processors or radiation-hardened CPUs, such as the RAD750, which offer high reliability but limited performance and

flexibility. As sensor resolutions and scientific data volumes have increased, these processors have proven inadequate for real-time data-intensive applications. NASA's Mars rovers and ESA's Rosetta mission reported challenges with bandwidth bottlenecks and processing delays, prompting investigations into more efficient onboard data handling mechanisms [1][2].

2.2 FPGA Usage in Space Applications

FPGAs have emerged as a promising solution for onboard processing due to their parallel processing capabilities, low power consumption, and reconfigurability. Missions such as NASA's Earth Observing-1 (EO-1) and the Lunar Reconnaissance Orbiter (LRO) demonstrated successful use of FPGA-based hardware for image processing and compression tasks [3][4]. These systems showed significant speedups and energy savings compared to CPU-based implementations. The use of radiation-tolerant FPGAs, such as Xilinx's Virtex-5QV and Microsemi's RTG4, has also made it feasible to deploy such platforms in space. However, early FPGA applications were largely static, with limited adaptability to changing mission requirements or onboard conditions.

2.3 Adaptive and Reconfigurable Architectures

Dynamic Partial Reconfiguration (DPR) has enabled FPGAs to modify their functionality at runtime without halting system operation. Studies like those by F. Méric et al. [5] and D. Koch et al. [6] have shown that DPR can be used to switch between processing modules (e.g., compression vs. classification) based on mission phase or available resources, reducing overall power consumption and silicon area usage. Recent efforts by ESA's Data Processing Units (DPUs) and NASA's High-Performance Spaceflight Computing (HPSC) initiative have further emphasized the shift toward adaptable, AI-capable, and modular hardware platforms that integrate FPGAs, CPUs, and AI accelerators to support intelligent autonomy and fault tolerance [7][8].

2.3 FPGA-Based AI and Signal Processing in Space

There is growing interest in implementing machine learning algorithms directly on FPGAs for tasks such as anomaly detection, feature extraction, and event classification. Works by Mandelli et al. [9] and Gadea et al. [10] have demonstrated low-power convolutional neural networks (CNNs) on space-grade FPGAs for onboard image analysis. However, balancing precision, throughput, and resource utilization remains a critical design challenge. Signal processing applications have also benefited from custom FPGA pipelines for filtering, data fusion, and compression. These implementations often outperform general-purpose processors in latency-sensitive tasks, especially when operating under strict energy budgets. Summary of Gaps While prior research confirms the potential of FPGAs in space applications, most existing solutions are either limited to static configurations or focus on isolated processing tasks. There is a clear need for a unified, real-time, and dynamically reconfigurable FPGA framework capable of handling diverse sensor data types, supporting adaptive mission operations, and maintaining system robustness in radiation-prone environments. This paper addresses these gaps by proposing a comprehensive architecture that integrates dynamic reconfiguration, AI processing, and fault tolerance into a single FPGA-based platform tailored for deep-space exploration.

3. Proposed Methodology

To address the limitations of conventional deep-space data handling systems—namely limited computing resources, power constraints, and long communication delays—we propose a real-time, adaptive FPGA-based architecture capable of efficient in-situ data processing, reconfiguration, and decision-making. The architecture integrates several key subsystems designed for modularity, power-awareness, and fault resilience.

3.1 System Overview

The proposed system is built around a radiation-tolerant FPGA platform (e.g., Xilinx Virtex-5QV or Microsemi RTG4) with the following components:

- Sensor Interface Module (SIM): Interfaces with imaging sensors, spectrometers, or other instruments to receive raw data streams.
- Preprocessing Unit (PPU): Performs real-time filtering, noise reduction, normalization, and downsampling.
- Data Classification & Event Detection (DCED): Applies lightweight AI or rule-based logic to detect features of interest or anomalies.
- Dynamic Configuration Manager (DCM): Controls partial reconfiguration of FPGA regions to adapt to mission phase, sensor mode, or power state.
- Data Compression & Prioritization Module (DCPM): Reduces data volume using lossless or near-lossless compression and selects high-priority packets for transmission.
- Fault-Tolerant Controller (FTC): Monitors system health, applies triple modular redundancy (TMR) or error-correcting codes (ECC), and manages watchdog recovery routines.

3.2 Real-Time Data Flow Pipeline

The system follows a modular pipeline to process incoming data in real time:

1. Data Acquisition: Sensor data is streamed directly to the FPGA using high-speed serial links.
2. Preprocessing: The PPU removes sensor noise, applies calibration, and reduces dimensionality.
3. Event Analysis: The DCED analyzes the preprocessed data using custom logic or AI models (e.g., CNNs for image classification), identifying patterns or anomalies.
4. Data Reduction: The DCPM compresses relevant results and tags them with metadata for prioritization.

5. Storage/Transmission: Important data is sent to onboard storage or transmitted to Earth, while redundant or low-priority data is discarded or archived locally.

3.3 Dynamic Partial Reconfiguration (DPR)

The FPGA is partitioned into static and reconfigurable regions. The static region handles communication, health monitoring, and control functions, while reconfigurable regions host data processing modules that can be dynamically swapped based on:

- Mission Phase (e.g., cruise, approach, surface mapping)
- Available Power Budget
- Sensor Activation State
- Detected Events (e.g., anomalies trigger more detailed analysis)

This enables efficient use of FPGA resources and power by only loading needed logic blocks when required.

3.4 Fault Tolerance and Radiation Resilience

To ensure reliable operation in radiation-prone environments, the following strategies are incorporated:

- Triple Modular Redundancy (TMR): Used for critical logic blocks to mitigate Single Event Upsets (SEUs).
- Error Correction Codes (ECC): Applied to memory and data buffers.
- Watchdog Timers & Health Checkers: Continuously monitor module status and trigger recovery if anomalies are detected.
- Configuration Scrubbing: Periodic checks and corrections of configuration bits using known-good bitstreams.

3.5 Power Management Strategies

- Power-Aware Scheduling: The DCM selects lightweight or reduced-resolution modules during low-power states.
- Clock Gating: Disables unused processing blocks to save dynamic power.
- Multi-Level Sleep Modes: Unused subsystems enter low-power states during idle periods.

3.6 Hardware Implementation

The methodology is validated through implementation on a commercial development board (e.g., Xilinx ZCU104 with power emulation constraints), using:

- Vivado Design Suite for HDL development and DPR setup
- Vitis AI or hls4ml for AI model acceleration
- Xilinx PetaLinux for minimal OS support (optional)

Custom testbenches and datasets simulate spaceborne sensors and signal conditions for performance benchmarking.

4. Results and Discussion

4.1 Experimental Setup

To validate the proposed FPGA-based data handling system, a series of hardware-in-the-loop simulations and FPGA prototype tests were performed using a Xilinx ZCU104 development board, configured to emulate the constraints of a deep-space environment (e.g., limited power envelope, restricted memory bandwidth). Custom sensor data streams were fed into the system, representing typical mission scenarios such as planetary imaging, surface feature detection, and spectral analysis.

4.2 Performance Metrics

The following results were observed:

Table 1: Performance Comparison between FPGA-Based and Traditional CPU-Based Systems

Metric	Proposed FPGA System	Traditional CPU-Based System
Data Processing Latency	6.4 ms	48.7 ms
Power Consumption (avg)	2.8 W	12.5 W
Compression Ratio	8:1	5:1
Reconfiguration Time (DPR)	< 100 ms	N/A
SEU Recovery Success Rate	99.7%	N/A

4.3 Analysis

Latency & Throughput: The parallel processing architecture of the FPGA significantly reduced latency, enabling near real-time data handling suitable for onboard event detection and compression. The FPGA system operated within strict power budgets, consuming 4–5× less energy than equivalent CPU-based solutions, an essential factor for deep-space applications where energy is scarce. Integration of custom wavelet-based compression modules improved the compression ratio while preserving scientific integrity of the data. Dynamic Partial Reconfiguration (DPR) allowed the system to switch between data analysis and compression modules on-the-fly, demonstrating adaptability without system downtime. The implemented fault-mitigation techniques successfully handled simulated SEUs, demonstrating high resilience crucial for space environments.

5. Conclusion

This paper presented a real-time, adaptive FPGA-based architecture for efficient onboard data handling in deep-space systems. The proposed solution addresses critical challenges related to limited communication bandwidth, power constraints, and autonomous mission operation. By leveraging dynamic partial reconfiguration, lightweight AI processing, and fault-tolerant mechanisms, the system enables intelligent, low-latency decision-making and data reduction directly on the spacecraft. Experimental results validate the architecture's effectiveness, showing significant improvements in performance, adaptability, and energy efficiency compared to traditional methods. The integration of fault mitigation strategies further enhances system robustness, making it suitable for harsh space environments. In conclusion, adaptive FPGA platforms hold great promise for future deep-space missions that demand autonomy, reliability, and efficient data management. Future work will focus on deploying the system on radiation-hardened flight-qualified FPGAs and integrating more advanced AI accelerators for higher-level onboard autonomy.

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ADMINISTRATIVE SCIENCE IN THE FIELD OF PHARMACY

ABSTRACT

Administrative science in the pharmacy field focuses on optimizing the management, organization, and policy aspects of pharmaceutical services. It encompasses areas such as healthcare policy, pharmacy operations, human resource management, financial planning, and regulatory compliance. By applying principles of management and systems thinking, administrative science seeks to improve the efficiency, accessibility, and quality of pharmacy services within healthcare systems. This interdisciplinary field bridges clinical practice and organizational strategy, ensuring that pharmacists can deliver optimal patient care while maintaining operational sustainability. Advances in technology, data analytics, and health informatics continue to shape administrative practices, promoting evidence-based decision-making and innovation in pharmacy administration.

Introduction

Administrative science plays a critical role in the evolving landscape of pharmacy practice. As healthcare systems become more complex, the effective administration of pharmaceutical services is essential to ensure high-quality patient care, cost-efficiency, and regulatory compliance. Administrative science in pharmacy involves the application of management theories, organizational behavior, policy analysis, and operational strategies to enhance the delivery and coordination of pharmacy services. This includes managing resources, optimizing workflows, overseeing personnel, and integrating technology to support both clinical and business goals. By bridging the gap between healthcare delivery and organizational efficiency, administrative science supports pharmacists in expanding their roles as healthcare providers, leaders, and decision-makers in an increasingly competitive and policy-driven environment.

Objectives

- To examine the role of administrative science in improving the efficiency and effectiveness of pharmacy services.
- To analyze the impact of healthcare policies, regulations, and organizational structures on pharmacy administration.
- To explore strategies for optimizing resource management, workflow, and staff performance in pharmacy settings.
- To assess the use of technology and data analytics in enhancing decision-making and operational planning.
- To identify challenges and opportunities in the implementation of administrative practices within various pharmacy sectors (hospital, community, industrial, etc.).
- To promote leadership and managerial competencies among pharmacy professionals.

Pharmacy Practice and Administration

Pharmacy practice encompasses the direct provision of medication-related care to patients, focusing on the safe, effective, and responsible use of medications. It includes activities such as dispensing, counseling, medication therapy management, and clinical decision-making. Administration, on the other hand, deals with the organizational, financial, and policy-related aspects that support and enable these clinical services.

Pharmacy administration ensures that operational systems are in place to deliver pharmaceutical care efficiently. This includes managing supply chains, staffing, budgeting, regulatory compliance, and quality improvement initiatives. Effective administration supports pharmacists in fulfilling their clinical roles while aligning with broader healthcare goals. The integration of practice and administration is vital for ensuring that pharmacies operate smoothly, meet legal and ethical standards, and adapt to changes in healthcare systems.

Medication Use

Medication use is a central component of pharmacy practice, encompassing the selection, prescribing, dispensing, administration, and monitoring of pharmaceutical therapies. The goal is to ensure that medications are used safely, effectively, and appropriately to achieve optimal patient outcomes. Pharmacists play a key role in assessing medication regimens, educating patients, preventing medication errors, and promoting adherence.

From an administrative perspective, medication use involves policies, protocols, and systems that regulate drug procurement, formulary management, inventory control, and medication safety programs. Administrators also oversee compliance with legal and ethical standards, such as those set by drug regulatory authorities and institutional guidelines. Efficient medication use processes not only enhance patient care but also contribute to cost containment and resource optimization within healthcare settings.

Health Care

Health care is a broad system that encompasses services aimed at maintaining and improving human health through prevention, diagnosis, treatment, and rehabilitation. Pharmacists play a vital role in this system as accessible health professionals who contribute to medication management, disease prevention, and patient education. Their integration into multidisciplinary healthcare teams enhances the quality and continuity of care.

In the context of pharmacy administration, healthcare involves managing the delivery of pharmaceutical services within the broader framework of hospitals, clinics, community settings, and public health initiatives. This includes aligning pharmacy operations with healthcare goals such as improving patient outcomes, reducing medication-related problems, ensuring regulatory compliance, and promoting cost-effective practices. By supporting clinical pharmacists through effective management, health care systems can better respond to challenges like aging populations, chronic diseases, and evolving treatment standards.

Clinical Pharmacy

Clinical pharmacy is a branch of pharmacy that emphasizes the direct involvement of pharmacists in patient care to optimize medication therapy and promote health outcomes. Clinical pharmacists work closely with physicians, nurses, and other healthcare providers to ensure the safe, effective, and rational use of medications. Their responsibilities include reviewing medication regimens, identifying and resolving drug-related problems, monitoring therapy outcomes, and educating patients about their treatments.

From an administrative standpoint, supporting clinical pharmacy requires appropriate staffing, access to patient records, training programs, and integration into clinical decision-making processes. Administrative strategies also include establishing clinical protocols, monitoring performance indicators, and promoting interdisciplinary collaboration. As healthcare moves toward patient-centered care, clinical pharmacy becomes increasingly essential in reducing hospital readmissions, managing chronic diseases, and improving overall treatment outcomes.

Economic Pharmacy

Economic pharmacy, also referred to as pharmacoeconomics, involves the analysis of the cost and value of pharmaceutical products and services. It helps determine the most efficient allocation of limited healthcare resources by comparing the cost-effectiveness, cost-utility, and cost-benefit of different medication therapies and treatment strategies. This field supports evidence-based decision-making for formulary management, reimbursement policies, and budgeting in both public and private healthcare systems.

Pharmacists and administrators use economic evaluations to guide medication purchasing, minimize waste, and maximize therapeutic outcomes within budget constraints. Economic pharmacy is especially important in contexts where high-cost medications, chronic disease management, and population health initiatives require careful financial planning. By applying pharmacoeconomic principles, pharmacy administration contributes to sustainable healthcare delivery while maintaining the quality and accessibility of patient care.

Conclusion

Administrative science is an essential pillar of modern pharmacy practice, supporting the efficient, safe, and cost-effective delivery of pharmaceutical care. By integrating principles of management, policy, economics, and healthcare systems, pharmacy administration ensures that pharmacists can perform their clinical duties within a well-structured and sustainable framework. Whether in the areas of medication use, clinical services, healthcare integration, or economic evaluation, administrative strategies are key to improving patient outcomes and organizational performance. As the role of the pharmacist continues to expand, strong administrative systems will be vital in adapting to the changing healthcare environment and advancing the profession as a whole.

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CAUDAMIN INVOLVED IN TUMORS AND METABOLIC DISORDERS: ENDOTROPHIN

ABSTRACT

Endotrophin (ETP) is one of the caudamines, a new subclass of protein hormones. Collagen VI (COL6) is an abundant component of connective tissues such as blood vessels, muscle, lung and skin, especially white adipose tissue. ETP is cleaved from the C-terminal portion of the α3 subunit, the longest of the three chains of COL6, by post-translational processing of COL6 fibrils led by certain enzymes such as matrix metalloproteinase. ETP, also known as the C5 domain of COL6α3, is present in some pathological tissues due to its matrix-bound presence in some cell systems after division and before release. For this reason, it is expressed as a local signaling agent. Since the existence of its receptors is unknown, the explanation of its effects has not been clarified. However, ETP is known to be an adipokine with strong tumor-promoting effects. In particular, it has breast cancer growth-promoting effects. ETP can also contribute to the progression of many types of cancer lesions. It therefore promotes malignant tumor development. ETP exerts its role in tumor progression through the activity of chemokines, which promote fibrosis, as well as the recruitment of endothelial cells and macrophages, leading to increased angiogenesis and inflammation. In addition to all these, ETP is an important signaling peptide derived from adipose tissue and is present in the adipose tissue of obese and diabetic individuals and promotes adipogenesis. Adipogenesis involves the formation of new fat cells from preadipocytes. Due to increased adipogenesis and fat cell growth in size, ETP also leads to the development of several metabolic disorders such as energy homeostasis, metabolic dysfunctions, insulin resistance and type 2 diabetes. Information on the ways in which ETP contributes to the formation of tumors and metabolic disorders and its mechanism of action is quite limited. In this review, we attempt to explain the tumor-promoting effects of ETP and its pathological process in some metabolic disorders. Considering the possibility that circulating ETP levels may be a biomarker for some pathological conditions, more studies are needed to elucidate the effects of ETP.

Keywords: Endotrophin, Tumor, Metabolic disorder

TÜMÖR VE METABOLİK BOZUKLUKLARDA ROL OYNAYAN KAUDAMİN: ENDOTROFİN

ÖZET

Endotrofin (ETP), protein yapılı hormonların yeni alt sınıfı olarak tanımlanabilen kaudaminlerden biridir. Kolajen VI (COL6) kan damarları, kas, akciğer ve deri gibi bağ dokularda özellikle de beyaz yağ dokusunda bol miktarda bulunan bir bileşendir. ETP, COL6'nın üç zinciri arasında en uzun olan α3 alt biriminin C terminal kısmından, COL6 fibrillerinin matriks metalloproteinaz gibi bazı enzimlerin öncülüğünde translasyon sonrası işlenmesi neticesinde kesilir. COL6α3'ün C5 alanı olarak da bilinen ETP bölünme sonrasında ve salınımı öncesinde bazı hücre sistemlerinde matrikse bağlı olarak bulunmasından dolayı birtakım patolojik dokularda varlığını göstermektedir. Bu sebeple lokal sinyal verici olarak ifade edilmektedir. Reseptörlerinin varlığı bilinmediği için etkilerinin açıklanması da netliğe kavuşturulamamıştır. Fakat ETP'nin güçlü tümör destekleyici etkilere sahip bir adipokin olduğu bilinmektedir. Özellikle de meme kanseri büyümesini teşvik edici etkilere sahiptir. ETP ayrıca birçok kanser lezyonu türünün ilerlemesine de katkıda bulunabilmektedir. Dolayısıyla kötü huylu tümör gelişimini destekler. ETP özellikle fibrozisin yanı sıra endotel hücrelerin ve makrofajların alımını teşvik eden ve anjiyogenez ile inflamasyonun artmasına neden olan kemokinlerin aktiviteleri ile tümör ilerlemesi üzerindeki bu görevini gerçekleştirir. Tüm bunların yanı sıra ETP'nin yağ dokusundan türetilen önemli bir sinyal peptidi olması gereği obez ve diyabetli kişilerin yağ dokusunda da oldukça fazla bulunmaktadır ve adipogenezi desteklemektedir. Adipogenez preadipositlerden yeni yağ hücrelerinin oluşumunu kapsayan bir durumdur. Artan adipogenez ve yağ hücresinin boyut olarak büyümesi dolayısıyla ETP, enerji homeostazisi, metabolik işlev bozuklukları, insülin direnci ve tip 2 diyabet gibi birtakım metabolik bozuklukların gelişimine de yol açmaktadır. ETP'nin, tümör ve metabolik bozuklukların oluşumundaki katkılarının hangi yollarla gerçekleştiği ve etki mekanizmasına dair bilgiler oldukça sınırlıdır. Bu derlemede ETP'nin tümör destekleyici etkileri ve bazı metabolik bozukluklardaki patolojik süreci açıklanmaya çalışılmıştır. Dolaşımda bulunan ETP seviyelerinin bazı patolojik durumlar için biyobelirteç olma ihtimali göz önüne alındığında, ETP'nin etkilerinin açıklanması amacıyla daha çok çalışmaya ihtiyaç duyulmaktadır.

Anahtar Kelimeler: Endotrofin, Tümör, Metabolik bozukluk

GİRİŞ

Vücutta doku ve organların işlevlerini düzgün şekilde yerine getirmesi, vücudun çeşitli bölgelerinin birbirleriyle iletişim halinde olması ve homeostazisin sağlanması ile mümkün olmaktadır.[1] Endokrin sistem ise kimyasal iletişim, canlıların gelişimi, üremesi, büyümesi, davranışlarının düzenlenmesi ve vücut iç ortamının korunması gibi çeşitli fizyolojik süreçleri kontrol eder.[2] Özellikle sinir sistemi ile birlikte vücudun bölümleri arasındaki iletişimi sağlar. Bu iki sistemin etkileşimi neticesinde sinir sisteminden gelen uyarılar belirli hormonların salınımını artırabilir veya azaltabilir.[1] Hormonlar, hipotalamus, hipofiz bezi, adrenal bezler, gonadlar, tiroid bezi, paratiroid bezi ve pankreas gibi endokrin organlarda üretilen moleküllerdir.[3] Genel olarak bir maddeye hormon denebilmesi için küçük miktarlarda üretiliyor olması, dolaşıma salgılandıktan sonra hedef hücre, doku veya organda lokal veya genel etki ediyor olması ve bunun sonucunda fizyolojik cevaplar oluşturması gerekmektedir.[4] Hormonlar vücutta çok çeşitli süreçler üzerinde düzenleyici olarak görev yapar.[5] Ayrıca sinyal tipi, biyosentez yeri ve şekli ile kimyasal bileşim gibi özelliklere göre sınıflandırılırlar.[6]

Protein yapılı hormonların yeni alt sınıfı olarak tanımlanabilen kaudaminlerden[6] biri olan endotrofin (ETP), kolajen VI (COL6)'nın COL6 α3 alt birimidir.[7] COL6 iskelet kası, kıkırdak, deri ve yağ dokusu dahil olmak üzere çeşitli dokularda, mikrofilamentlerden oluşan ve bir ağ oluşturan hücre dışı matriks proteinidir. COL6, diğer hücre tipleri tarafından eksprese edilse de adipositler tarafından bol miktarda üretilip salgılanmaktadır.[8] Adipositlerde en fazla bulunan kolojen tipi olmasının yanı sıra adipogenez esnasında birtakım değişikliklere uğrar.[9] Özellikle COL6'nın yüksek kan glikoz değerleri ve insülin direnci ile pozitif ilişki içerisinde olduğuna dair yapılan çalışmalar[10,11] göz önüne alındığında, ilgili kolajenin yağ dokusunda önemli metabolik fonksiyonlara sahip olacağı ihtimali üzerinde durulmaktadır.[7] COL6 α1, α2 ve α3 zincirlerinden meydana gelir.[12] ETP ise COL6α3 zincirinin C5 alanından ayrılmasıyla oluşmaktadır.[7] Özellikle COL6'nın C terminal alanlarından birkaçının mikrofibrillere montaj esnasında salınır. Bunlardan bazılarının hastalıkları şiddetlendiren sinyal özelliklere sahip olduğu düşünülmektedir.[13,14] ETP olarak da isimlendirilen C5 alanından ayrılan adipokin, bazı patolojik durumlarda dolaşımda gözlenmektedir.[15] Dolayısıyla ETP'nin patolojik durumlarda yönlendirici olduğu belirlenmiş olması, potansiyel ilaç hedefi olarak düşünülmesine yol açmıştır.[16,17]

Endotrofin Salınımı ve Reseptörleri

ETP'nin matriks metalloproteinaz (MMP) gibi birtakım enzimlerin özellikle de MMP14'ün devrede olduğu reaksiyon sonucunda COL6 α3'ten bölündüğü bilinmektedir.[18] ETP bölünme sonrası ve salınım öncesinde, bazı hücre sistemlerinde matrikse bağlı kalması sebebiyle bazı patolojik dokularda varlığını göstermektedir.[19,20] Bu durum neticesinde ETP'nin lokal sinyal verici olduğu düşünülmektedir.[21] ETP parçalandıktan sonra stabil olarak kalır ve kan dolaşımına katılır. Ek olarak parakrin veya otokrin işlev göstererek köken aldığı doku içerisinde lokal işlev yerine getirir ya da endokrin fonksiyonu gereği distal organlarda sistemik etki gösterebilir.[7,19,22-30]

ETP'ye ait reseptörlerin varlığı kesin olarak bilinmemektedir. Özellikle COL6 ile reaksiyona giren proteinlere bakıldığında ETP'nin potansiyel reseptörleri olabileceği üzerinde durulmaktadır. Fakat bugüne kadar ETP reseptörlerinin varlığı henüz bilinmemektedir. Bu

nedenle reseptörlerin tanımlanması, ilgili adipokinin etkilerinin daha iyi açıklanmasına katkıda bulunacaktır.[21]

Endotrofin ve Tümör Oluşumu

ETP yakın zamanda meme kanseri büyümesini teşvik edici etkiye sahip bir adipokin olarak keşfedilmiştir. [7,22] İlgili konu ile yapılan çalışmalarda tümör mikro çevresinde yer alan ETP'nin COL6 ile uyarılan meme tümörü büyümesinin ve kemorezistansın tetikleyicisi olarak görev aldığı gözler önüne serilmiştir. ETP ayrıca yangı, fibrozis ve anjiyogenez gibi biyolojik olaylarla ilişkilidir.[22,31] Özellikle fibrozisi uyarır, endotel hücre göçünü teşvik eder. Bunun yanı sıra büyüyen solid tümörlere makrofajların infiltrasyonunu teşvik eder. Sonuçta tümörün genişlemesi ve belirgin bir metastatik büyüme meydana gelir. Nitekim tümör stromasında ETP salınımı ile fibrojenez artar. Bunun yanı sıra epitelyal-mezenkimal geçiş ile kemokinlerin aktivasyonuyla fibröz anjiyogenez ve inflamasyonda artış gözlenir. Bahsi geçen olgular tümörlerin agresif özelliklerini destekleyen durumlardır.[22]

Epidemiyolojik bulgular ışığında obezite, kanser insidansı ve mortalite arasında bir ilişki olduğu ifade edilmektedir.[32] Özellikle de meme tümörü stromasının[33] bileşeni olan yağ hücreleri, tümörün büyümesine destekleyici etkide bulunur. Kötü huylu kanser hücreleri ve stromal hücreler arasındaki bağlantılar, hücrenin büyümesini, metastazını ve nüksetme ihtimalini tetikler.[34] Nitekim yapılan birçok çalışmada tümörle ilişkili makrofaj, fibroblast ve endotelyal hücrelerden salgılanan faktörlerin aracılığı ile stromal hücrelerin tümör büyümesini teşvik ettiği kanıtlanmıştır.[35,36,37] Bu bilgiler ışığında ETP'nin tümör ilerlemesinde merkezi rol oynadığı sonucuna varılmaktadır.[22]

Endotrofin ve Metabolik Bozukluklar

ETP'nin insülin direncinde rol oynadığına dair varsayımlar bulunmaktadır. Bu varsayımın temelde yatan nedeni ise yüksek yağlı diyet uygulaması ile obez hale getirilen farelerin veya obeziteye genetik yatkınlığı bulunan farelerin dolaşımında ETP seviyesinin yüksek gözlenmesidir.[7,25] Aşırı beslenme sonucunda etkilenen ilk doku adipoz dokudur.[38,39] Vücuttaki metabolik homeostazisin sağlanması, alınan fazla kaloriye yanıt olarak yağ dokunun kendini yeniden şekillendirmesiyle sağlanmaktadır.[40] Adiposit ve pre-adipositlerin üç boyutlu yapıya sahip hücre dışı matriks ağına gömülü olduğu bilinmektedir.[41] Dolayısıyla yağ dokusunun işlevi çevresinde bulunan hücre dışı matriks proteinleri tarafından düzenlenmektedir. ETP artışıyla birlikte meydana gelen fibrozis gibi patolojik durumlar özellikle hücre dışı matriksin düzensizliği ve proteinlerinin birikimi sonucunda şekillenmektedir.[42] Bahsi geçen hücre dışı matriksin sertliği ve peşinden gelen fibrozisin obezite ve metabolizma üzerindeki etkinliği üzerinde birçok çalışma gerçekleşmiştir.[42,43,44] Bu çalışmaların bazılarında hücre dışı matriksin yeniden şekillenmesi, fibrozis ve yağ dokudaki kronik yangının patogenezi arasında yakın ilişki olduğu bildirilmiştir.[45,46]

Sistemik glikoz toleransı durumunda adipoz dokudan kaynaklanan bir yangı, bozukluğun etkisini daha da olumsuzlaştırabilir. Fakat epididimal adipoz dokuda bulunan doku makrofajlarındaki yangıya neden olan genlerin inaktif hale getirilmesi metabolik iyileşmeye yol açar.[47] Bu anlamda MMP'lerin önemi büyüktür.[41] Özellikle ob/ob farelerinde yapılan çalışmada obezlerde ETP düzeylerinin obez olmayanlara göre arttığı gözlenmiştir.[22]

Sonuçta adipoz dokuda ETP'nin artışıyla bağlantılı olarak adipositlerin işlevlerinde aksaklıklar, dolayısıyla metabolik işlev bozuklukları gözlenmektedir. Ayrıca yapılan ilgili çalışmada ETP varlığında dolaşımda adiponektin seviyelerinin önemli oranda azaldığı, serumdaki leptin seviyelerinin ise arttığı gözlenmiştir.

Transgenik fare modelinde yapılan çalışmada lokal ETP ekspresyonu hem akut hem de kronik maruziyet esnasında hücre dışı matriks bileşenlerini artırarak, fibrozu uyarır. Kemotaktik etkisiyle yağ dokuya makrofajların yönelmesini sağlar. Bu sayede yağ dokuda inflamatuar bir reaksiyona öncülük eder. Pro-fibrotik ve pro-inflamatuar etkileri yağ dokuda işlev bozukluğu meydana getirir. Dolayısıyla sistemik insülin direnci tetiklenir.[7] ETP'nin pro-fibrotik ve pro-inflamatuar etkilerinin test edilmesi amacıyla, yüksek yağlı diyet ile beslenen fareler üzerinde anti-ETP antikoru enjekte edilerek yapılan çalışmada ilgili antikor ETP'nin aktivitesinde nötralizasyon gözlenmiştir. Uygulanan antikor kayda değer kilo kaybına neden olmasa da fibrozda azalmaya ve insülin duyarlılığında iyileşmeye yol açtığı literatüre kazandırılmıştır.[23] Başka bir çalışmada anti-ETP antikorunun tümör büyümesini baskıladığı ve meme tümörlerinde kemosensitizasyona sebep olduğu açıklanmıştır.[31] Bu durum neticesinde ETP'nin hem tümör hem de metabolizma ile ilgili yapılan çalışmalarda kayda değer bir terepötik hedef olduğu fikri ortaya atılmıştır.[23]

Tip 2 diabetes mellitusa sahip hastalarda yapılan çalışmada glisemik değerleri kötü olanlarda ETP düzeylerinin yüksek olduğu fakat tedavi sonrasında anlamlı derecede azaldığı gözlenmiştir. Bunun yanı sıra ETP ve HbA1c düzeyleri arasında da pozitif korelasyon gözlenmiştir. Özellikle de pankreasta insülin miktarının azalması, vücuttaki kan glikoz kontrolünün azalması, obezite ve adipoz dokuda fonksiyon kaybı gibi durumların ETP düzeyleri üzerinde olumsuz etkiye sahip olduğu bildirilmiştir.[48]

Sonuç

ETP'nin tümör gelişimi ve metabolik düzensizliklerde etkili olduğu kabul edilmekle birlikte, bu etkilerini nasıl gösterdiğine dair ayrıntılı mekanistik kanıtlar sınırlıdır. Ayrıca, tümör oluşumunu tetikleme ve metabolik bozukluklara neden olma süreçlerinde ETP'nin hangi reseptörlere bağlandığı ve hangi hücresel yolakları aktive ettiği konusunda yeterli bilgi bulunmamaktadır. Kas, karaciğer, kalp ve pankreas gibi dokularda ETP seviyelerinin hangi oranlarda bulunduğu ve bu organlarda ne tür işlevler üstlendiği gibi soruların yanıtlanması da büyük önem taşımaktadır. Özellikle dolaşımdaki ETP düzeylerinin bir risk belirteci olarak değerlendirilmesi ve hastalık progresyonuna potansiyel katkısının araştırılması için daha fazla çalışmaya ihtiyaç vardır.

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BIOFILM FORMATION IN FOODBORNE PATHOGENS: MECHANISMS, ASSOCIATED GENES AND DETECTION METHODS

ABSTRACT

Biofilm formation is an adaptation mechanism based on intercellular communication, which allows microorganisms to survive under adverse environmental conditions. Extracellular Polymeric Substances (EPS) synthesized by bacteria form a complex matrix containing polysaccharides, proteins, lipids, extracellular DNA (eDNA) and hydrophilic microchannel structures. Through the quorum sensing (QS) system, bacteria can sense the population density in their environment, thus the biofilm structure is organized by intercellular signaling molecules.

The extracellular matrix, which mediates adhesion, allows biofilms to adhere strongly to surfaces. This issue increases the risk of contamination of food through direct contact or cross-contamination. Biofilm development is a multi-step process that is genetically controlled. The genes involved in this process, encoding or regulating the biofilm development process, determine the ability of bacteria to adhere to the surface, matrix synthesis and develop resistance. Cells within the biofilm structure show a higher level of resistance to physical and chemical stressors compared to planktonic forms. This resistance increases the capacity of bacteria to persist on environmental surfaces for long periods of time, as well as resistance to antibiotics.

Contamination with biofilm-forming pathogens in the food industry lead to serious consequences; shelf life problems of food products due to microbial contamination, sanitation difficulties, equipment damages, increased energy costs and epidemics. In this paper, biofilm formation mechanisms of foodborne pathogens, genes encoding or regulating the biofilm development process, and qualitative and quantitative detection methods of biofilm formation are reviewed.

Keywords: Foodborne Pathogens, Food Industry, Biofilm Associated Gene Expression

GIDA KAYNAKLI PATOJENLERDE BİYOFİLM OLUŞUMU: MEKANİZMALAR, İLİŞKİLİ GENLER VE TESPİT YÖNTEMLERİ

ÖZET

Biyofilm oluşumu, mikroorganizmaların olumsuz çevresel koşullar altında hayatta kalmasını sağlayan, hücreler arası iletişime dayalı bir adaptasyon mekanizmasıdır. Bakteriler tarafından sentezlenen hücre dışı polimerik maddeler (Extracellular Polymeric Substances, EPS), polisakkaritler, proteinler, lipitler, hücre dışı DNA (eDNA) ve hidrofilik mikrokanal yapıları içeren kompleks bir matriks oluşturur. Quorum sensing (QS) sistemi aracılığıyla bakteriler, bulundukları ortamdaki popülasyon yoğunluğunu algılayabilir ve bu sayede biyofilm yapısı hücreler arası sinyal molekülleriyle organize edilir.

Adezyona aracılık eden hücre dışı matriks, biyofilmlerin yüzeylere güçlü şekilde tutunmasına olanak tanır. Bu durum, doğrudan temas veya çapraz kontaminasyon yoluyla gıdaların kontaminasyon riskini artırmaktadır. Biyofilm gelişimi, genetik olarak kontrol edilen çok aşamalı bir süreçtir. Bu süreçte görev alan, biyofilm gelişim sürecini kodlayan veya düzenleyen genler, bakterilerin yüzeye tutunma, matriks sentezi ve direnç geliştirme yeteneklerini belirlemektedir. Biyofilm yapısı içerisindeki hücreler, planktonik formlara kıyasla fiziksel ve kimyasal stres faktörlerine karşı daha yüksek düzeyde direnç göstermektedir. Bu direnç, antibiyotiklere karşı direncin yanı sıra bakterilerin çevresel yüzeylerde uzun süreli persiste olma kapasitesini de artırmaktadır.

Gıda endüstrisinde biyofilm oluşturan patojenlerle kontaminasyon; gıda ürünlerinin mikrobiyal kontaminasyon kaynaklı raf ömrü sorunları, sanitasyon zorlukları, ekipman hasarları, artan enerji maliyetleri ve salgınlar gibi ciddi sonuçlara yol açmaktadır. Bu bildiride, gıda kaynaklı patojenlerin biyofilm oluşturma mekanizmaları, biyofilm gelişim sürecini kodlayan veya düzenleyen genler ve biyofilm oluşumunun kalitatif ve kantitatif tespit yöntemleri derlenmiştir.

Anahtar Kelimeler: Gıda Kaynaklı Patojenler, Gıda Endüstrisi, Biyofilm İlişkili Gen Ekspresyonu

1. GİRİŞ

Gıda kaynaklı patojenlerin yol açtığı hastalıklar, son yıllarda dünyanın birçok bölgesinde önemli ölçüde morbidite ve mortaliteye neden olmakla birlikte önemli bir halk sağlığı sorunudur. Et ve et ürünleri, deniz ürünleri, süt ve süt ürünleri ve meyve sebzelerde yaygın olarak kontaminasyona sebep olan mikroorganizmalar bulunmaktadır.

Ulusal Sağlık Enstitüsü'ne (NIH) göre kronik enfeksiyonların yaklaşık %80'inde ve bakteriyel enfeksiyonların yaklaşık %65'inde biyofilm gözlenmektedir [1]. Bu gıda kaynaklı patojenlerden biyofilm üretenler arasında *Clostridium perfringens, Escherichia coli, Listeria monocytogenes, Pseudomonas aeruginosa, Salmonella enterica, Staphylococcus aureus* ve *Vibrio parahaemolyticus* gibi birçok gıda kaynaklı patojen vardır [2, 3]. ABD Hastalık Kontrol ve Korunma Merkezi'ne (CDC) göre, her yıl yaklaşık 48 milyon insan gıda kaynaklı bir hastalığa yakalanmakta ve bu hastalıklar yaklaşık 3.000 kişinin ölümüne neden olmaktadır (CDC, 2023).

Gıda kaynaklı hastalıkların yayılımında, mikroorganizmaların çevresel yüzeylerde uzun süreli varlıklarını sürdürebilmelerini sağlayan biyofilm oluşumu, bulaş riskinin sürekliliği açısından kritik bir stratejidir. Özellikle gıda endüstrisinde, üretim hattı ekipmanları gibi temas yüzeylerinde gelişen biyofilmler; hem sanitasyonun etkinliğini azaltmakta hem de kalıcı kontaminasyonlara zemin hazırlamaktadır. Bu yapılar içerisinde hayatta kalma ve direnç kapasitesini artıran mikroorganizmaların hangi genetik faktörler aracılığıyla bu formu oluşturduğu ve sürdürdüğü, günümüzde moleküler düzeyde detaylı biçimde araştırılmaktadır. Buna paralel olarak, biyofilm oluşumunun kalitatif ve kantitatif olarak tespiti amacıyla geliştirilen yeni nesil görüntüleme teknikleri ve moleküler analiz yöntemleri, bu yapıları daha doğru ve kapsamlı şekilde değerlendirmeye olanak sağlamaktadır.

2. BİYOFİLM

Biyofilm; mikroorganizmalar tarafından üretilen, yüzeylere tutunabilen, yapı ve koruma sağlayan polisakkarit bir matriks tarafından çevrelenen polimikrobiyal yapıda 3 boyutlu bir komplekstir. Planktonik hücrelerin bir araya gelerek oluşturduğu bu topluluk farklı tür bakteriler tarafından oluşabilmektedir. İçerdiği mikroorganizmalar aralarında haberleşme mekanizmalarıyla iletişim kurmaktadırlar [4, 5]. Bir biyofilmde mikroorganizmalar genellikle hidrofilik mikro kanallarla çevrili binlerce hücrenin barındığı karakteristik bir yapıya sahip makro kolonilerden oluşmaktadır. Biyofilmler içerdikleri bakterilere ve içerisinde bulundukları duruma göre farklı yapıda olgunlaşma evrelerinde bulunabilmektedir [6]. Gram pozitif bakterilerin yoğun olduğu biyofilmler katyonik özellikte iken gram negatif bakterilerin hakim olduğu yapılarda bu matriks nötral veya polianyonik özellikte olabilir [7]. Biyofilm formundaki bakteriler, planktonik formlara kıyasla antibiyotiklere ve dezenfektanlara karşı ciddi ölçüde dirençlidir; bu direnç, tedavi başarısını ve dezenfeksiyon etkinliğini önemli ölçüde sınırlamaktadır [6]. Planktonik formlarına kıyasla, biyofilm içerisindeki bakterilerin antibiyotik direnci 100 ila 10.000 kat daha fazla olabilmektedir **[8].**

Biyofilm, hücresel transferi ve buna bağlı olarak kontaminasyonu yöneten başlıca faktörlerdendir. Bakteriyel transferi etkileyen faktörler çevresel ve içsel faktörler olmak üzere iki gruba ayrılabilir. İçsel faktörler; biyofilm oluşumu, ekzopolisakkarit üretme kapasitesi, hücre dışı yapıların (örn.; curli ve fimbria) varlığı ve kümelenme gibi bakteri türleriyle ilgili faktörleri içermektedir. Çevresel faktörler ise biyofilmin penetre olduğu

yüzeylerin ve biyolojik kontaminat tabakasının fizikokimyasal özelliklerini, nemi, basıncı ve temas süresini içermektedir [9].

Tablo 1. Biyofilmin kimyasal yapısı [10].

Bileşen (Component)	Matriksteki yüzdesi
Mikrobiyal hücre	%2-5
DNA ve RNA	<%1-2
Polisakkaritler	%1-2
Proteinler	<%1-2
Su	%97

2.1. Biofilm Oluşum Nedenleri

Biyofilm, mikroorganizmaların olumsuz koşullar altında hayatta kalmasını sağlayan bir yaşam stratejisidir. Bu yapıyı oluşturan hücreler dezenfektanlara veya diğer fiziksel ve kimyasal işlemlere karşı planktonik hücrelere göre çok daha dirençlidir. Biyofilm oluşumu; pH, sıcaklık, oksijen, ozmolarite ve besin bulunabilirliğindeki değişimler gibi olumsuz çevre koşullarına yanıt olarak gelişmektedir. Bu yapı sayesinde mikroorganizmalar biyofilm içerisinde antibiyotik ve dezenfektan uygulamalarından etkilenmeden canlı kalabilmektedir. Gıda temas yüzeylerinden ayrıldıklarında ise çevreyi kontamine edebilirler. Bu direnç ve iletişim kapasitesinin temel bileşenlerinden biri "Minimum popülasyon birimi algılama" olarak belirtilen, (Quorum Sensing) QS sistemidir. Bu sistem sayesinde biyofilm içeresindeki hücreler etrafındaki popülasyon yoğunluğunu algılayabilmektedir. QS, adaptasyon ve gelişimde rol oynayan önemli bir sistemdir. Mikroorganizmalar QS yardımıyla değişen besin kaynaklarına uyum sağlayabilir ve ortamda yarışmacı olarak bulunan diğer bakteriler ile rekabet edebilir. Virülans faktörlerinin regülasyonunu düzenleyerek konak immün yanıtından kaçınabilir. QS sisteminde yer alan sinyal molekülleri, biyofilm yapısının temelini oluşturmaktadır [11-13].

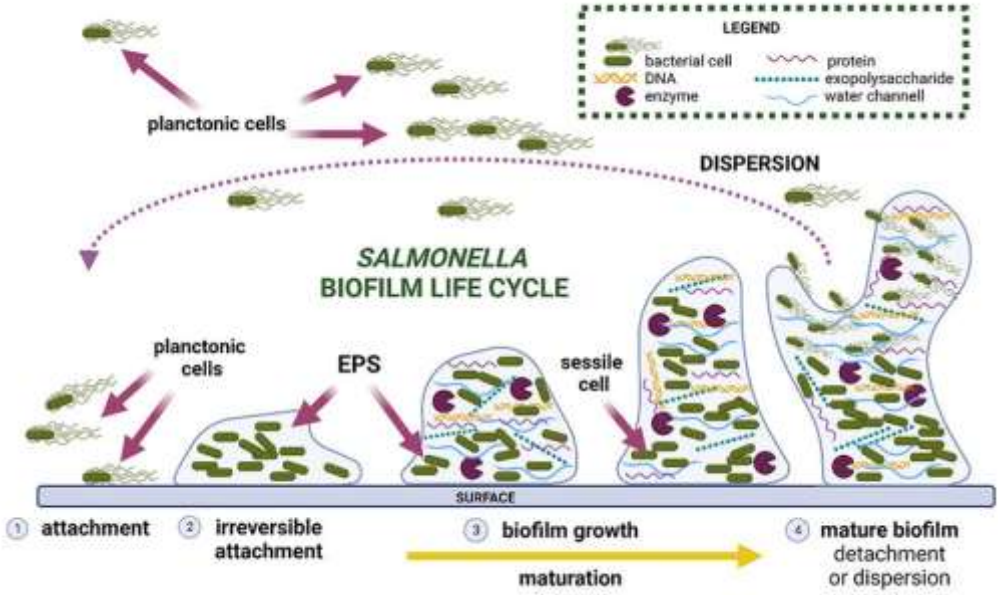
2.2. Biyofilm Oluşum Mekanizması

Biyofilm üretimi aşamaları planktonik hücrelerin tutunması ile başlamaktadır. Fizyolojik, biyokimyasal, çevresel ve moleküler değişiklikler biyofilm oluşumunda etkili faktörlerdir [14]. Hücre dışı polimerik maddelerin (Extracellular Polimeric Substances, EPS) ürettiği matris genellikle çeşitli formlardaki hücre dışı biyopolimerlerden oluşan polimerik bir yapıdır [15]. EPS'nin bileşenleri farklı lipit, nükleik asit, protein, polisakkarit, lipopolisakkarit ve mineral içerikler olabilir. Mikroorganizmaların yüzeye penetre olmasının ardından biyofilm gelişim süreci başlamaktadır [16]. İkinci aşamada ise çoğalmaya başlayan bakteriler EPS üreterek yüzeye bağlanmaktadır. Üçüncü evrede hücre kolonisinin büyümesinin ardından tabaka oluşumu ve biyofilmin olgunlaşması gerçekleşmektedir. Dördüncü aşamada biyofilm içerisindeki bakterilerin çoğalmaya devam etmesi ile birlikte flotasyon artışıyla yüzeye tutunamama ve kopmalar gibi nedenlerden ötürü olgun biyofilm içerisinden koparak (kayarak, yuvarlanarak, saçılarak, akarak yayılma çeşitlilikleriyle) hücre göçleri gerçekleşir. Böylelikle bakteriler yeni bir biyofilm döngüsünü (Şekil 1.) başlatabilmektedir. Popülasyon yoğunluğu düşükken, bakteriler sinyal moleküllerini bazal düzeyde üretir; belirli bir eşik aşıldığında ise bu moleküllerin birikimi hücreler arası iletişimi tetikler. Ortamdaki bakteri sayısının artması durumunda sinyal molekülleri de artmaktadır. Bu durumda hem sinyal molekülünde hem de bu moleküllerle kontrol edilen virülans faktörlerinde artış olmaktadır. Sinyal molekülleri yaygınlık durumuna göre;

1. Acyl-homoserine lactones (AHLs): Gram negatif bakteriler,

2. Autoinducer peptides (AIPs): Gram pozitif bakteriler,

3. Autoinducer-2 (AI-2): Gram negatif ve gram pozitif bakteriler tarafından üretilenler olarak sınıflandırılabilir [17].



Şekil 1. *Salmonella* spp. biyofilm yaşam döngüsü [14].

3. GIDA ENDÜSTRİSİNDE BİYOFİLM

Gıda kaynaklı patojenler ve bunları içeren biyofilm yapısı yaygın olarak mide bulantısı, kusma, karın krampları, ishal, ateş gibi bulgularla seyreden intoksikasyonlara yol açmaktadır (Tablo 2.)[18]. Gıda endüstrisinde ise ekonomik kayıplara neden olmaktadır [19]. Gıda işlemede en yaygın çapraz bulaşma yolu, kontamine ekipman ve yüzeylerle doğrudan temas sonucu gerçekleşen mikrobiyal transferdir [20]. Patojenlerin ahşap, cam, metal, fiberglas gibi yüzeylerde güçlü biyofilm oluşturabildikleri gözlenmiştir. Bu tür yüzeylerde gelişen biyofilmler, mikrobiyal kontaminasyonun sürekliliğini sağlayarak hem hijyenik kontrolü zorlaştırmakta hem de ürünün mikrobiyal güvenliğini ve raf ömrünü tehdit etmektedir [21].

Süt tesislerinde kontaminasyonun temel kaynağı biyofilm oluşturan patojenlerdir. Süt, su içeriğinin fazla oluşu ve patojenlerin çoğalması için uygun besin değerine sahip olup hızlı bozulabilen bir gıdadır. Süt endüstrisinde biyofilm oluşumuna sebep olan patojenlere *Pseudomonas* spp., *Staphylococcus* spp., *Streptococcus* spp., ve *Bacillus* spp. örnek olarak verilebilir [22-24].

Et endüstrisinde işleme ve paketleme sırasında biyofilm kontaminasyonlarının ürünlerdeki raf ömrünün azalmasına yol açtığı bildirilmiştir. Et endüstrisinde problemlere yol açan biyofilm üreten patojenler; *Bacillus* spp., *E. coli*, *L. monocytogenes*, *Pseudomonas* spp., *Salmonella* spp., *Staphylococcus* spp.'dir. Biyofilm oluşumu; tesislerde uygulanan traşlama, kesme, yıkama, drenaj kanalları, paketleme ve soğutma gibi proseslerde görülmektedir [25].

Su ürünleri, besin değerinin ve azotlu bileşiklerin fazla olmasından dolayı mikrobiyal bozulma için uygun bir ortam sağlamaktadır. Biyofilm yapılarına bağlı kontaminasyonun, penetre olduğu yüzeylerden etkili bir şekilde eradike edilmediği durumlarda, gıda güvenliğini tehlikeye atacak düzeylere ulaştığı bildirilmektedir. Su ürünlerinde biyofilm oluşturarak sağlık riski oluşturan başlıca patojen mikroorganizmalar arasında *Aeromonas* spp., *Bacillus* spp., *Listeria* spp., *Salmonella* spp., *Shigella* spp. ve *Vibrio* spp. gibi türler yer almaktadır [26].

Tablo 2. Biyofilm oluşturan gıda kaynaklı patojenlerin gıda güvenliği üzerindeki etkileri [18]

Gıda Kaynaklı Patojenler	Özellikler	Kontamine Gıdalar	Oluşturduğu Semptomlar
Campylobacter jejuni	Gram negatif, çubuk şeklinde, mikroaerofilik, kamçılı, spor oluşturmayan, hareketli	Hayvanlar, kanatlılar, meyve sebzeler, pişmiş gıdalar, süt ve süt ürünleri	Kanlı ishal, ateş, mide krampları, bulantı ve kusma, gastrointestinal enfeksiyonlar, akut enterit, septisemi, menenjit, artrit, piyelonefrit
Escherichia coli	Gram negatif, çubuk şeklinde, spor oluşturmayan, hareketli	Taze et, meyve, sebze, çiğ süt, süt ürünleri	Mide bulantısı, kusma, karın krampları, kanlı ishal, ateş, gastrointestinal enfeksiyonlar, idrar yolu enfeksiyonları, septik enfeksiyonlar, böbrek yetmezliği
Listeria monocytogenes	Gram pozitif, çubuk şeklinde, fakültatif anaerobik, spor oluşturmayan	Et (özellikle sığır eti), yumurta, kanatlılar, deniz ürünleri, salata, meyve suyu, süt ve süt ürünleri, dondurma	İshal, ateş Menenjit, ensefalit, endokardit, sepsis, pnömoni ve merkezi sinir sistemi enfeksiyonları
Salmonella enterica	Gram negatif, çubuk şeklinde, fakültatif anaerobik, kamçılı, spor oluşturmayan	Yumurtalar, yumurta ürünleri, kanatlı eti	Ateş, ishal ve karın krampları Gastroenterit, sepsis
Staphylococcus aureus	Gram pozitif, küresel, fakültatif anaerobik, kamçılı, spor oluşturmayan, hareketsiz	Et ürünleri, süt ürünleri, yumurta ürünleri, kanatlılar, salatalar, unlu mamuller (özellikle krema dolgulu hamur işleri ve kekler, sandviç dolguları)	Bulantı, kusma, orta ve üst karın bölgesinde spazmodik ağrı, ishal Osteomiyelit, endokardit, kronik yara enfeksiyonu, göz enfeksiyonu, multimikrobiyal biyofilm enfeksiyonu, böbrek apsesi

4. BİYOFİLM TESPİT YÖNTEMLERİ

4.1.Kültür Temelli Yöntemler

4.1.1. Tüp yöntemi (TM)

Modifiye Christensen yöntemi olarak da bilinen standart cam tüp yönteminde belirli miktarda triptik soy buyyon (TSB) besiyeri içeren cam tüplere bakteri inoküle edilir. Genellikle 37°C de 18-48 saat inkübasyon gerçekleştirilir. İnkübasyon sonunda tüp aspire edilerek PBS ile yıkanır ve 30 dk. kurumaya bırakılır. Metilen mavisi, safranin veya %1'lik kristal viyole eklenir. 15 dk. beklendikten sonra tüp içeriği tekrar boşaltılır [27, 28] Tüp içeriğinde renkli bir film tabakasının kalıntısı biyofilm formasyonu pozitif olarak değerlendirilirken; oluşumun düzeyi (+), (++), (+++) ve (-) olarak derecelendirilmektedir (Şekil 2.) [10].

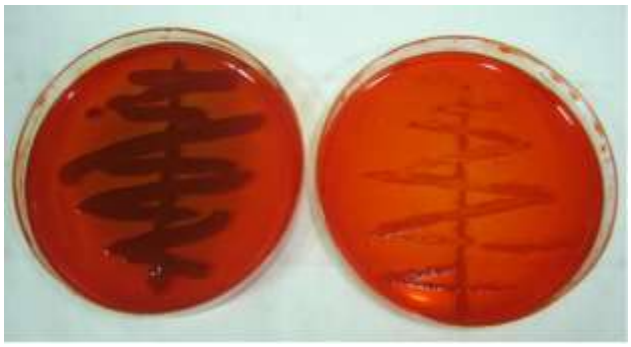


Şekil 2. *P. aeruginosa* izolatlarında biyofilm oluşumunun tüp yöntemiyle saptanması [27].

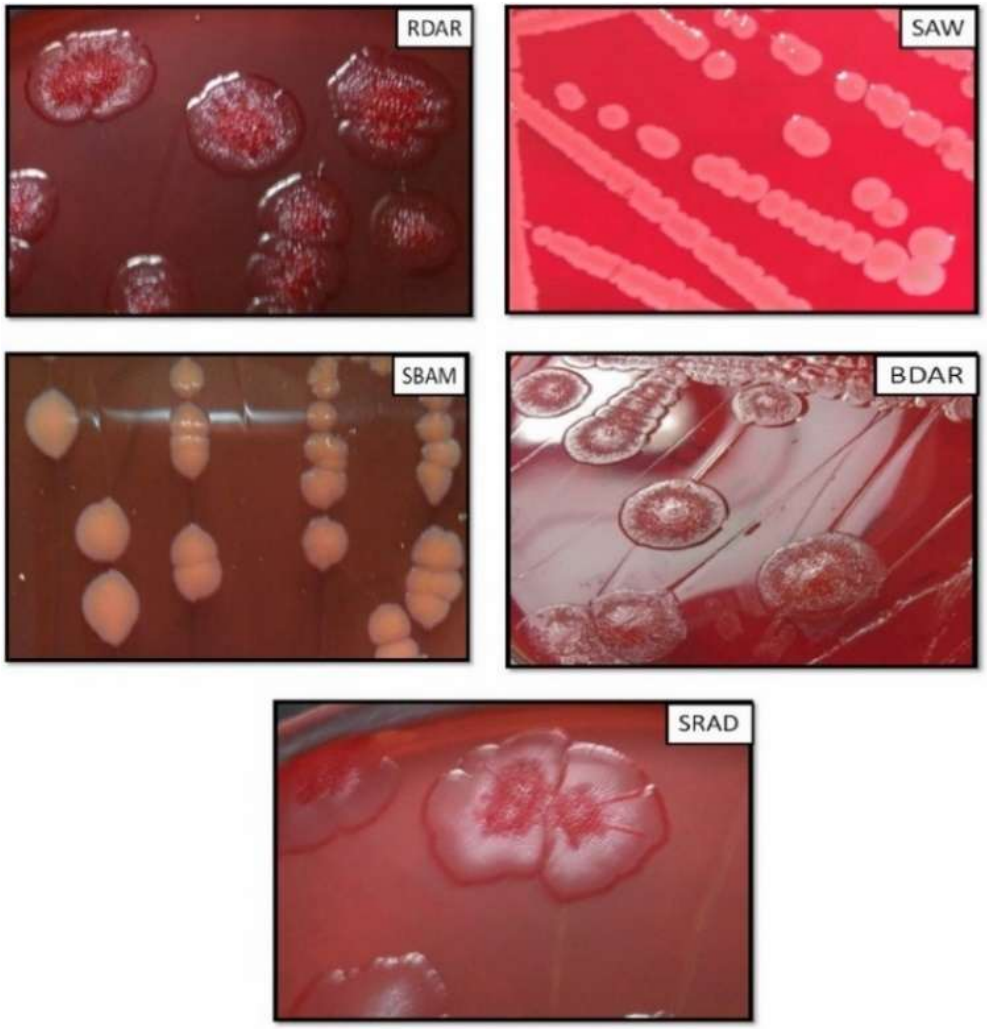
4.1.2. Congo Red Agar (CRA) ve Calcofluor Agar (CA) yöntemi

Biyofilm üretimi, koagülaz negatif stafilokoklarda ilk kez Freeman ve ark. [29] tarafından kongo kırmızılı agar tekniği kullanılarak araştırılmıştır [29]. Kongo Kırmızısı Agar ve Calcofluor Agar testleri, *Salmonella* tarafından oluşturulan biyofilmin ana bileşenleri olan curli ve selülozun varlığını tespit etmek için yaygın olarak kullanılmaktadır [30].

Bu yöntem ile; Congo Red Agar (CRA) besiyerine ekim yapılmasının ardından 37°C'de 24 saat inkübasyona bırakılır. İnkübasyon sonrası kolonilerde oluşan morfotipe göre değerlendirme yapılmaktadır. Siyah koyu kırmızı-kahverengi (Brown Dry and Rough (BDAR)) renkli koloni oluşumu görülen biyofilmlerin saptanması ve biyofilm üretimi açısından pozitif, pembe-kırmızı renkli (Red Dry and Rough (RDAR)) koloni oluşumu (Şekil 3.) veya renksiz (Smooth and White (SAW)) görülenler ise biyofilm üretimi açısından negatif (Şekil 4.) olarak yorumlanmaktadır [30, 31].



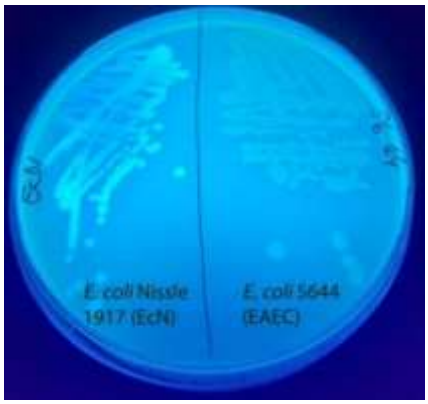
Şekil 3. CRA testinde, metisiline dirençli *S. aureus* (MRSA) [32].
*Siyah renk koloni morfolojisiyle pozitif, pembe renk koloni morfolojisiyle negatif biyofilm formasyonu.



Şekil 4. Kongo kırmızısı agarda *Salmonella* kolonilerinin farklı morfolojileri [33].
*Kırmızı, kuru ve pürüzlü (RDAR), pürüzsüz ve beyaz (SAW), pürüzsüz, kahverengi ve mukoid (SBAM), kahverengi, kuru ve pürüzlü (BDAR), pürüzsüz kırmızı (SRAD) morfotip.

Salmonella spp. suşlarının biyofilm üretiminin karşılaştırılması için Shatila ve ark. [30], CRA ve kalkoflor agar (CA) testlerini kullanmıştır. Araştırmacılar, NaCl içermeyen LB üzerinde

24 saat inkübasyon sonucu güçlü biyofilm yapıları tespit etmiştir. Biyofilm içeriği olan selüloz üretimini CA ile desteklemiş NaCl içermeyen LB agar üzerinde doğrulamışlardır. 27 °C ve 37 °C'de 96 saat inkübe edilmiştir. İnkübasyon sonrası CRA'ya kültürlerin ekimi yapılmıştır. CRA (Congo Red Agar) üzerinde farklı morfotipler belirlenirken, CA (Calcofluor Agar) kültürlerinde selüloz üretimi, UV transilluminatör altında floresan boyama yöntemiyle kontrol edilmiştir [30] (Şekil 5.).

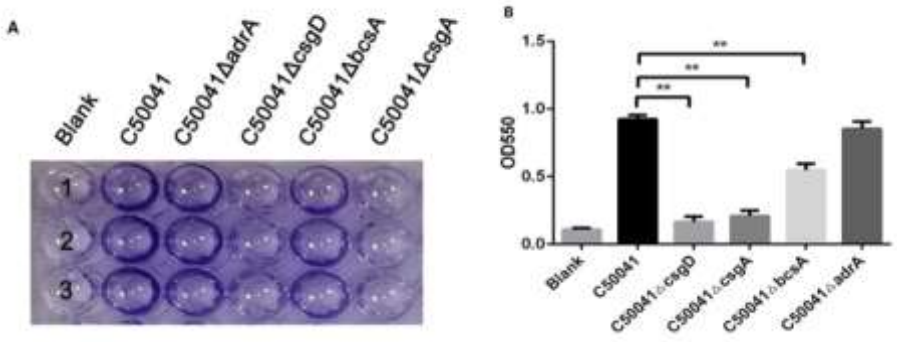


Şekil 5. *E. coli* izolatlarının kalkoflor agar üzerindeki floresansı [34].
*Selüloz üreten (*E. coli* Nissle 1917) pozitif floresan koloni morfolojisi göstermiştir. *E. coli* izolatı 5644 (EAEC) selüloz üretimi açısından negatiftir.

4.1.3. Mikroplak yöntemi

Yöntemde 96 adet kuyucuk bulunan mikroplaklar (Şekil 6.) ve bu kuyucuklar içerisindeki biyofilm yoğunluğunu belirlemek için spektrofotometre kullanılmaktadır [13]. Kuyucuklara besiyeri (%1-3 glukoz içeren TSB veya beyin-kalp infüzyon buyyon- BHB), içerisinde bakteri bulunan süspansiyon eklenir ve bakteriye özgü sıcaklık ve zamanda inkübasyona bırakılır. Süre bitiminde mikroplaklar ters çevrilerek kuyucuk içeriği boşaltılır. PBS ile yıkandıktan sonra kuyucuklara yine tüp testinde olduğu gibi metilen mavisi veya safranin veya en çok kullanılan boyalardan olan %1'lik kristal viyole gibi boyalar eklenir ve biyofilme penetrasyonu için belirli bir süre beklenir. Kuyucuklar boşaltılarak PBS ile yıkama işlemi tekrarlanır. Yıkama adımında boyar madde biyofilm içerisindeki hücreleri boyarken yapıya katılmamış diğer debrisler ve maddeler uzaklaştırılmaktadır. Oda sıcaklığında en az 30 dk. kurumaya bırakılan mikroplaklar daha sonra etanol, asetik asit veya aseton gibi ajanlarla fiksasyon sağlanır. Örnekler için optik dansite (OD) değeri belirlenir. Mikroplak okuyucu spektrofotometrede belirli bir dalga boyunda ölçüm yapılır. Numune değerleri ve kontrol kuyucuklarının ortalama OD değerleri karşılaştırılarak biyofilm oluşumunun varlığı ve derecesi değerlendirilebilir [12].

Salmonella spp.'nin farklı serotiplerine ait biyofilm oluşturma düzeyinin tespiti için mikroplak testinin kullanıldığı bir araştırmada [35], 69 serotipe ait izolattan oluşan toplam 151 suşta biyofilm üretim düzeyleri karşılaştırılmıştır. *Salmonella* izolatları, 48 saat süreyle LB besiyerinde inkübe edilerek çoğaltılmıştır. Hücrelerin ısı ile sabitlenmesi (80 °C, 30 dakika) ve % 0.5 kristal viyole ile boyanması sonrası %20'lik aseton çözeltisi kullanılarak kristal viyole absorbansı ölçülmüştür. Suşların çoğunluğu (%57.61) orta derecede biyofilm üreticisi iken, 34 (%22.52) suşun zayıf ve 29 suşun (%19.21) güçlü biyofilm üreticisi olduğu tespit edilmiştir. Numunelerden *S.* Muenster'ın biyofilm üretmediği gözlenmiştir. Araştırmacılar, gıda endüstrisi için önem taşımakta olan *Salmonella* suşlarının büyük çoğunluğunun plastik yüzeylerde biyofilm oluşturduğunu tespit etmiştir [35].



Şekil 6. *S. enteritidis* biyofilm ölçümünde mikroplak testi [36].
*(A) Kristal viyole boyanmış suşların olduğu 96 kuyucuklu mikroplak. (B) Optik yoğunluk (OD550) ölçümü ile kristal viyole penetrayonunun değerlendirilmesi ile biyofilm miktarının belirlenmesi amaçlanmıştır.

4.2.Moleküler yöntemler

4.2.1. Polimeraz Zincir Reaksiyonu (PCR)

PCR teknolojisi, biyofilm oluşumu üzerine etkili olan hücre dışı DNA'nın (eDNA) analizinde de yaygın olarak kullanılan bir yöntemdir. Biyofilm formasyonunda eDNA'nın inhibihe edici veya stimüle edici etkisi mevcuttur. eDNA ile ilgili Özdemir ve ark.[37], tarafından yapılan bir çalışmada 17 farklı *Salmonella* serovarının mikrobiyal yapışma ve farklı biyofilm oluşum aşamalarında eDNA etkisinin analizi yapılmıştır. Kültürel yöntemlerle izole edilen ve PCR ile çoğaltılan farklı suşlardaki eDNA'lar %1'lik agoroz jelde görüntülenmiştir. Farklı suşların karşılaştırılması bakımından DNase I varlığında bazı serotiplerin erken biyofilm oluşumu aşamalarında 28°C'de daha fazla biyofilm ürettiği, aynı suşların optimum üreme koşullarını sağlayan 37°C'de biyofilm oluşturmadığı bulgular arasında yer almıştır. Araştırmacılar bu çalışma ile, çeşitli serovarların biyofilm oluşturma yetenekleri arasındaki farklılığın, büyüme ve gelişim için çeşitli sıcaklıklarda farklı seviyede gen ekspresyonlarından kaynaklanabileceğini öne sürmüştür. Çalışmaya göre, serovarların ilk yüzeye yapışmasında eDNA'nın önemli derecede inhibe edici etkisinin olduğu gözlemlenmiştir [37].

4.2.2. RT - PCR / qPCR

Gerçek zamanlı PCR (RT-PCR) biyofilm yapısında görev alan genlerin ekspresyon düzeylerinin yanı sıra, bu genler arasındaki ilişkilerin, mikrobiyal yükün ve hücre canlılığının kantitatif olarak analiz edilmesine olanak sağlamaktadır. Gen ifadelerine örnek olarak bir çalışmada, *VirSR* (iki bileşenli sinyal iletim sistemi) ve *VirAB*'den (ATP bağlayıcı kaset taşıyıcısı) oluşan bir sistemin *L. monocytogenes'*in saha suşu olan EGD-e'nin biyofilm oluşumundaki rolü araştırılmıştır. Biyofilm oluşumu kristal viyole boyama, SEM ve CLSM ile mikroplak testi kullanılarak ölçülmüştür. EGD-e suşu ve mutant suşlar arasında bağlanma kapasitesi ve sürü şeklinde hareket kabiliyetleri qPCR ile karşılaştırılmıştır. Saha suşu ve izogenik delesyon mutantlarında biyofilm oluşturulmasına ilişkin genlerin ifade düzeyleri belirlenmiştir. Elde edilen bulgular *flaA, motA* ve *motB* genlerinin; mutant suşlar Δ*virAB* ve Δ*virS*'de aşağı yönde düzenlendiğini göstermiştir. Araştırmacılar, bu genlerin aşağı regülasyonunun, mutant suşlarda gözlenen biyofilm oluşumu ve yüzeye bağlanma kapasitesindeki azalmanın muhtemel nedeni olabileceğini öne sürmüştür [38].

4.2.3. Floresan In-situ Hibridizasyon (FISH)

FISH metodu biyofilm yapısını oluşturan polimikrobiyal topluluklar ve içerdikleri türlerin varlığının ve çevresel dağılımını kantitatif olarak ölçmek için kullanılmaktadır. FISH metodunun CLSM ile desteklenmesiyle, mikroorganizmalar arası etkileşimler ve bu türlerin çevresel değişikliklerden etkilenmelerini görüntülemek mümkündür. Peptidonükleik asit-floresans in situ hybridization (PNA-FISH) yönteminin bu amaçla kullanıldığı bir araştırmada *E. coli*, *L. monocytogenes*, *S. enterica* türlerinin biyofilm yapısının karakterizasyonu yapılmıştır. Nicel olarak 56 farklı biyofilm popülasyonu 48 saat izlenmiştir. *E. coli* çoğalması ve EPS salınımının, *L. monocytogenes* ve *S. enterica* 'nın iki katı düzeyde olduğu ve bu sonuçların *E. coli*'yi diğer iki patojen ile rekabete yönlendirdiği belirtilmiştir. Araştırmacılar FISH ile doğru bir konsantrasyon belirleyebildiklerini ancak biyofilm yapısının ve içeriğinin kalitatif olarak anlaşılmasının CLSM ile mümkün olduğunu savunmuştur [39].

4.2.4. Western Blot- SDS PAGE

Sodyum dodesil sülfat–poliakrilamid jel elektroforezi (SDS-PAGE) yöntemi, biyofilm oluşumu sürecinde meydana gelen protein profil değişimlerinin ve biyofilm yapısına özgü protein içeriklerinin analizinde yaygın olarak kullanılmaktadır [40]. Bu yöntemin kullanımına örnek olarak, *Leptospira* spp. tarafından oluşturulan biyofilm yapısında *Gro*EL stres proteininin aşırı ekspresyonunun gösterildiği çalışma verilebilir. Abiyotik yüzeylerde biyofilm oluşturma kapasitesine sahip olan *Leptospira* spp., bu çalışmada biyofilm ve planktonik hücreler arasında karşılaştırmalı protein ekspresyonu açısından analiz edilmiştir. Çalışmaya göre biyofilmde ifade edilen ısı şoku proteini, SDS-PAGE ile birlikte MALDI-TOF kütle spektrometrisi ve immünoblotlama yöntemleri kullanılarak araştırılmıştır. Planktonik hücrelerde ve biyofilmde ifade edilen protein analizleri ve karşılaştırmaları yapılmıştır. Çalışma sonucunda, biyofilm formunda aşırı ekspresyon gösteren 60 kDa moleküler ağırlığındaki bir proteinin, MALDI-TOF analizi ile *Gro*EL stres proteini olarak tanımlandığı rapor edilmiştir [41].

4.2.5. Flow Sitometri (FCM)

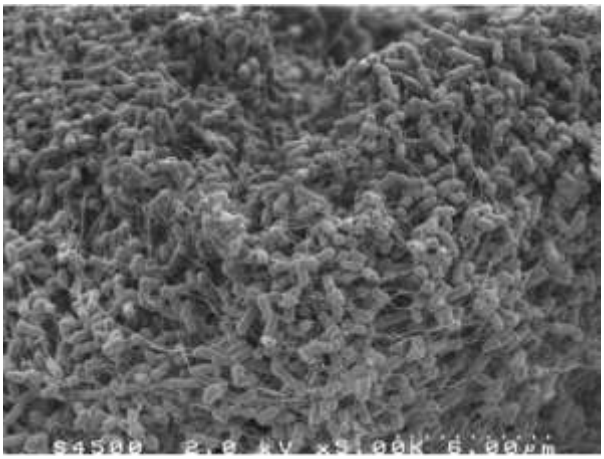
Akış sitometrisi ile biyofilm içeriğindeki mikrokolonilerin karakterizasyonu, hücre fizyolojisi ve metabolik aktivitesi, türlerin tanımlaması gibi karışık kültür analizleri yapılabilmektedir. [42]. Konieczny ve ark (2021), görüntüleme akış sitometrisi verilerini makine öğrenimi tabanlı bir yorumlama protokolüyle desteklemiştir. Gıda işleme hatlarından toplanan biyofilm örnekleri metabolik aktivite ve karmaşık agregatlar açısından gözlemlenmiştir. Mikroorganizmaların planktonik formları ve agregatlarının ve biyofilm yapılarını oluşturan mikrobiyal hücrelerin fizyolojisini değerlendirmek için aynı anda aktif, orta aktif ve ölü hücre yüzdeleri incelenmiştir. Araştırmacılar tarafından geliştirilen makine öğrenmesi yorumlama protokolü, biyofilm yapısı içindeki bakteri kümelerinin özelliklerini daha ayrıntılı değerlendirmiştir. Araştırmacılara göre bu çalışma, gıda endüstrisinde biyofilm formlarının tespitini kolaylaştırma olasılığını göstermiştir [43].

4.3.Mikroskobik Yöntemler

4.3.1. Taramalı Elektron Mikroskobu (SEM)

Taramalı Elektron Mikroskobu (SEM), biyofilmin morfolojik yapısını, hücreler arası etkileşimleri ve ekstraselüler polimerik madde (EPS) matrisinin organizasyonunu yüksek

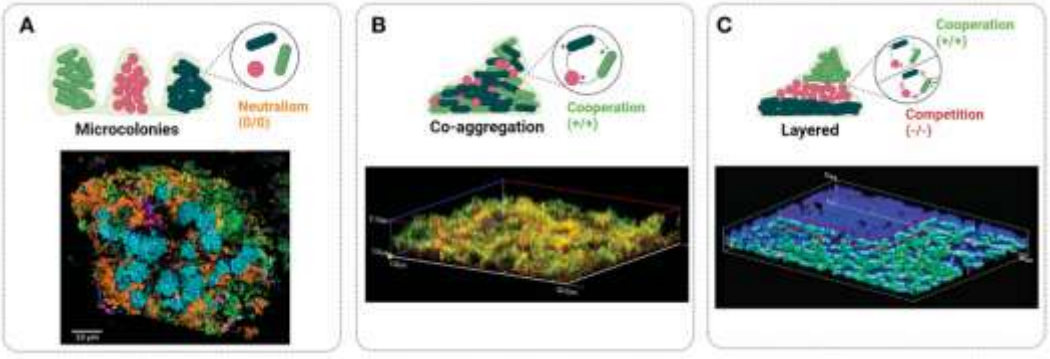
çözünürlükte incelemek amacıyla kullanılan temel görüntüleme yöntemlerinden biridir. Biyofilm örnekleri, liyofilizasyon işleminden geçirildikten sonra, ince bir tabaka halinde altın (Au) veya paladyum (Pd) ile kaplanarak Taramalı Elektron Mikroskobu (SEM) ile görüntülenmeye uygun hale getirilmektedir (Şekil 7). Al-Shabib ve ark.[44], bakır(I) kompleksinin biyofilm üzerindeki QS mekanizması ve bu mekanizmayı baskılayan QS aktivitesi üzerindeki etkilerini incelemiştir. Her üç kompleks de *P. aeruginosa* (elastaz, piyosiyanin ve aljinat üretimi), *C. violaceum* (violacein) ve *S. marcescens'teki* (prodigiosin) QS tarafından düzenlenen işlevleri önemli derecede etkilemiştir. Bakır(I) ile muamele edilen *E. coli*, *Chromobacterium violaceum*, *Klebsiella pneumoniae*, *L. monocytogenes*, *P. aeruginosa* ve *Serratia marcescens*'de, geniş spektrumlu ve güçlü biyofilm inhibisyonu gözlenmiştir. Biyofilm inhibisyonu SEM ve CLSM kullanılarak görselleştirilmiştir. Komplekslerin, sürü hareketi ve EPS üretimi gibi biyofilm oluşumunda rol oynayan iki önemli QS düzenlemeli işlev üzerindeki etkisinde azalma bildirilmiştir [44].



Şekil 7. *L. monocytogenes* LO28 biyofilminin taramalı elektron mikroskobu ile görselleştirilmesi [45].

4.3.2. Konfokal Lazer Tarama Mikroskopisi (CLSM)

Uygun boyama protokolleriyle birlikte kullanılan Konfokal Lazer Taramalı Mikroskopi (CLSM), biyofilmin üç boyutlu yapısını, hücre dağılımını, canlılık durumunu ve EPS matrisini detaylı biçimde görüntüleme imkânı sunmaktadır. Biyofilmin mimarisini oluşturan eDNA'nın temel işlevlerinden biri biyofilm stabilitesini sağlamaktır. Bu yapı CLSM ile görüntülenebilir [46]. Bakterilerin 24 ve 48 saatlik biyofilm popülasyonları üç boyutlu olarak CLSM ile görüntülenmiştir [39]. CLSM ile her bakteriyi ayırt eden ve üç alanın üst üste gelmesini gösteren görüntüleri mevcuttur [47]. Şekil 8.'de gösterilen (C) *E. coli* tarafından oluşturulan biyofilm tabakasını göstermek için bir kırmızı dikdörtgen çıkarılmıştır; bu tabakanın altında karışık *Salmonella* ve *Listeria* tabakası bulunmaktadır.



Şekil 8. Polimikrobiyal biyofilm yapısı [5].
*(A) ayrı mikro koloniler [48] (B) ko-agregasyon [47]; (C) düzenlenmiş katmanlar; kırmızı *Salmonella*, yeşil *Listeria*, mavi *E.coli* [39].

5. BİYOFİLM İLİŞKİLİ GENLER

Genom düzeyinde yapılan gen ekspresyonu analizleri, biyofilm oluşumu sırasında farklı şekilde ifade edilen genlerin önemli bir kısmını işlevi henüz tanımlanmamış genlerin oluşturduğunu ortaya koymuştur [49].

Planktonik formdaki mikroorganizmaların gen ekspresyon profilleri, biyofilm yapısı içerisindeki hücrelerle karşılaştırıldığında belirgin farklılıklar göstermektedir. Mikroorganizmaların çevresel stres faktörlerine karşı geliştirdiği adaptasyon yanıtları, yalnızca biyofilm oluşumunu değil, aynı zamanda belirli genetik mutasyonların ortaya çıkmasını da tetikleyebilmektedir [50]. Mar (multiple antibiotic resistance operon), *E. coli*'de çoklu antibiyotik direncinin gelişiminde rol oynayan, transkripsiyon düzeyinde gen ekspresyonunu düzenleyen bir kontrol sistemidir. Stres yanıtı, hücrelerin zararlı çevresel etkenlere maruz kalmasından sonraki birkaç saat içerisinde aktive olur ve direnç mekanizmalarında artış gözlemlenir. *OxyR* ve *soxR* gibi çeşitli düzenleyici genlerin, hücre içi redoks potansiyelini dengeleyerek, bakterilerin oksidatif stres koşullarında yanıt sistemlerini aktive ettiği gösterilmiştir [1].

Biyofilm dinamikleri ile ilgili *C. jejuni* için otuz kadar tanımlanmış gen bulunmaktadır. *C. jejuni* tarafından *cydB* geninin biyofilm oluşumundaki rolünün araştırıldığı bir çalışmada Transpozon kütüphanesinde, *Campylobacter* için biyofilm oluşumu ile daha önce ilişkilendirilmemiş olan solunum ile bağlantılı *cydB* geninin biyofilm oluşumundaki rolü incelenmiştir. Tanımlanmış mutant suşu ile birlikte bir *cydB* delasyon mutantı oluşturmuşlardır. *cydB* mutantın ana suşa göre daha gevşek, zayıf yapıda ve daha düşük hacimde bir biyofilm tabakası oluşturduğu gözlenmiştir [51].

S. Tyhimurium için curli major alt birimi ve biyofilmin önemli bileşenleri olan curli ve fimbrial sentezi *CsgA* geni tarafından kodlanır [52]. *BcsA* ve *BcsB* genleri ise biyofilmin önemli bir bileşeni olan selülozun sentezini kodlar [53]. *CsgD* geni *adrA* transkripsiyonunu teşvik eder. *AdrA* geni diguanilatsiklaz, ikincil haberci sinyal molekülü (3'-5') -siklik diguanozin monofosfat (c-di-GMP) üretimi yoluyla selüloz sentezini pozitif olarak düzenler [54].

*E. coli'*de biyofilm yanıtının önemli bir bölümü, durağan (stationary) faz sırasında indüklenen genlerin ekspresyonuna dayanmaktadır. Biyofilm formasyonunun düzenlenmesinde birçok genetik regülatör rol oynamaktadır. Bunlardan *barA/uvrY* iki bileşenli sistemi biyofilm oluşumunu sağlayan gen ekspresyonunu aktive etmektedir. Yüzey

uyaranlarını algılamaya yardımcı *cpxRA* geni hücreler arası etkileşimlerde rol oynar. Katabolit baskılama geni olan *crp* ise biyofilm oluşumunu baskılayan genlerdendir. *csrA* ve *csrB* genleri biyofilm üretimini baskılayarak aynı zamanda olgun biyofilmlerde ayrılma evresini başlatır [55, 56]. Anoksik koşullarda ise *hns* geni yüzey adezyonunu azaltır [57].

P. aeruginosa ve *E. coli*'de *rpoS* geni, çevresel koşullara bağlı olarak biyofilm üretiminin artmasını veya azalmasını düzenleyen önemli bir stres yanıt regülatörüdür. Bununla birlikte, durağan faz sigma faktörü olan *rpoS*'nin ifadesinin *E. coli* ile karşılaştırıldığında *P. aeruginosa* tarafından üretilen biyofilmde 2-3 kat baskılandığı belirtilmiştir [49, 58, 59]. Biyofilm mimarisinin oluşumunda ve yüzeye ilk adezyon aşamasında rol oynayan alternatif sigma faktör *rpoN*, QS sistemine ait *rhlI* geninin önemli bir düzenleyicisidir [60].

*S. aureus'*un biyomateryaller üzerinde biyofilm üretme yeteneği bulunmaktadır. Abiyotik yüzeylerde ise *S. aureus* tarafından olgun biyofilm oluşumunu üstlenen gen olarak *rbf* geni tanımlanmıştır [61]. *rlR-arlS* lokusu ise hücre dışı proteolitik aktiviteyi değiştirmektedir. *AgrC-AgrA*, virülans faktörlerinin üretiminde yer alan iki bileşenli bir düzenleyici sistem olarak tanımlanmıştır [62, 63]. Biyofilm tabakasının adezyonu ve kalıcılığı gibi faktörlerde rol oynayan gen bölgeleri *ica* lokusu ve *hemB* lokusudur. Biyofilm yapısında *clfAB* , *fnbAB* , *cna* ve *ica* genleri tarafından düzenlenen virülans faktörleri bulunmaktadır [64, 65].

6. SONUÇ

Biyofilm yapıları, gıda endüstrisinde hem gıda güvenliğini sağlama hem de halk sağlığını koruma açısından kritik bir risk faktörüdür. Biyofilm oluşumunun tespiti ve kontrol stratejilerinin geliştirilmesi amacıyla hem kalitatif hem de kantitatif analiz yöntemleri kullanılmaktadır. Biyofilm yapılarındaki mikrobiyal çeşitlilik ve dinamiğin tam olarak anlaşılabilmesini amaçlayan çeşitli moleküler yaklaşımlar geliştirilmiştir. Bu yaklaşımları destekleyen yeni nesil görüntüleme tekniklerinin entegrasyonu sayesinde, biyofilmlerin yapısal ve fonksiyonel özelliklerine ilişkin geliştirilen analiz yöntemlerinin sayısı her geçen gün artmaktadır.

Farklı patojen türleri, çevresel koşullara adaptasyon süreçlerinde tür spesifik genetik ve fizyolojik mekanizmalar geliştirmiştir. Biyofilm matriksinin temel yapı taşları olan EPS, QS mekanizmaları, eDNA ve hidrofilik su kanalları gibi unsurların fonksiyonlarına yönelik yapılan güncel çalışmalar; farklı mikroorganizmalarda bu sistemlerin ne ölçüde benzerlik gösterdiğini ve hangi yönlerden çeşitlilik taşıdığını ortaya koymaktadır. Bu alanda yürütülen çalışmaların artmasıyla biyofilm ilişkili genler ve mekanizmalarının anlaşılması, biyofilm üreten patojenlerin antibiyotikler, dezenfektanlar gibi kimyasal maddelere ve çevresel stres faktörlerine direnci azaltılabilir. Bu nedenle, gıda üretim alanlarında biyofilm oluşumunu kaynağında engellemek ve çapraz kontaminasyon riskini azaltmak amacıyla, mikroorganizmaların yüzeylere tutunma yeteneğini minimuma indiren malzeme ve kaplama teknolojilerinin tercih edilmesi kritik bir kontrol stratejisi olarak öne çıkmaktadır.

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ANGIOKERATOMA CIRCUMSCRIPTUM:A CASE REPORT

ABSTRACT

Aim Angiokeratoma is a capillary malformation that presents with vascular ectasia, papillomatosis in the papillary dermis, and hyperkeratosis and acanthosis in the epidermis. The rarest form of angiokeratoma is angiokeratoma circumscriptum (1). The other four subtypes are Mibelli angiokeratoma, Fordyce angiokeratoma, solitary angiokeratoma, angiokeratoma corporis diffisum (Fabry disease)(2). In our study, we aimed to define the rare angiokeratoma circumscriptum, to describe its histopathological features and accompanying syndromes, and to explain treatment options through our case (1).

Method Our case report describes an 18-year-old male patient who presented to the Dermatology-1 outpatient clinic of the SBU Van Training and Research Hospital in February 2025 and had a painful plaque with linearly located vesicles containing serous and hemorrhagic material in the right gluteal region, occasionally spreading to the left gluteal region. In the first stage, dermoscopic examination was performed with the DL-5 dermoscopy device, blood tests were requested, and herpes zoster treatment was given due to the zosteriform localization. Since the disease did not regress with treatment, a skin biopsy was taken from the patient with a 5-hole punch.

Result The incidence of angiokeratoma circumscriptum is 0.16% worldwide, which is quite rare and there is a slight male predominance in incidence (3). Although the developmental mechanism is not fully known, some syndromes and trauma are primarily blamed (3). Our patient who applied to our polyclinic was male and 18 years old. Our patient had no known additional disease and his examination results were normal. He had no other symptoms other than pain and mild itching. Dermoscopic examination revealed plaques with hemorrhagic lacunae separated by septa and a blue-white veil on top. Angiokeratoma circumscriptum was considered in the preliminary diagnosis and for definitive diagnosis, a punch biopsy was taken from the patient with the preliminary diagnoses of angiokeratoma circumscriptum, lymphangioma circumscriptum, and verrucous hemangioma. Biopsy results showed hyperkeratosis and acanthosis in the epidermis, papillomatosis in the papillary dermis, widespread erythrocyte accumulation in the epidermis and dermis, and capillary ectasia. The patient's biopsy result supported angiokeratoma circumscriptum.

Conclusion Standard treatments for angiokeratoma are laser treatment or total excision treatment. Laser treatment is the primary treatment because of its low risk of complications and better cosmetic results. Argon, Nd:yag and CO2 pulse-dye laser can be tried. If complete

remission is not achieved, total excision may be recommended (4). We was planned Nd:yag laser treatment at our clinic to our patient.

Keywords: angiokeratoma circumscriptum, Nd:yag laser, verrucous hemangioma

ANJİOKERATOMA SİRKUMSİKRİPTUM: BİR OLGU SUNUMU

ÖZET

Giriş ve Amaç Anjiokeratom vasküler ektazi, papiller dermiste papillomatozis, epidermiste hiperkeratoz ve akantoz ile giden bir kapiller malformasyondur. Anjiokeratomun en nadir görülen formu anjiokeratoma sirkumskriptum'dur (1). Diğer dört alt tipi ise Mibelli anjiokeratomu, Fordyce anjiokeratomu, soliter anjiokeratom, anjiokeratoma korporis diffizum (Fabry hastalığı)'dur(2). Çalışmamızda vakamız üzerinden nadir görülen anjiokeratom sirkumskriptumu tanımlamak, histopatolojik özellikleri ve eşlik edebildiği sendromları tanımlamak tedavi seçeneklerini anlatmak amaçlanmaktadır (1).

Materyal ve Yöntem Vaka sunumumuz Şubat 2025 tarihinde SBÜ. Van Eğitim ve Araştırma Hastanesi Dermatoloji-1 polikliniğine başvuran sağ gluteal bölgede yer yer sol gluteal alana da yayılan lineer yerleşimli seröz ve hemorajik materyal içeren veziküllerin olduğu ağrılı plağı olan 18 yaşında erkek hastayı tanımlamaktadır. İlk aşamada DL-5 dermoskopi cihazı ile dermoskopik inceleme yapılıp, kan tetkikleri istenmiştir ve zosteriform yerleşiminden dolayı herpes zoster tedavisi verilmiştir. Tedavi ile gerilememesi üzerine hastadan 5'lik punch ile deri biyopsi alınmıştır.

Bulgular Anjiokeratoma sirkumskriptumun görülme oranı dünya geneli %0,16 olup oldukça nadirdir ve insidansta hafif bir erkek baskınlığı izlenmektedir (3). Gelişim mekanizması tam olarak bilinmemekle beraber bazı sendromlar ve travma ön planda suçlanmaktadır (3). Bizimde polikliniğimize başvuran hastamız erkekti ve 18 yaşındaydı. Hastamızın bilinen bir ek hastalığı yoktu ve tetkikleri doğaldı. Ağrı ve hafif kaşıntı dışında başka bir semptomu yoktu. Dermoskopik incelemede septalarla ayrılmış hemarojik lakünlerle beraber üstünde mavi-beyaz peçe bulunan plaklar izlendi. Ön tanıda anjikoeratoma sirkumsikriptum düşünüldü ve kesin tanı için anjiokeratoma sirkumskriptum, lenfanjioma sirkumskriptum, verrüköz hemanjiom ön tanılarıyla hastadan puch biyopsi alındı. Biyopsi sonucunda epidermiste hiperkeratoz ve akantoz, papiller dermiste papillomatozis, epidermis ve dermiste yaygın eritrosit birikimi ve kapiller ektazi izlendi. Hastanın biyopsi sonucu anjiokeratoma sirkumskriptumu destekler nitelikteydi.

Sonuç Anjiokeratom tedavisinde standart tedaviler lazer tedavi veya total eksizyon tedavisinden oluşmaktadır. Komplikasyon riskinin düşük olması ve kozmetik sonuçlarının daha iyi olması nedeniyle lazer tedavisi öncelikli tedavidir. Argon, Nd:yag ve CO2 pulse-dye lazer denenebilir. Tam remisyon sağlanamazsa total eksizyon önerilebilir(4). Hastamıza kliniğimizde bulunan Nd:yag lazer işlemi planlanmıştır.

Anahtar Kelimeler*:* anjiokeratoma sirkumskriptum, Nd:yag lazer, verrüköz hemanjiom

GİRİŞ VE AMAÇ

Anjiokeratom, dermal damarlarda ektazi ve epidermiste hiperkeratoz ve akantoz ile seyreden derinin vasküler bir hastalığıdır. 5 varyantı bulunmaktadır: Mibelli anjiokeratomu, Fordyce anjiokeratomu, soliter anjiokeratom, anjiokeratoma korporis diffizum, anjiokeratoma sirkumsikriptum (2). Anjiokeratom çok nadir görülen bir hastalıktır ve 5 farklı çeşidi olmasıyla beraber genel olarak histopatolojileri ortaktır. Soliter anjiokeratom anjiokeratom tipleri arasında en sık görülen tipken, anjiokeratoma sirkumsikriptum en nadir görülen varyanttır. Anjiokeratoma korporis diffizum daha çok Fabry hastalığının bir paterni olarak izlenirken, Fordyce anjiokeratomu genelde skrotal yerleşir, Mibelli anjiokeratomu ise el ve ayak parmaklarının dorsal yüzünde yerleşir (5). Bununla beraber anjiokeratom mukozal alanlarda da yerleşebilir. Genelde soliter yerleşimli mukozal lezyonlar ek bir hastalıkla ilişkili olmazken, multipl lezyonlar Fabry hastalığı veya Fukosidoz ile ilişkili olabilir (5). Ancak genel olarak mukozal yerleşimli anjiokeratomlar kutanöz anjiokeratomlara göre sistemik hastalıklarla daha yakından ilişkilidir (4). Anjiokeratomlar genelde spontan remisyon göstermezler ve hastalar için kozmetik problemler oluşturabilirler. Damar bazlı lazer tedavileri ve total eksizyon gibi tedavi yöntemleri tedavi seçiminde kullanılabilir (6).

VAKA SUNUMU

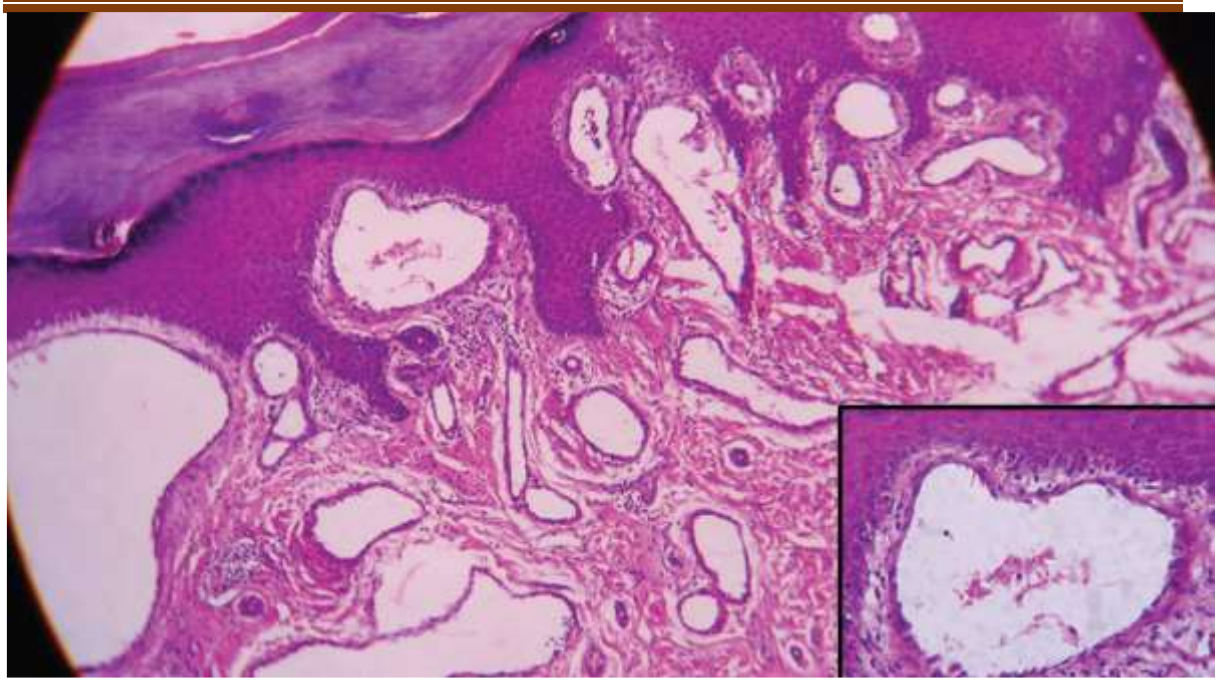
Vaka sunumumuz Şubat 2025 tarihinde SBÜ. Van Eğitim ve Araştırma Hastanesi Dermatoloji-1 polikliniğine başvuran sağ gluteal bölgede yer yer sol gluteal alana da yayılan lineer yerleşimli seröz ve hemorajik materyal içeren veziküllerin olduğu ağrılı plağı olan 18 yaşında erkek hastayı tanımlamaktaydı. İlk aşamada DL-5 dermoskopi cihazı ile dermoskopik inceleme yapılıp, kan tetkikleri istendi ve zosteriform yerleşiminden dolayı herpes zoster tedavisi verildi. Tedavi ile lezyonların gerilememesi üzerine hastadan 5'lik punch ile dermiside içerecek şekilde derin deri biyopsi alındı. Dermoskopisinde mavi-mor hemorajik lakünlerin septalarla ayrıldığı üzerinde mavi beyaz peçe ve hiperkeratozik skuamların olduğu plaklar mevcuttu. Biyopsisinde dermisteki kapillerlerde dilatasyon ve ektazi epidermiste akantoz ve hiperkeratoz yaygın eritrosit dağılımı izlenmiş olup histopatoloji anjiokeratom ile uyumlu görüldü. Kan tetkikleri doğal izlendi. Hastanın oturmakla, hareketle ve travmayla artan ağrısı olmaktaydı. Biyopsi sonucu anjiokeratom ile uyumlu olan hastanın kliniğimizde olan damar bazlı lazer cihazımız Nd:yag lazer ile tedavisi planlanıp seanslarına başlandı.



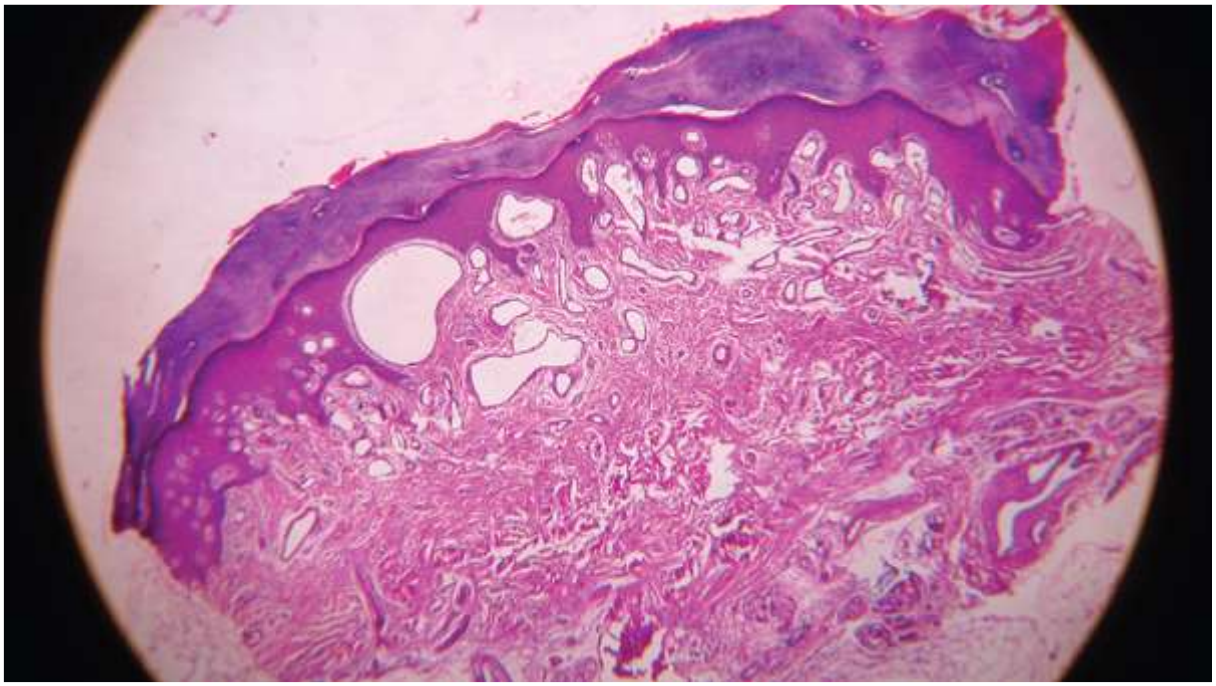
Resim 1: *Çoğunlukla sağ gluteal alan medialinde olmak üzere yer yer sol gluteal alan medialinde de yerleşen yer yer seröz yer yer hemorajik vasıflı grube veziküllerin olduğu plakların izlendiği fotoğrafta bulgular anjiokeratoma sirkumsikriptum ile uyumlu izlenmiştir.*



Resim 2: *Çoğunlukla sağ gluteal alan medialinde olmak üzere yer yer sol gluteal alan medialinde de yerleşen yer yer seröz yer yer hemorajik vasıflı grube veziküllerin olduğu plakların izlendiği fotoğrafta bulgular anjiokeratoma sirkumsikriptum ile uyumlu izlenmiştir.*



Resim 3: *Kapiller endotelde incelme ve dilatasyon ile giden vasküler ektazi, uzamış retelerin görüldüğü histopatolojik görüntü anjiokeratomun histopatolojik bulgularından biridir (7).*



Resim 4: *Mikroskobik görüntüde papiller dermisteki kapiller endotelde incelme ve dilatasyon, retelerde uzama, epidermiste hiperkeratoz ve akantoz izlenmektedir (7).*

TARTIŞMA

İlk anjiokeratom terimi Mibelli tarafından 1889 yılında el parmak dorsumlarında yerleşen damar anomalileri için kullanılmış sonrasında günümüzde bildiğimiz diğer 5 tipi tanımlanmıştır. Anjiokeratomların gelişiminin sebebi tam olarak bilinmemekle beraber hamilelik konjenital sebepler, chilblain, travma, doku asfiksisi olabilecek sebepler arasında gösterilmiştir (8). Subtipler klinik olarak farklı karakteristik ve lokalizasyon göstersede histopatoloji tüm tiplerde ortaktır (8). Vakamız bu subtiplerden anjiokeratoma sirkumsikriptum tipine aitti ve biyopside diğer tiplerde olduğu gibi epidermiste hiperkeratoz ve akantoz, dermiste kapiller ektazi izlendi. Lezyon gluteal alanda yerleşmişti patoloji konjenital olarak değil erken çocukluk döneminde fark edilmiş sonrasında gluteal alana giderek yayılmış ve ağrı yapmaktaydı.

Anjiokeratomlar genelde sistemik hastalıklarla ilişkili bulunmamış olsada Fabry hastalığı, Fukosidoz sendromları, Klippel Trenaunay veya Cobs sendromunun kutanöz bulgusu olarak da görülebilir (9). Bunun dışında IDH-1 (İzositrat Dehidrojenaz-1)mutasyonunun sebep olduğu çok nadir bir sendrom olan Enkondromatozis ile giden D-2 hidroksiglutarik asiduri sendromunun bir patenti olarak da görebiliriz (10). Vakamızda eşlik eden başka bir sendrom görülmedi. Anjiokeratomu tetikleyen bir travma ve doku asfiksisine neden olacak bir hastalık yoktu.

Sendromlar ve tetikleyici faktörler dışında hemanjiom kategorisinde yer almasına rağmen görüntü olarak özellikle anjiokeratoma sirkumsikriptuma çok benzeyen başka bir patoloji ise verrüköz hemanjiomdur (11). Verrüköz hemanjiomlarla anjiokeratomları ayırmak için histopatolojik inceleme gereklidir. Histopatolojide epidermiste ortak hiperkeratoz ve akantoz görülürken anjiokeratomlardaki damar patolojisi daha yüzeyel papiller dermisteyken, verrüköz hemanjiomlarda vasküler patoloji daha derin yerleşimli derin dermis ve subkutan dokudaki kapillerlerde meydana gelmektedir (11). Vakamızda klinik görünüm verüköz hemanjiomada benzemekte ancak histopatolojide vasküler patoloji papiller dermiste yerleşmekte ve anjiokeratom histopatolojisiyle uyumlu görünmekteydi.

SONUÇ VE ÖNERİLER

Anjiokeratomlar nadir görülen klinik olarak kolay tanısı konabilen aynı zamanda dermoskopik görüntüleme ve histopatolojik özelliklerini belirgin olması nedeni ile kolay teyit edilebilen bir hastalıktır (4). Tedavi planı ağrı kanama ve kozmetik nedenlerle planlanabilir. Tedavi çeşitleri damar bazlı ablatif ve non-ablatif lazer cihazları ile veya total eksizyondan oluşmaktadır. Kozmetik sonuçların daha iyi olması birkaç seansta tama yakın remisyonun sağlanabilmesi açısından öncelikli tedavi seçeneği olarak kabul edilebilir. Ancak lazer tedavileri sonrasında da atrofik skar hipo-hiperpigmente plaklar kalabilmektedir (4).

Puls-dye lazer, argon lazer, fraksiyonel lazer, Nd-yag lazer çeşitleri tedavide kullanılabilen ışık sistemleridir. Bu lazerler vasküler patolojilerde olumlu sonuçlar verseler de anjiokeratomların özellikle anjiokeratoma sirkumsikriptumun yoğun hiperkeratoz içermesi nedeniyle sürekli dalga argon ve karbondioksit fraksiyonel lazer gibi ablatif lazerlerin kullanılması hem hiperkeratinizasyona hem de vasküler anomalilerin tedavi edilmesinde daha efektif rol oynayabilir (4). Lazer tedavileriyle istenilen sonuç alınamayan hastalar total eksizyona yönlendirilebilir. Vakamızda kliniğimizde bulunan Nd- yag lazer tedavisine

başladık seansların seyrine göre total eksizyon gerekliliğini gündemimize taşıyıp taşımama kararı aldık (4).

Sık rastlanılan bir hastalık olmasa da özellikle yerleşim yerleri ve kanamalara sebep olması dolayısıyla hızlı tanı konulup büyük alanları kaplamadan erken teşhis edilmesi varsa eşlik edebilecek sendromlar açısından hastaların incelenmesi çok önemlidir. Morbitidesi nedeni ile hasta konforunu çok azaltan bir hastalık olmasıyla beraber lazer bazlı tedavilerle yüz güldürücü sonuçlar alınmaktadır.

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POWER ANALYSIS AND SAMPLE SIZE: THEORETICAL FOUNDATIONS, TYPES, AND THEIR ROLE IN RESEARCH PLANNING

ABSTRACT

Statistical techniques are used to estimate population parameters through point or interval estimation, to develop models, and to test hypotheses. For each of these objectives, it is necessary to obtain an appropriate sample from the target population. When statistical studies such as surveys, experiments, and observational designs are carefully planned, the validity and reliability of the results significantly increase. The first step in research planning is typically to answer the question: “How many observations should be included in this study?” To answer this question scientifically, it is essential to calculate the sample size or conduct a power analysis. Power analysis is a fundamental statistical method used to assess the probability that a statistical test will detect an existing effect or relationship. It is a crucial step in the design of any research. An insufficient sample size may lead to inconclusive results and weak statistical power, whereas an excessively large sample may cause resource waste and the detection of statistically significant but practically irrelevant effects. Moreover, including more subjects than necessary may raise ethical concerns. Therefore, determining the minimum required sample size is essential to ensure both statistical adequacy and cost-effectiveness. The aim of this study is to emphasize the necessity of sample size estimation, provide an overview of the types of power analysis—including a priori (theoretical), post hoc (empirical), sensitivity, compromise, and criterion analyses—and explain the core components of power analysis such as null and alternative hypotheses, effect size, Type I error (α), and Type II error (β).

Keywords: Power analysis, Sample size, Effect size, Type I error, Type II error

1. Introduction

Conducting scientifically valid and ethically sound research requires meticulous planning at every stage. From hypothesis formulation to the selection of appropriate analytical strategies, each decision in the planning phase directly impacts the reliability and interpretability of the findings (Hulley et al., 2013). Among these considerations, determining an adequate sample size and ensuring sufficient statistical power are particularly crucial. A study lacking power may fail to detect meaningful effects, leading to incorrect conclusions and raising ethical concerns, especially when human subjects are involved (Cohen, 1988; Biau et al., 2008).

Ideally, researchers would study an entire target population to achieve maximum accuracy. However, practical limitations related to time, budget, and accessibility often make this infeasible (Sedgwick, 2015). Therefore, researchers rely on representative samples, and the credibility of a study hinges on both the sampling methodology and the accuracy of sample size calculations. In this context, determining an appropriate sample size is not merely a technical task but a scientific and ethical obligation.

From an economic standpoint, studies with unnecessarily large samples can lead to wasted resources and may produce statistically significant but practically insignificant results (Biau et al., 2008; Hickey et al., 2018; Cohen, 1992). Conversely, an insufficient sample size may prevent the detection of true effects, increasing the likelihood of a Type II error (Cohen, 1988). Therefore, sample size planning should strike a balance between statistical power and cost-effectiveness (Moher, 1994). Determining the minimum sample size necessary for reliable statistical inference is essential for both scientific rigor and ethical practice (Dell et al., 2002).

2. Basic Components of Power Analysis

The power of a statistical test is the probability of detecting a true difference or relationship. In other words, it is the ability to reveal this effect when H_0 (null hypothesis) is false. Sample size is calculated in different ways depending on whether the variable is qualitative or quantitative, hypothesis testing, effect size, Type I error and Type II error probabilities. In general, some factors need to be determined in order to calculate the appropriate minimum sample size that can be used in studies with power analysis.

There are factors that need to be considered in calculating the appropriate sample size, and each of these factors affects the sample size independently. In order to estimate the sample size, researchers need to determine (1) the statistical analysis to be applied (2) the power of the study (3) the significance level and (5) the effect size (Althubaiti, A. 2023).

When the results obtained in a given sample are used to make inferences about a society, four results emerge (Table 1). As can be seen from the table, there are two types of errors that can be made when testing hypotheses. The first type of error is the probability of a Type I error, which indicates the probability of rejecting the H_0 hypothesis when it is actually true, and is expressed as alpha (significance level). The probability of making a Type I error is partly a standard value used in testing the hypothesis (sometimes called α error). Alpha is usually considered as 0.05 or 0.01. As the alpha value decreases, the sample size increases. The second type of error is the probability of a Type II error, which indicates the probability of accepting the H_0 hypothesis when it is actually false, and is expressed as beta. Statistical power analysis deals with Type II error (the probability of making a Type II error is β, power: $1-\beta$). In other words, power is the probability of avoiding a Type II error.

Table 1. Hypothesis Test Result

Result of Hypothesis Test	True State	
	H_0 True	H_0 False
H_0 Acceptance	1 - α Correct Decision	β (Type II Error)
H_0 Rejected	α (Type I Error)	1 - β Correct Decision (Power of the Test)

Effect size is a critical concept for both interpreting research results and planning sample size (power analysis) and is an objective measure. It is a statistical measure that expresses the magnitude of the difference or relationship between groups in a study. In other words, it shows how important a statistically "significant" result is in practice. In short, it answers the question, "There is a difference, but how big is this difference? Is it important?" (Aberson, C. L., 2019).

If the researcher cannot answer the question of "how much of a difference should be considered clinically significant?", it can be obtained from studies in the literature or a pilot study can be conducted. For cases where effect sizes cannot be determined, it can be determined by using effect sizes categorized as small, medium and large, which were suggested by Cohen and developed for different hypothesis tests (Cohen, 1988).

The smallest effect that can be detected statistically provides information about the smallest effect size that will be statistically significant when observed, given a certain alpha level and sample size (Cook, J., (2014).

3. Types of Power Analysis

- **Theoretical Power Analysis (A Priori Power Analysis):** It is used to determine the sample size required to reach the targeted power level before starting the research. It is the analysis performed to determine whether the statistical test has sufficient power before starting a research (Faul et al., 2007). Thanks to this analysis, a certain effect size, significance level (alpha) and statistical power (usually 80% or 90%) is targeted and the required sample size is calculated. Thus, it is predicted whether the study has the capacity to statistically detect a difference or relationship that actually exists.

- **Experimental Power Analysis (Post Hoc Power Analysis):** After the research is completed, the analysis is done to calculate the statistical power of the test according to the sample size and results**.** In other words, the probability of the test actually

detecting a difference or relationship is evaluated according to the effect size, sample size and significance level found in the study. However, its interpretation requires caution because low power can give meaningless results.

- **Sensitivity Power Analysis:** Calculates the smallest effect size that can be detected with a given sample size. It is a type of power analysis where the sample size is fixed and the minimum detectable effect size is determined. This analysis is used to evaluate how small a difference the sample size will be enough to detect. Generally, researchers conduct this type of analysis to discover the smallest difference they want to see. This is especially important to determine when starting a new study, especially if there are limited resources. This is especially useful in studies with limited sample sizes to understand which differences can be reliably detected. (Lakens, D. 2022).
- **Compromise Power Analysis:** It aims to determine the most appropriate sample size under certain constraints by optimizing the α and β values together (Faul et al., 2007). If the sample size is fixed, both the Type I error (α) and Type II error (β) rates are determined together. It is generally used when the sample cannot be increased due to ethical or practical reasons (clinical studies, rare patient groups, expensive tests, etc. if there are limited data sources). Thus, it allows more realistic decisions to be made with a limited sample and allows for conscious risk distribution. (Erdfelder, E., 1996).
- **Criterion Analysis:** It is applied after the research is done. It is an alternative to experimental power analysis. α ;1-β is a function of the effect size and the number of observations (n). It is applied when β is more important than α, i.e. when we want to minimize the Type II error. Researchers use it to determine the alpha level compatible with β =0.05 (Faul et al., 2007).

A summary of the power analysis types is given in Table 2.

Table 2 : Summary of Power Analysis Types

Type of Power Analysis	When It Is Used	Purpose
A Priori (Theoretical)	Before conducting the study	To determine required sample size for a desired power level
Post Hoc (Empirical)	After the study is completed	To assess actual power given sample size and effect size
Sensitivity Analysis	When sample size is fixed	To determine the smallest detectable effect size
Compromise Analysis	When both α and β need adjustment under constraints	To find optimal α and β values given limited sample resources
Criterion Analysis	After data collection, when minimizing Type II error is key	To determine the α level corresponding to a fixed β (usually 0.05)

4. Conclusion and Recommendations

Sample size calculation and power analysis are fundamental steps that should not be overlooked in research planning. It is important for researchers to manage this process consciously in terms of both scientific validity and resource efficiency. Therefore, calculating the sample size is important to establish a balance between risk and benefit. Researchers should not focus on producing large sample sizes. Instead, the focus should be on selecting an appropriately sized sample that has sufficient power for the statistical test to detect true positives, comprehensively reporting analysis techniques, and interpreting the results in terms of p-values, effect size, and confidence intervals.

This study discusses the importance of sample size calculation in scientific research and the basic components and types of statistical power analysis. Sample size calculations made during the planning phase of the research process play a critical role not only in terms of statistical significance, but also in terms of scientific validity, ethical compliance, and effective use of resources. Appropriate sample size is an indispensable element for a study to reveal real effects and generalizability of results.

Power analysis ensures the statistical adequacy of the study by balancing Type I and Type II error probabilities. In addition, considering the effect size ensures that the research results are not only meaningful but also practically important. In this context, it is recommended that researchers perform an A priori power analysis before starting the study, evaluate post hoc analyses after the data obtained, and consider compromising approaches in sample limitations.

Power analysis should be considered a mandatory step before every study, effect size should not be ignored, conscious and balanced decisions should be made by preferring alternative methods such as compromising power analysis in limited resource situations, and not only the level of significance but also practical significance should be considered in statistical analyses.

In conclusion, sample size calculations and power analyses are one of the cornerstones of scientific research. Neglecting these calculations can damage the reliability of the research. Therefore, including the power analysis process from the first steps of research planning will ensure that more valid and reliable results are obtained.

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CELLULAR DAMAGE AND THE EFFECT OF SUSPENSION ENVIRONMENT ON BLOOD FLUIDITY

ABSTRACT

Purpose: Blood is a vital tissue for the continuation of life in vertebrates. Blood is a tissue containing blood cells in liquid medium called plasma, which circulates throughout the body within the vascular system filled by the pumping power of the heart. The fluidity of this tissue depends primarily on erythrocytes, the properties of plasma, and the relationship between these two. In particular, the physical properties of erythrocytes can be decisive here. Accordingly, the fluidity of blood is affected by the viscosity of plasma, the hematocrit value of blood, and the rheological properties of erythrocytes. The aim of this study was to compare the sedimentation rates of blood samples prepared by changing the cellular properties of erythrocytes and plasma composition with the viscosity of whole blood.

Materials and Methods: Venous samples taken from adult male volunteers were divided into four groups as control, Glutaraldehyde, $Dextran_{500}$ and isotonic phosphate buffer. After the hematocrit value of all blood samples was adjusted to 0.4 l/l, their sedimentation was measured by the Westergren method and their viscosity was measured by a rotational viscometer with a cone-plate type measuring system at a shear rate of 1500 s^{-1} at 37 ˚C.

Results: As a result of measurements made with samples prepared by modifying two different approaches (plasma composition and cellular properties of erythrocytes), sedimentation rate and whole blood viscosity were found to be significant between the groups compared to the control after change of suspension medium or cellular damage ($p<0.05$).

Conclusion: Since plasma acts as a suspension medium for cellular elements in blood, a change in its fluidity and/or changes in the deformability of erythrocytes are directly reflected in blood viscosity. As a result; in our study, modification of the cellular properties of erythrocytes and/or the suspension medium in which these cells are located causes changes in the physical properties of blood, which was revealed by viscosity and sedimentation measurements.

Keywords: Erythrocyte; plasma; viscosity; sedimentation; fluidity

HÜCRESEL HASAR VE SÜSPANSİYON ORTAMININ KANIN AKIŞKANLIĞINA ETKİSİ

ÖZET

Amaç: Kan, omurgalı canlılarda canlılığın devamı için hayati öneme sahip bir dokudur. Kan, kalbin pompa gücü sayesinde içini doldurduğu damar sistemi içinde tüm vücudu dolaşan, plazma adı verilen sıvı ortam içinde kan hücrelerinin bulunduğu bir dokudur. Bu dokunun akışkanlığı, öncelikle eritrositlere, plazmanın özelliklerine ve bu ikisinin birbiriyle olan ilişkisine bağlıdır. Özellikle de eritrositlerin fiziksel özellikleri burada belirleyici olabilmektedir. Buna göre, kanın akışkanlığı; plazmanın viskozitesi, kanın hematokrit değeri ve eritrositlerin reolojik özelliklerinden etkilenir. Bu çalışmada eritrositlerin hücresel özelliklerini ve plazma bileşimini değiştirerek hazırlanan kan örneklerinin sedimentasyon hızlarıyla tam kan viskozitelerinin karşılaştırması amaçlanmıştır.

Materyal ve Yöntem: Yetişkin erkek gönüllülerden alınan venöz örnekleri kontrol, Glutaraldehid (GA), $Dextran_{500}$ ve izotonik fosfat tamponu (PBS) olmak üzere dört gruba ayrıldı. Bütün kan örneklerinin hematokrit değeri 0.4 l/l olacak şekilde ayarlandıktan sonra, Westergren yöntemiyle sedimentasyonları, koni-plak tipi ölçüm sistemine sahip bir rotasyonel viskozimetre ile viskoziteleri $1500s^{-1}$ kayma hızında 37 ˚C'de ölçülmüştür.

Bulgular: İki farklı yaklaşımla (plazma bileşimini ve eritrositlerin hücresel özelliklerini) modifiye ederek hazırlanan örneklerle yapılan ölçümler sonucunda süspansiyon ortamının değişmesi veya hücresel hasar sonrasında sedimentasyon hızı ve tam kan viskoziteleri kontrole göre gruplar arasında anlamlı bulunmuştur ($p<0.05$).

Sonuç: Plazma, kandaki hücresel elemanlariçin süspansiyon ortamı olarak görev yaptığından, akışkanlığındaki bir değişiklik ve/veya eritrositlerin şekil değiştirme yeteneklerindeki (deformabilite) değişimler doğrudan kan viskozitesine yansır. Sonuç olark; yaptığımız çalışmada eritrositlerin hücresel özelliklerinin (GA) ve/veya bu hücrelerin bulundukları süspansiyon ortamının (Dekstran-PBS) modifikasyonu kanın fiziksel özelliklerinin değişmesine neden olmakta, bu da viskozite ve sedimantasyon ölçümleri ile ortaya konmuştur.

Anahtar Kelimeler: Eritrosit; plazma; viskozite; sedimentasyon; akışkanlık

GİRİŞ

Kan, çok hücreli organizmalarda yaşamın devamı için hayati önem taşıyan bir dokudur. Eritrosit, lökosit, trombosit gibi kan hücrelerinin plazma adı verilen sıvı bir ortamda süspansiyon halinde dağıldığı, damar sisteminin içini dolduran ve kalbin pompalama gücü sayesinde bu sistemde tüm vücudu dolaşabilen dokuya kan denir. Eritrositler, hemoglobin içeren ve oksijeni akciğerlerden vücut dokularına taşıyan, omurgalı canlıların kanında bulunan özelleşmiş hücrelerdir. Özellikle memeli eritrositleri, olgunlaşma süreçlerinin sonunda basit bir hücre haline gelirler ve hemoglobin içerikleri kuru ağırlıklarının %90'ına yaklaştığında, yalnızca oksijen taşımaya özgü yapılar olarak mükemmel hale gelirler. Bu oldukça uzmanlaşmış sürecin bir sonucu olarak, eritrositler oksijen taşıma işlevleri için hemoglobine daha fazla yer açmak adına çekirdeklerini ve organellerini feda etmektedirler. Bu fedakârlık ayrıca eritrositlerin mekanik özelliklerini de etkilemiş ve bazı yerlerde çaplarının üçte birinden daha küçük çaplara sahip olan kılcal damar yatağından geçebilmek için şekil değiştirmelerine izin vermiştir[1,2]. Kan dokusu akışkanlığı öncelikle eritrosit kütlesine, plazmanın özelliklerine ve bu ikisi arasındaki ilişkiye bağlı olarak değişir[3-5]. Fakat eritrositlerin fiziksel özellikleri bu sistemde belirleyici bir rol oynamaktadır. Kan dokusunun vasküler sistemdeki hareketi her şeyden önce kendi özelliklerine ve akışkanlığına bağlıdır. Buna göre kanın akışkanlığı; plazma viskozitesi, hematokrit değeri ve kan hücrelerinin reolojik özelliklerinden etkilenir. Eritrositlerin deformabilite yeteneği ve geri dönüşümlü agregasyon eğilimleri (agregasyon), farklı koşullar altında kanın akışkanlığını belirlemede önemli rol oynar[1].

Yüksek akım hızı koşullarında, eritrosit deformabilitesi kan viskozitesini belirleyen ana faktörler arasındadır[6]. Akım yavaşlarsa, hücreler üzerinde etkili olan kuvvetler küçülür ve kümelenme eğilimi belirginleşir. Eritrosit agregatlarının oluşumu bu koşullar altında viskoziteyi artırır[7]. Bu kümeler eritrosit süspansiyonu (kan) akmaya başladığında (hücreler üzerinde etkili olan akım kuvvetleri tarafından) parçalanır. Başka bir deyişle, eritrosit agregasyonu geri dönüşümlüdür. Eritrosit agregasyonu plazmanın ve eritrositlerin hücresel özelliklerindeki değişikliklerden etkilenmektedir. Özellikle plazma bileşenleri arasında fibrinojen konsantrasyonu eritrosit agregasyonunu etkileyen en önemli faktörlerden biridir[8]. Fibrinojenin yanı sıra diğer akut faz reaktanları, plazma globulin değişiklikleri, ozmolarite ve pH'daki değişimler ve hematokrit değerindeki artış eritrosit agregasyonunu etkiler[8,9]. Eritrosit özellikleri, şekil değiştirilebilmesi, eritrosit morfolojisi ve yüzey yükü farklılıkları ve IgG'nin membrana bağlanması gibi hücresel özelliklerin eritrositlerin agregasyon eğilimlerini önemli ölçüde değiştirebileceği deneysel kanıtlarla bulunmuştur[10]. İn vitro ortamda deneysel olarak eritrosit agregasyonunu belirlemek için çeşitli yaklaşımlar ve yöntemler kullanılmaktadır. Bu yöntemler arasında eritrosit süspansiyonlarından ışık geçirgenliği veya ışık yansımasının ölçülmesi[11,12], eritrosit agregasyonunun mikroskobik endeksleri[13], eritrosit sedimantasyon hızı, düşük kayma viskozitesi[14] ve eritrosit süspansiyonlarının elektriksel ölçümleri[15,16] yer almaktadır. Bu çalışmada eritrosit agregasyonunu, iki farklı yaklaşımla (plazma bileşimini değiştirerek ve eritrositlerin hücresel özelliklerini değiştirilerek) modifiye ederek hazırlanan bu örneklerin sedimantasyon hızlarıyla viskozitelerinin karşılaştırılması amaçlanmaktadır.

MATERYAL VE YÖNTEM

Kan Örnekleri ve Eritrosit Süspansiyonunun Hazırlanması

Çalışmada, 18-25 yaş aralığındaki erkek gönüllülerden venöz kan örnekleri (20 ml) alınmıştır. Geçmişinde herhangi bir sağlık sorunu olan donörlerin olmamasına dikkat edilmiştir. Örnek toplanmasından önceki 24 saat içinde herhangi bir ilaç kullanmış olanlar donör olarak kullanılmamamıştır. Kan örnekleri, antikoagülan olarak sodyum heparin (15 IU/ml) içeren enjektörlere ön dirsek damarlarından alınmıştır. Örnekler kan toplanmasından hemen sonra değerlendirimiş ve her örnek üzerindeki çalışmalar kan toplanmasından yaklaşık dört saat sonra tamamlanmıştır.

Gönüllülerden alınan kan örnekleri, plazma ve eritrosit paketlerini ayırmak için 5 dakika boyunca 1400 g'de santrifüj edilmiştir. Eritrosit paketi iki kez izotonik fosfat tamponu (PBS) ile yıkandı ve bir kısmı 0.4 l/l hematokrit değerine kadar otolog plazmada (tam kan) süspanse edildi. Yıkanmış eritrosit paketinin bir kısmı PBS ile 0.4 l/l'lik hematokrit değerine kadar süspanse edildi. Ayrıca, plazmaya %1 konsantrasyonda dekstran 500 (MW: 500 kD, D5251; Sigma Chemical Co., St. Louis, MO, ABD) eklendikten sonra, PBS ile iki kez yıkanan eritrosit paketi bu plazmada 0,4 l/l hematokrit değerine kadar süspanse edilmiştir. PBS ile yıkanmış eritrosit paketi, 0,05 l/l hematokrit değerine ulaşana kadar PBS'de yeniden süspanse edildi. Glutaraldehit (GA, Merck, Darmstadt, Almanya) ile oda sıcaklığında (22°C) 30 dakika boyunca %0,003'lük son konsantrasyonda inkübe edildi. İnkübasyondan sonra, örnekler üstteki sıvıyı uzaklaştırmak için 5 dakika boyunca 1400 g'de santrifüj edildi. Eritrosit paketi, PBS ile iki kez yıkanacak ve 0,4 l/l hematokrit değerine ulaşana kadar otolog plazmada süspanse edilmiştir.

Ölçümü Yapılacak Parametreler

Eritrosit Sedimantasyon Hızı (Westergren Yöntemi)

Hematokriti ayarlanmış (%10) kan örnekleri, %3 trisodyum sitrat ile 1/5 (1 hacim sitrat, 4 hacim kan) seyreltilerek antikoagüle edilmiştir. 300 mm uzunluğunda ve 2.55 mm iç çaplı bir Westergren tüpü kanla doldurulmuş ve dikey olarak yerleştirilmiştir. Kırmızı kan hücreleri olmayan plazma kolonunun yüksekliği 1 saat sonra okundu. Bu çalışma için ticari olarak temin edilebilen tek kullanımlık Westergren tüpleri kullanılmıştır.

Plazma ve Tam Kan Viskozitesi

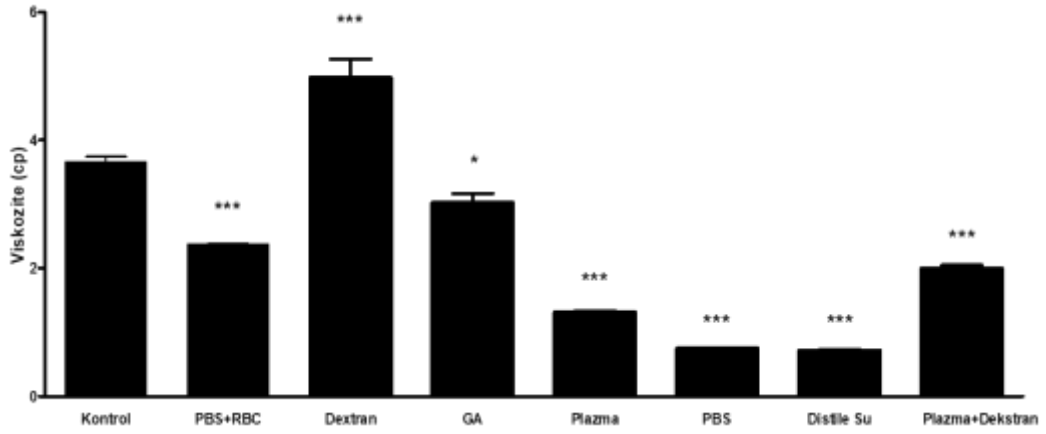
Hazırlanan eritrosit süspansiyonlarının viskozitesi, koni plaka tipi ölçüm sistemine sahip bir viskozimetre (Brookfield Engineering Labs., Middleboro, MA, ABD) kullanılarak 37 °C'de 487,5 ve 1500 s-1 kayma hızlarında ölçülmüştür. Plazma viskozitesi 1500 s-1 kayma hızında ve kan örnekleri 487,5 s^{-1}'de belirlenmiştir. Her örnek hazırlama işleminden sonra, 40X-100X objektif kullanılarak bir ışık mikroskobu ile görüntüleme yapıldı ve kaydedilmiştir.

İstatistiksel Analiz

Veriler ortalama ± standart hata olarak gösterilmiş $p<0.05$ değeri istatistiksel olarak anlamlı kabul edilmiştir. Değişkenlerin gruplar arası karşılaştırmalarında tek yönlü varyans analizi kullanılmıştır. İstatistiksel olarak önemli bulunan değişkenler için grupların ikili karşılaştırmalarında Bonferroni's post hoc testi kullanılmıştır.

BULGULAR

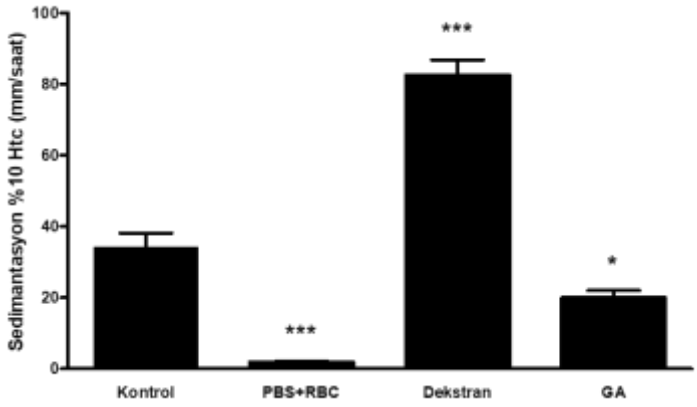
Plazma kandaki hücresel yapılar için bir süspansiyon ortamı görevi gördüğünden, akışkanlığındaki bir değişiklik doğrudan kan viskozitesine yansır. Normal plazma viskozitesi 37 °C'de 1.10 ile 1.35 centipoise (cp) arasında bir değere sahiptir. Suyun viskozite değeri ise 1 cp olarak kabul edilir. Yaptığımız ölçümler sonucunda distile su ve PBS viskozite değeri yaklaşık olarak 1 cp, plazmanın ise 1.5 cp yakın değerlerde ölçülmüştür (Şekil.1). Bu sonuçlar literatür bilgisi ile uyumlu bulunmuştur. Benzer şekilde %40 hematokrite sahip PBS+RBC grrubunun viskozitesi kontrol grubuna göre anlamlı şekilde azalmıştır (Şekil.1) Eritrositlerin düşük konsantrasyonda (%0.003) Glutaraldehid ile 30 dakika inkübasyonu eritrosit deformabilitesini azaltır. Bu muameleden sonra da eritrosit agregasyonunun etkilendiği tahmin edilmektedir. Şekil 1'de GA grubunda viskozite değerinin kontrole göre hafifte olsa azaldığı ve bu azalmanın anlamlı olduğu bulunmuştur.



Şekil.1. Hazırlanan kan örnekleri ve süsüpansiyon ortamlarının viskozite değerleri.

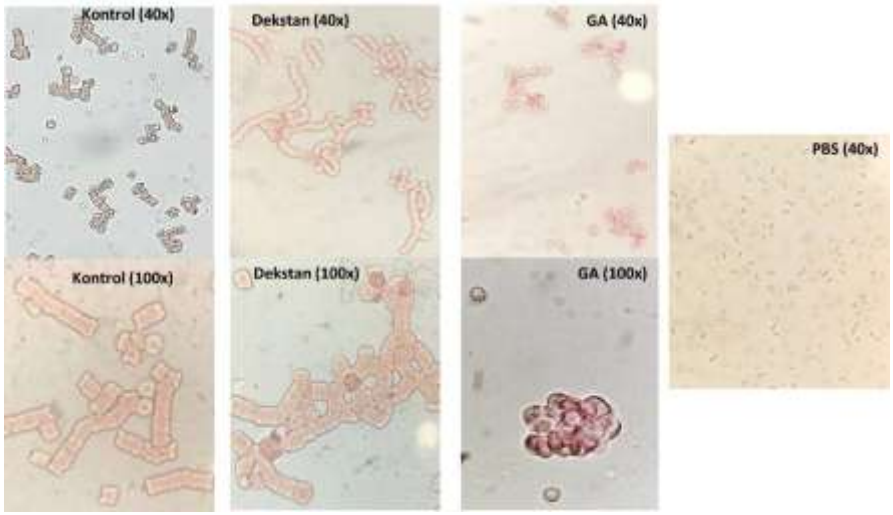
"Kontrol (tam kan)"dan fark; *****: $p<0.05$; *******: $p<0.001$. (cp: centi poise)

Hücreler yıkanıp protein ya da polimer içermeyen tamponlarda tekrar süspanse edilirlerse, eritrosit agregasyonu ortadan kalkar. Yani bu hücreler basit tuz çözeltileri (PBS gibi) içinde süspansiyon haline getirilmeleri durumunda rulo formasyonu gözlenmez. Büyük molekül ağırlığına sahip bir polimer ($Dekstran_{500}$) plazmanın içine eklendiği zaman kontrolden daha büyük bir viskozite değerine sahip olduğu gözlenmektedir (Şekil.1).



Şekil.2. Hazırlanan kan örneklerine ait sedimantasyon değerleri. "Kontrol (tam kan)"dan fark; *****: $p<0.05$; *******: $p<0.001$. (mm/saat)

Birçok hastalıkta tanıya yardımcı bir inceleme yöntemi olan eritrosit sedimentasyon hızı (ESH), oldukça yaygın kullanılan, basit ancak duyarlılığı düşük bir testtir. Kan dik bir tüpe alındığında, eritrositler dibe doğru çökmeye meyillidir. Belirli bir süre içerisinde eritrositlerin çökme mesafesinin ölçümü ESH olarak adlandırılır. ESH agregasyonun derecesinin belirlenmesinde kullanılmaktadır. Çalışmamızda hazırlamış olduğumuz kan örneklerinden PBS+RBC grubunda beklendiği gibi neredeyse eritrosit sedimentasyon hızı sıfıra yakın bir değerde ölçülmüş, GA grubunun kontrole göre azaldığı, dekstran grubunda ise kontrole göre iki katından fazla arttığı ve bu değerlerin istatistiksel olarak anlamlı olduğu bulunmuştur (Şekil.2). Yapılan ölçümler sonucu süspansiyon ortamı değiştirilerek (hücre dışı) veya GA (hücresel hasar) uygulamasından sonra ölçülen sedimantasyon ve tam kan viskoziteleri kontrole göre tüm gruplarda istatistiksel olarak anlamlı bulunmuştur.



Şekil.3. Hazırlanan kan örneklerine ait 40x ve 100x ışık mikroskop görüntüleri

Ölçümü yapılan kan örneklerininden hazırlanan prepatlardan ışık mikroskobu altında elde edilen görüntülerde de hücrelerin davranışları (rulo formasyonu) net bir şekilde izlenmiştir (Şekil.3). Normal bikonkav şekilden aşırı değişiklikler ve/veya hücresel deformabilite

kabiliyetinin azalması (GA grubu), agregasyonu azaltacaktır. Mikroskopta yapılan incelemelerin ve kaydedilen görüntülerin de diğer sonuçlarımızı desteklediği gözlenmiştir.

SONUÇ

Kırmızı kan hücresinin zarının moleküler organizasyonu, hücrenin morfolojisini ve işlevini kontrol eder. Bu nedenle dolaşımdaki kırmızı kan hücresi homeostazının ana belirleyicisidir. Membran organizasyonunun rolü kırmızı kan hücresi deformabilitesi ve agregasyonunda belirgin bir şekilde rol oynar. Ancak, aynı membran özelliği tarafından kontrol edilip edilmedikleri ve eğer öyleyse, ne ölçüde kontrol edildikleri konusunda çok az bilgi vardır. Kırmızı kan hücresi agregasyonunu belirleyen faktörler hücre dışı ve hücresel faktörler olarak iki gruba ayrılabilir. Hücre dışı faktörler şunlardır: akım, plazma proteinlerinin konsantrasyonu (fibrinojen, immünoglobulinler, albümin vb.), diğer makromoleküllerin varlığı (örneğin dekstranlar, polietilen glikol (PEG) vb.), pH değeri, ozmotik basınç. Hücresel faktörler şunlardır: glikokaliks, kırmızı kan hücresi şekli ve şekil değiştirilebilirliği. Kırmızı kan hücrelerinin glutaraldehit ile muamele edilmesi, hücre deformabilitesinde azalma ile birlikte membran viskoelastik ve sitosol viskoz özelliklerinin büyük ölçüde değişmesiyle intra ve intermoleküler çapraz bağlama membranı ve sitosol bileşenleriyle sonuçlanır. Kırmızı kan hücresi deformabilitesinin azalması, bitişik hücreler arasında yakın temasların oluşumunu engeller.

Plazma viskozitesi, tam kan viskozitesini etkileyen önemli bir faktördür ve protein ve lipit konsantrasyonuyla doğrudan ilişkilidir. Plazma viskozitesindeki değişiklikler hem akut hem de kronik durumlarda meydana gelebilir. Birkaç faktör tam kan viskozitesini etkiler. Bunlar arasında vasküler yatağın özellikleri, tam kan, kırmızı kan hücrelerinin intrinsik özellikleri ve çeşitli plazma faktörleri (protein vb.) bulunur. Kan dokusu, organizmada homeostatik dengeyi ve hücrelerin hayatta kalmasını sağlamak için sürekli hareket halinde olmalıdır. Kan akım hızının yüksek olduğu koşullarda (arter), eritrosit deformabilitesi kan viskozitesini belirleyen ana faktördür. Kan akım hızı yavaşladığında (ven), hücreler üzerinde etkili olan kuvvetler azalır ve kümeleşme (agregasyon/rulo formasyonu) eğilimi ön plana çıkar. Eritrosit agregatlarının oluşumu bu koşullar altında viskoziteyi artırır. Sonuç olarak; eritrositlerin hücresel özelliklerinin ve/veya bu hücrelerin bulundukları süspansiyon ortamının değiştirilmesi kanın viskozite, agregasyon, akışkanlık gibi fiziksel özelliklerinin değişmesine neden olmaktadır.

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COMPARISON OF ANTIOXIDANT ACTIVITIES OF ORGANIC TOMATO (*SOLANUM LYCOPERSICUM* L.) AND RED PEPPER (*CAPSICUM ANNUUM* L.) EXTRACTS AGAINST H_2O_2 TOXICITY

ABSTRACT

In our study, the antioxidant effects of methanolic extracts of organically grown tomatoes and red peppers against H_2O_2 toxicity on *Saccharomyces cerevisiae* were compared. Malondialdehyde (MDA) analysis from these antioxidant activities was performed on a Shimadzu (Kyoto Japan) brand HPLC device. The analyses of antioxidant enzymes Superoxide Dismutase (SOD), Catalase (CAT) and Glutathione-S-transferase (GST) were determined by reading them at 480 nm, 240 nm and 340 nm, respectively, with a spectrophotometer device.

At the end of the study, a decrease was detected in MDA values in H_2O_2+extracts compared to both control and H_2O_2 in both extract groups ($p<0.01$, $p<0.001$). While statistically insignificant partial changes were observed in GST enzyme values, CAT enzyme values increased at varying rates in all groups except D1+D group compared to control ($p>0.05$, $p<0.05$, $p<0.01$, $p<0.001$), and when the groups given extract with H_2O_2 were compared, increases were observed at varying rates in both tomato and red pepper groups. While SOD levels showed values close to control in all groups compared to the control group ($p>0.05$), a partial increase was observed in tomato groups compared to the H_2O_2 group ($p>0.05$, $p<0.05$, $p<0.01$). While a decrease was observed in the SOD inhibition level in all groups except D2-KB, D3-KB and D4-KB groups compared to the control ($p>0.05$, $p<0.05$), it decreased in varying amounts compared to H_2O_2 except for D2-KB+H_2O_2 and D3-KB+H_2O_2 groups. ($p>0.05$, $p<0.05$, $p<0.01$).

As a result, we determined that both tomato and red pepper plant extracts added to S cerevisiae nutrient medium developed a defense mechanism against hydrogen peroxide radicals in the groups added, however, some samples collected from different regions showed slight differences in antioxidant activity. The decrease in MDA values in the extract groups and the increase in CAT and SOD enzymes mostly support this antioxidant effect. We hope that our study will be useful for other studies, both in isolating the compounds of both plants that will contribute to human nutrition and using them as food additives, and in understanding the importance of encouraging the consumption of these products naturally ($p<0.01$, $p<0.001$).

Keywords: *Solanum lycopersicum* L., *Capsicum annuum* L., Antioxidant activity

H_2O_2 TOKSİSİTESİNE KARŞI ORGANİK DOMATES (*SOLANUM LYCOPERSICUM* L.) VE KIRMIZIBİBER (*CAPSICUM ANNUUM* L.) EXTRAKTLARININ ANTİOKSİDAN AKTİVİTELERİNİN KARŞILAŞTIRILMASI

ÖZET

Çalışmamızda, organik olarak yetiştirilen domates ve kırmızıbiberin metanolik ekstraktlarının *Saccharomyces cerevisiae* L. üzerinde oluşturulan H_2O_2 toksisitesine karşı antioksidan etkileri karşılaştırıldı. Bu antioksidan aktivitelerden malondialdehyde (MDA) analizi Shimadzu (Kyoto Japan) marka HPLC cihazında yapıldı. Antioksidan enzimler Superoksit Dismutaz (SOD), Katalaz (CAT) ve Glutation-S-transferaz (GST)'in analizleri spektrofotometre cihazı ile sırasıyla 480 nm, 240 nm ve 340 nm'e karşı okunarak tespit edildi.

Çalışmanın sonunda hem kontrole kıyasla ekstrelerde hem de H_2O_2'e kıyasla H_2O_2+ekstrelerde MDA değerlerinde her iki ekstre grubunda da azalma tespit edildi ($p<0.01$, $p<0.001$). GST enzim değerlerinde istatiksel olarak anlamlı olmayan kısmi değişiklikler gözlenirken, CAT enzim değerlerinin kontrole kıyasla D1+D grubu dışında diğer bütün gruplarda değişen oranlarda artış ($p>0.05$, $p<0.05$, $p<0.01$, $p<0.001$), H_2O_2 ile ekstrakt verilen gruplar karşılaştırıldığında ise hem domates hem de kırmızıbiber gruplarında değişen oranlarda artış gözlenmiştir ($p<0.01$, $p<0.001$). SOD düzeyi kontrol grubuna göre bütün gruplarda kontrole yakın değerler gösterirken ($p>0.05$), H_2O_2 grubuyla karşılaştırıldığında ise domates gruplarında kısmen de olsa artış gözlenmiştir ($p>0.05$, $p<0.05$, $p<0.01$). Kontrole kıyasla SOD inhibisyon düzeyinde D2-KB, D3-KB ve D4-KB grupları hariç diğer gruplarda azalma gözlenirken ($p>0.05$, $p<0.05$), H_2O_2'e kıyasla ise D2-KB+H_2O_2 ve D3-KB+H_2O_2 grupları dışında değişen oranlarda azalma göstermiştir ($p>0.05$, $p<0.05$, $p<0.01$).

Sonuç olarak, *S. cerevisiae* L. besi ortamına eklenen domates ve kırmızıbiber bitkisinin her ikisinin ekstrelerinin eklendiği gruplarda hidrojen peroksit radikaline karşı savunma mekanizması geliştirdiği, bununla birlikte farklı bölgelerden toplanan bazı örneklerin antioksidan aktivitede ufak da olsa farklılıklar gösterdiğini tespit ettik. Ekstre gruplarında MDA değerlerinin azalma göstermesi, CAT ve SOD enzimlerinin çoğunlukla artış göstermesi bu antioksidan etkiyi desteklemektedir. Her iki bitkinin hem insan beslenmesinde katkı sağlayacak bileşiklerinin izole edilip gıda katkı maddesi olarak kullanılması için, hem de doğal olarak bu ürünlerin tüketilmesinin teşvik edilmesinin öneminin anlaşılması için çalışmamızın diğer çalışmalara faydalı olacağını ümit ediyoruz.

Anahtar kelimeler: *Solanum lycopersicum* L., *Capsicum annuum* L., Antioksidan aktivite

GİRİŞ

Oksidatif stres tüm canlıları olumsuz etkileyen bir faktör olmakla birlikte yaşam sürecinde normal fizyolojik şartlarda da meydana gelebildiği için kaçınılmaz bir olaydır. Bitkiler dünya çapında büyümeyi ve üretkenliği olumsuz etkileyen çeşitli abiyotik streslerle sürekli olarak karşı karşıyadır. Bitkiler evrimleri ölçüsünde; belirli streslere tolerans derecesi türden türe farklılık göstermesinin yanısıra, çevresel koşullara uygun şekilde tepki vermek için, dış sinyalleri tanımak için karmaşık mekanizmalar geliştirmiştir. Bitkisel mekanizmalarda bu reaktif oksijen türlerinin aşırı üretimi ise, bitkisel makromoleküllerde ve hücresel yapılarında oksidatif hasara neden olan, bitki büyümesini ve gelişmesini engelleyen veya ölümüne bile neden olabilen abiyotik ve/veya biyotik stresler altında artmaktadır. Çeşitli ROS'lar arasında daha serbest yayılabilen ve diğerlerine göre daha uzun ömürlü olabilen H_2O_2, stres sinyalinin iletim yollarında merkezi bir oyuncu olarak işlev görür. Stresi ileten bu yollar, daha sonra çeşitli abiyotik ve biyotik kaynaklı olabilen stres faktörlerine karşı direnci güçlendiren mekanizmaları aktive de edebilir [1]. Antioksidanlar ise hücrelere zarar veren ROS türlerini indirgeyerek daha düşük toksitititeye sahip ya da toksik olmayan ürünlere dönüştürme yeteneğine sahiptir. Antioksidan mekanizmalar, vücut hücreleri tarafından üretildikleri gibi, gıdalar yoluyla dışarıdan da alınabilmektedir. Gıdalardan (meyve ve sebze) alınan ve serbest radikallere karşı koruyucu özellikleri olan başlıca doğal antioksidanlar; vitaminler (A, C, E), flavonoidler, karotenoidler ve polifenollerdir. Meyve antioksidanlarının dokuları stres ve hastalıklara karşı koruduğu bilinmektedir [2].

Solanum lycopersicum L. 3000’ den fazla türe sahip Solanaceae familyasına mensuptur [3]. Domates (*Solanum lycopersicum* L.), dünyada insan beslenmesinin önemli bir bileşenidir. Karotenoidler (likopen), askorbik asit, potasyum, folat ve fenolik bileşikler dahil olmak üzere doğal antioksidanların ve zengin bir mikro besin kaynağıdır. Rutin, kersetin, naringenin, kalkonaringenin ve kaempferol türevleri gibi flavonoidlerin yanı sıra klorojenik asitler ve ilgili bileşiklerde (hidroksisinnamatlar) ana fenolik bileşikler olarak rapor bildirilmiştir [4]. Bu ikincil metabolitler arasında klorojenik asit, antioksidan, antiinflamatuar, hepatoprotektif, kardiyoprotektif, hipoglisemik, antimikrobiyal ve antiviral ajan gibi çeşitli terapötik roller oynayan önemli ve biyolojik olarak aktif bir diyet polifenolüdür [5]. Ayrıca başka bir çalışmayla domatesin sahip olduğu kuersetinin invivo olarak kalple ilgili önemli faydaları ve anti-inflamatuar, antiagregan ve vazodilatör etkileri sergilerken [6] ve P vitamini olarak da bilinen rutinin antikanserojenik etkiye ve kan damarlarının kırılganlığını azaltma yeteneğine sahip olduğu bildirilmiştir [7].

Capsicum annuum (biber), dünya genelinde bulunabilen, Solanaceae familyasının çift çenekli çiçekli bir bitkisi olup genellikle ılıman bölgelerde yetişir ve çevresel etkilerin çoğuna dayanaklı bir bitkidir. Biber, tropik bölgelerde yayılan çok yıllık çalı formunda bulunmasının yanı sıra yıllık olarak da bulunabilir [8]. Uçucu yağ, vitaminler, lif, proteinler, karotenoidler, kapsaisinoidler, mineral elementler ve yağlı yağlar dahil olmak üzere çeşitli ikincil metabolitler içeren bir bitkidir [9]. Ayrıca, kendi savunması için de besin değeri, aroma, doku, lezzet ve renk bakımından önemli bileşenler içerir. C vitamini özellikle olgun meyvelerinde bulunur [10]. Bunun yanında provitamin A, B1, B2, B3, B6, E ve insan vücudunun oksidatif hasarını önleyen, kardiyovasküler hastalıklardan ve kanserden koruyan antioksidanlar [11] bulundurur. Biber yüksek antioksidan aktiviteye sahip büyük bir polifenol içeriğine sahiptir [10]. Bütün bu bileşikler, hayvanlar ve insanlar üzerindeki farmasötik uygulamaları için tanınmasını arttırmış ve bu uygulamalar gıda ve ilaç idaresi (FDA ve EFSA) tarafından onaylanmaktadır [12]. Kırmızıbiberdeki kapsantin, yağ asitleri ile açillendiği bir formda bulunur ve oksijen içerir ve β-karotenden daha polardır; kapsan'ın

farklı yapıları, ince insan vücudunda farklı fonksiyonel etkiler gösterebilir [13]. Kapsantin bir serbest radikal süpürücü olarak etkilidir [14] anti-tümör aktivite sergiler [15], obezite kaynaklı iltihabı hafifletir [16] ve plazma yüksek yoğunluklu lipoprotein (HDL) kolesterol seviyelerini yükseltir [17].

S. cerevisiae özellikle de ksenobiyotik ve diğer toksik madde etkilerinin incelenmesinde en çok kabul gören ökaryotik hücre modelidir [18]. Çünkü bu hücreler toksik maddelere karşı direnç gösterirler [19]. Maya hücreleri de diğer canlılar gibi gerek doğal olarak ve gerekse insanların yol açtığı diğer etkiler sonucu oluşan stres koşulları altında yaşamak zorunda kaldıklarından ve bunla mücadele etmek için adaptasyon geliştirdikleri, bununla ilgili bir çalışmada ise sıcaklık, oksijen ve besin sınırlanması gibi bazı çevresel faktörlerin değişimine karşı *S. cerevisiae* hücresinin açık bir şekilde etkilenip plazma membranında bazı adaptasyonlar meydana getirdiği ve bu adaptasyonların ise lipit bileşimindeki modifikasyonlara neden olduğu [20], bunun sonucunda, lipid peroksidasyonunun son ürünü olan ve miktarının fazla olması hücresel hasarın bir göstergesi olan MDA [21], hücre düzeyinde metabolize edilerek ya da diffüze olarak diğer hücrelere de zarar vermektedir [22]. Maya hücrelerindeki başlıca antioksidan savunma sistemleri olarak ise süperoksit dismutaz (sitoplazma), katalaz, glutatyon redüktaz enzimleri ile glutatyon, metallotiyonein, poliamin kimyasalları gösterilmiştir [20]. Bu moleküller hücrede normal fizyolojik şartlarda oluşan reaktif oksijen moleküllerini etkisiz hale getirirler.

Bu çalışmada, H_2O_2 ile oksidatif hasar oluşturulmuş *Saccharomyces cerevisae* L. (Ekmek mayası) kültürüne ilave edilen, insanların beslenmesinde çok önemli yeri olan ve normal mevsiminde organik olarak yetiştirilen domates ve kırmızıbiber ekstraktlarının hücre peletlerindeki antioksidan aktiviteler üzerine (MDA, SOD, CAT ve GST) biyokimyasal etkilerinin analizleri yapılarak, domates ve kırmızıbiber ektraktlarının H_2O_2'in oluşturduğu dejeneratif etkiye karşı koruyuculuğunun olup olmadığının anlaşılması amaçlanmıştır. Domates ve kırmızıbiber genellikle her mevsimde bulunmakla birlikte, en faydalı olan dönemin mevsiminde organik olarak yetiştirilmiş olması önemli bir faktördür. Bu dönemde daha yüksek oranda antioksidan moleküller içerebilmektedir. Bu anlamda bu çalışma ile domates ve biber ekstrelerinin içeriklerinin mayada H_2O_2 ile oluşan serbest radikallerin etkilerini azalttığı gösterilirken, bu sonuçların ışığında kronik hastalıkların önlenmesi için beslenme alışkanlıklarının daha fazla meyve, sebze ve tahıl tüketecek şekilde değiştirilmesi yönünde etkin bir yaklaşım sunmaya katkıda bulunmayı amaçlanmıştır.

MATERYAL METOD

Saccharomyces *cereviaiae* L. Kültür Ortamının Hazırlanması

20 g peptone water, 20 g yeast extraktı, 40 g D-Glukoz ve her amino asit karışımından 500 mg artılarak 1 L'lik saf su içerisinde ultrasonik su banyosunda 20 dakika süre ile çözdürülerek, 250 ml'lik şişelere etiketleme yapılarak eşit şekilde aktarıldı. Şişelerin her birine 200 ml besiyeri eklendi. Sonrasında otoklav 121 ^oC'ye programlanıp 15 dakika sterilize edildi. Soğutma işleminden sonra steril olarak 1 ml stok maya hücresi, 100 µL H_2O_2 eklendi. İnkübatör 30 °C' ayarlanıp elde edilen karışım 72 saat boyunca inkübasyona bırakıldı.

Bitkisel Materyallerin Toplanması

Bu çalışmada, yaz mevsimi döneminde organik olarak yetiştirilen domates ve kırmızıbiber örnekleri Elazığ'ın 4 farklı bölgesinden toplandı. Bu bölgeler Baskil (D1), Cip (D2),

Doğukent (D3) ve Sivrice (D4) olarak belirlendi. Ve örnek materyaller bu bölgelerden ayrı ayrı taze olarak toplanıp deneylerin yapılacağı laboratuvara getirildi.

Bitki Ekstraktların Hazırlanması

Domates ve kırmızıbiber örneklerinden 100'er g tartılarak 250 mL %85'lik metanol ile blender yardımıyla homojenize edilip, filtre kâğıdı yardımıyla filtre edildi. 50 °C'deki döner buharlaştırıcı ile çözücü madde uçurularak uzaklaştırıldı. Geride kalan kısım dimetil sülfoksit (DMSO) içinde çözünerek 50 mL hacime getirildi. Bu karışımdan 1 mL alınarak *S. cerevisiae* kültürlerine ilave edilerek 30 C'de inkübasyona bırakıldı. Bu süre sonunda hücre pelletleri toplanarak biyokimyasal işlemler uygulandı ve sonuçlar ortalama±SEM şeklinde ifade edildi.

Besiyeri ortamı hazırlandıktan sonra gruplar aşağıdaki şekilde oluşturuldu:

1-Kontrol Grubu: Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su, 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı olacak şekilde hazırlandı.

2-Hidrojen Peroksit Grubu (H_2O_2): Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı hazırlandı. Ayrıca inkübasyon başlangıcında 100 µL H_2O_2 çözeltisi eklendi.

3-Domates Ekstraktı Verilen Gruplar: Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su içinde 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı kullanıldı ve besi ortamına 1 mL domates ekstraktı ilave edildi.

4- Kırmızıbiber Ekstraktı Verilen Gruplar: Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su içinde 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı kullanıldı ve besi ortamına 1 mL kırmızıbiber ekstraktı ilave edildi.

5- Domates Ekstraktı+H_2O_2 Verilen Gruplar: Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su içinde 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı kullanıldı ve besi ortamına 1 mL domates ekstraktı ile inkübasyonun başlangıcında 100 µL H_2O_2 çözeltisi eklendi.

6-Kırmızıbiber Ekstraktı+H_2O_2 Verilen Gruplar: Bu gruptaki *S. cerevisiae* hücreleri için, 200 mL saf su içinde 2 g maya ekstraktı, 4 g baktopepton ve 4 g glukoz içeren besiyeri ortamı kullanıldı ve besi ortamına 1 mL kırmızıbiber ekstraktı ile inkübasyonun başlangıcında 100 µL H_2O_2 çözeltisi eklendi.

Kültür ortamına steril şartlarda maya hücresi aşılanmasından sonra, kültürler 30 °C'de 72 saat inkübasyona bırakıldı. Bu sürenin sonunda kültürler laboratuvar şartlarında 600 nm'de hücre yoğunlukları ölçüldükten sonra, 6000 rpm'de 5 dakika süreyle + 4 ° C'de santrifüj edilip hücreler toplandı. Hücreler pellet olarak toplandıktan sonra yaş ağırlıkları belirlendi. Hücre pelletleri, 20 mM Tris HCl-baz (pH= 7.4) ve 20 mM ETDA karışımı ile homojenize edilip santrifüj edildikten sonra süpernatant kısmı ile antioksidan enzimler ve MDA ölçümleri yapıldı.

Lipid peroksidasyon (MDA) Miktarlarının HPLC cihazı ile Tayini

MDA değerlerinin belirlenmesi için 1mL alınan süpernatant kısım kullanıldı. Bunun üzerine %10'luk perklorik asit (PCA) eklenip proteinlerin çökmesi sağlandı. Elde edieln bu karışım

5000 rpm'de 5 dakika santrifüj edilerek, supernatant kısım otosampler viallere alınarak Shimadzu (Kyoto Japan) marka HPLC cihazında analizler yapıldı. Mobil faz için 30 mmol KH_2PO_4 ve metanol karışımı (%82-%18, H_3PO_4 ile pH=3.6) oluşturuldu. ODS-3 kolonu (150 mm x 4.6, 5 µm) analiz için kullanıldı. Mobil fazın akış hızı 1,0 mL/dk olarak ve DAD dedektörünün dalga boyu ise 244 nm olarak ayarlandı [23].

Antioksidan Enzim Aktivitelerinin Tayini

Superoksit Dismutaz (SOD) Enzim Aktivitesi

SOD enzim tayini adenokroma oksidasyonunu inhibe eden, epinefrin-ksantin ve ksantinoksidaz sisteminden oluşan bir metodla yapıldı. Örneklerin inceleneceği tüplere sırasıyla 0.05 M potasyum fosfat tamponu (pH 7.8), 0.1 mM EDTA, epinefrin, ksantin ve örnek materyal eklenip, son olarak da ksantin oksidaz ilave edilerek reaksiyon başlatıldı. Bu olaylar sonunda oluşan absorbanlar spektroda 480 nm'e karşı okundu [24].

Katalaz (CAT) Enzim Aktivitesi

Katalaz enzim aktivitesinin analizi için ise hidrojen peroksitin 240 nm dalga boyundaki absorbans değerinin ölçülmesine dayanan UV metodu kullanıldı. Deney tüplerine 50 µl örnek materyal ve üzerine ise 250 µl 67 mm fosfat tamponu (pH 7.0) ve 20 mM H_2O_2 eklendi. Meydana gelen reaksiyon sonucu hidrojen peroksit, katalaz yardımı ile oksijen ve suya ayrışması sonucunda spektroda 240 nm'deki absorbans değerinin azalmasından faydalanılarak doku içerisindeki katalaz aktivitesi hesaplandı. Bu hesaplama da bir birim katalazın dakikada 1 µmol H_2O_2'yi ayrıştıran enzim miktarını göstermektedir [24].

Glutation-S-transferaz (GST) Enzim Aktivitesi

Glutation-S-transferaz enzim analizi için 100 mM potasyum fosfat tamponu (pH 6.5) içeren deney tüplerine sırasıyla, 1 mM 1-kloro-2,4-dinitrobenzen (CDNB) ve 1 mM GSH ve son olarak örnek materyal eklenerek reaksiyon başlatıldı ve spektroda 340 nm'deki değeri ölçülerek belirlendi [25].

İstatistik Analizi

İstatistik analizler SPSS 20.0 (SPSS Inc., Chicago, IL, USA) paket programı kullanılarak yapıldı. Kontrol grubu ile deneysel gruplar arasındaki karşılaştırmalar ANOVA (tek yönlü varyans analizi; one-way ANOVA) testi ile grupların kendi aralarındaki karşılaştırılması ise LSD testi kullanılarak yapıldı. Sonuçlar ortalama ± standart hata olarak verildi.

BULGULAR

Domates ve Kırmızıbiber Ekstraktı ile Oluşturulan Grupların MDA ve Antioksidan Enzim Aktiviteleri

Lipid peroksidasyon (MDA) düzeyi kontrol grubuna göre bütün bölgelerde kırmızıbiber gruplarında belirgin düştüğü gözlendi ($p<0,001$). H_2O_2 verilen gruplarda ise yine kırmızıbiber daha belirgin olmak üzere ($p<0,001$) domateste de bariz düşüşler ($p<0,01$) belirlendi (Tablo 1 ve 2).

GST düzeyinde kontrol grubuna göre D1, D2 ve D3 bölgesinde domates ve kırmızıbiber grupları kontrole yakın değerlerde gözlenirken, D4 bölgesindeki kırmızıbiber gruplarında istatiksel olarak anlamlı olmasa da artış olduğu saptanmıştır ($p<0,05$). H_2O_2 ve ekstrakt verilen gruplar H grubu ile karşılaştırıldığında D2, D3 bölgesi hariç GST düzeyi yine artış göstermiştir ($p>0,05$, $p<0,05$).

Katalaz aktivitesi incelendiğinde kontrol grubuna göre D1-D grubu dışında diğer bütün gruplarda değişen oranlarda artış gözlenmiştir ($p>0.05$, $p<0.05$, $p<0.01$, $p<0.001$), H_2O_2 ile ekstrakt verilen gruplar karşılaştırıldığında hem domates hem de kırmızıbiber gruplarında değişen oranlarda katalaz enzim düzeyinde artışlar gözlenmiştir ($p<0,01$, $p<0,001$).

SOD düzeyi kontrol grubuna göre bütün gruplarda kontrole yakın değerler gösterirken ($p>0.05$), SOD düzeyi H_2O_2 verilen gruplarda H2O2 grubuyla karşılaştırıldığında; domates gruplarında kısmen de olsa artış gösterirken ($p>0.05$, $p<0.05$, $p<0,01$), kırmızıbiber gruplarında azalma gözlenmiştir ($p>0.05$, $p<0.05$).

Kontrole kıyasla SOD inhibisyon düzeyi ise D2-KB, D3-KB ve D4-KB grupları hariç diğer gruplarda azalma gözlenirken ($p>0.05$, $p<0.05$), H_2O_2'e kıyasla ise D2-KB+ H_2O_2 ve D3-KB+ H_2O_2 grupları dışında değişen oranlarda azalma göstermiştir ($p>0.05$, $p<0.05$, $p<0,01$) (Tablo 1 ve 2).

Tablo 1. Domates ve Kırmızıbiber ekstraktı ilave edilen *S. cerevisiae* peletlerinde MDA, GST, SOD ve CAT değerlerinin kontrol grubuna göre değişimi

Gruplar	Analizler				
	MDA (nmol/g)	**GST (µg/g)**	**CAT (µg/g)**	**SOD (µg/g)**	**SOD (%) inhibisyon)**
Kontrol	26,21±0, 87	11,61±0,34	64,37±2,02	5,01±0,25	83,73±0,97
D1-D	27,59±1, 09 ^{a}	11,82±0,22 ^{a}	48,63±1,91 ^{d}	4,82±0,16 ^{a}	83,53±0,17 ^{a}
D1-KB	15,31±1,12 ^{c}	11,99±0,22 ^{a}	69,24±1,91^{d}	5,46±0,16 ^{a}	82,86±0,17 ^{a}
D2-D	25,15±0, 88 ^{a}	11,47±0,69 ^{a}	71,89±3,26 ^{d}	5,33±0,25 ^{a}	80,73±0,80 ^{b}
D2-KB	15,17±0,78 ^{c}	11,87±0,69 ^{a}	67,61±3,26 ^{d}	3,93±0,2 ^{b}	87,07±0,80 ^{c}
D3-D	28,26±1, 61 ^{a}	11,22±0,32 ^{a}	65,14±4,67 ^{d}	5,09±0,18 ^{a}	81,07±0,73 ^{a}
D3-KB	14,33±1,11 ^{d}	9,71±0,32 ^{b}	112,44±4,67 ^{c}	3,96±0,18 ^{b}	86,54±0,73^{b}
D4-D	29,14±1, 51 ^{b}	11,71±0,36 ^{a}	95,89±2, 66 ^{b}	5,32±0,21 ^{a}	80,08±0, 63 ^{b}
D4-KB	13,88±,59 ^{d}	14,12±0,36 ^{b}	133,03±2,66 ^{d}	4,84±0,21 ^{a}	84,21±0,63 ^{a}

a: $p>0.05$, b: $p<0.05$, c: $p<0.01$, d: $p<0.001$

D1-D=D1 bölgesi domates, D1-KB= D1 bölgesi kırmızıbiber, D2-D= D2 bölgesi domates, D2-KB= D2 bölgesi kırmızıbiber, D3-D= D3 bölgesi domates, D3-KB= D3 bölgesi kırmızıbiber, D4-D= D4 bölgesi domates,

D4-KB= D4 bölgesi kırmızıbiber

K= Kontrol, D1= Baskil, D2 = Cip, D3= Doğukent, D4= Sivrice

Tablo 2. Domates ve Kırmızıbiber ekstraktı ve H_2O_2 ilave edilen *S. cerevisiae* peletlerinde MDA, GST, SOD ve CAT değerlerinin H_2O_2 grubuna göre değişimi

Gruplar	**Analizler**				
	MDA (nmol/g)	**GST (µg/g)**	**CAT (µg/g)**	**SOD (µg/g)**	**SOD (%) inhibisyon)**
H_2O_2	42,86±1,17	10,59±0,79	30,14±1,61	4,76±0,25	84,80±0,86
D1-D + H_2O_2	20,89±0,51 [d]	11,45±0,53 [a]	38,77±0,86 [c]	5,16±0,11 [a]	81,47±0,80 a
D1-KB + H_2O_2	15,11±0,51 [d]	12,45±0,53 [a]	50,51±0,86 [d]	4,56±0,11 [a]	82,87±0,80 [a]
D2-D + H_2O_2	34,81±0,43 [c]	10,19±0,26 [a]	73,76±1,63 [d]	5,15±0,16 [a]	81,01±0,81 [a]
D2-KB+ H_2O_2	13,92±0,29 [d]	10,19±0,26 [a]	63,42±1,63 [d]	3,95±0,16 [b]	86,54±0,81 [a]
D3-D+ H_2O_2	28,16±1,11 [d]	10,51±0,17 [a]	110,11±2,93 [d]	5,56±0,3 [a]	77,73±1,29 [b]
D3-KB+ H_2O_2	12,64±0,33 [d]	10,51±0,17 [a]	108,66±2,93 [d]	3,93±0,3 [a]	85,80±1,29 [a]
D4-D+ H_2O_2	27,93±0,7 [c]	12,37±0,31 [a]	87,63±2,26 [d]	6,34±0, 21 [b]	77,06±0, 81 [b]
D4-KB+ H_2O_2	15,03±0,72 [d]	12,37±0,31 [a]	130,72±2,26 [d]	4,11±0,21 [a]	83,92±0,81 [a]

a: $p>0.05$, b: $p<0.05$, c: $p<0.01$, d: $p<0.001$

TARTIŞMA

Doğal olarak veya çevresel kaynaklı oluşabilen hücresel reaktif oksijen türlerinin organizmalarda hasara neden olduğu bildirilmiştir [26]. Hücredeki bu reaktif oksijen türlerinin miktarı arttıkça enzimatik olan ya da enzimatik olmayan antioksidan savunma sistemlerinin bozulduğu ve bu durumun canlıdaki homeostasiyi bozduğu ifade edilmiştir. Antioksidanlar hücrelerdeki çevresel veya diğer stres kaynaklarının oluşturduğu bu serbest radikallerin neden olduğu hasarı önleme veya azaltılma kapasitesine sahip maddeler olarak tarif edilmiştir. Geçmişten günümüze kadar yapılan çalışmalarda bitkisel ekstraktların ve bunlardan elde edilen bileşiklerin yüksek antioksidan özelliğe sahip oldukları bildirilmiştir [27].

Bu besinlerden önemli bir tür olan domates dünya genelinde çoğu ülkede tarla veya serada yetiştirilir. Genellikle sebze olarak telaffuz edilip aslında bir meyve olan domates, tadıyla da popüler bir besin olup insan diyetinde önemli bir vitamin ve antioksidan kaynağıdır. Domatese antioksidan özellik verdiği gibi kırmızı renginden de sorumlu olan pigment likopen olup bu pigmentin kanser gibi dejeneratif hastalıkları önleyebildiği ve bu hastalıklarla savaşabileceği bildirilmiştir [28]. Likopen lipitte çözünebilir bileşik olduğu için, yağ ile tüketilmesi faydasını da arttırmaktadır [29]. Geçmişten günümüze kadar antioksidan özelliği bilinen likopenin sağlık üzerine etkilerinin araştırıldığı birçok çalışma rapor edilmiştir [30]. Likopen tekli oksijeni yakalamada diğer karotenoidlerden daha etkilidir. Karotenoidlerin aktif radikalleri elektron transferi yoluyla veya H_2 vererek ya da direkt radikale bağlanarak oksidatif özellikli bu maddeleri inaktive edebildiği bildirilmiştir [31]. Yapılan bazı çalışmalarda antioksidan özelliği (zincir kırma özelliği sayesinde) yüksek

olan β-karotenin ortamın oksijen basıncının artması söz konusu olduğunda antioksidan etkinliğinin azaldığı rapor edilmiştir [32]. Ayrıca vücuda alınan karotenoid miktarı arttıkça kalp damar tıkanıklığı, kemik kalsifikasyonu ve sinirsel rahatsızlıkların görülme oranının azalma gösterdiği rapor edilmiştir [33].

Domateste β-karotenin dışında ayrıca phytoene, phytofluene gibi karotenoidler, kumarik ve klorojenik asitler gibi fenolik bileşikler, yüksek oranlarda C vitamini ve tokoferol maddelerinin de domatesin besleyiciliğini arttırdığı bildirilmektedir. Diğer taraftan domates üzerinde yapılan çalışmalara bakıldığında domatesteki fitokimyasalların sağlık üzerinde etkilerini anlamaya yönelik çalışmaların sayısının az olduğu görülmektedir. Yapılan bu çalışmalarda ise ağırlıklı olarak, A vitaminin önemli bir öncülü olduğu bilinen ve kanseri önleme bakımından likopene benzerliğinden dolayı daha çok β-karoten ilgi odağı olmuştur [34].

Aerobik türler yapılarındaki yağlı yapıdaki partiküller vasıtasıyla çeşitli peroksitlerle (OH, hidroksil, süper oksit ve lipoid peroksitler) açıkça sitotoksik bir etki oluşturacak şekilde birlikte çalışır [35]. Bu bilgiyle uyumlu olan, domatesin çeşitli bakteriler üzerinde antimikrobiyal etkisinin incelendiği bir çalışmada, aerobik hücrelerin olası metabolizmaları serbest radikal oluşumu ile ilişkilendirilmiştir. Ve bu çalışmada, serbest radikallere karşı söz konusu aktivitenin domatesin ekstraktındaki aktif bileşenlerinin varlığından kaynaklandığı gösterilmiştir [36].

Şimdiye kadar domatesle ilgili yapılan çalışmalar, ya domatesin antioksidan içeriklerinin belirlenmesine yönelik ya da domatesle ilişkili faydalı mikroorganizmaların bu bitkinin büyümesini teşvik edici özelliklere katkıda bulunup bulunmayacağının anlaşılmasını [37] konu edinmiştir. Ancak domatesin içeriklerinin maya hücrelerinin gelişimi üzerine etkilenin incelendiği çalışma mevcut değildir.

Bitkilerdeki fitokimyasal bileşiklerin aflatoksin gibi maddeleri detoksifiye ettiği bilinmektedir. Bununla ilgili bir çalışmada özellikle Çin ve Güneydoğu Asya'da birçok geleneksel ilaç yapımında kullanılan ve Piperaceae familyasından olan beyaz biber (*Piper negrum*)'in olgunlaşmış meyvelerinin çekirdekleri güneşte kurutularak antioksidan fitokimyasal içerikleri araştırılmıştır. Bu çalışmayla beyaz biberin antioksidan, anti-inflamasyon, anti-aterojenik ve anti-platelet agregasyon aktiviteleri gibi çeşitli faydalarının olduğu gösterilmiştir. Ve *Piper negrum*'un fitokimyasal içeriklerinin toksijenik mantarların aflatoksin üretimini engellediği rapor edilmiştir [38].

Yüksek yağ içerikli ve yüksek kolesterollü diyetle beslenen sıçanların diyetlerine farklı dozlarda kırmızıbiber tohumlarının etanol ekstraktlarının eklendiği bir başka çalışmada ise antioksidan savunma sistemi ve oksidatif stres üzerindeki etkiler incelenmiştir. Çalışmanın sonunda kırmızıbiberin etanollü tohum ekstraktlarının eklendiği gruplarda karaciğerde glutatyon, peroksidaz ve katalaz gibi antioksidan aktivitelerin önemli ölçüde arttığı tespit edilmiştir. Ayrıca bu gruplarda karaciğer mikrozum ve mitokondrilerinde (H_2O_2) süperoksit radikal miktarlarının büyük ölçüde azaldığı görülmüştür. Yine aynı çalışmada kırımızı biber tohumlarının eklendiği gruplarda; hepatik TBARS değerleri ve hepatik mitokondrial karbonil değerlerinin önemli derecede azaldığı rapor edilmiştir. Bu çalışma ile elde edilen sonuçların, kırmızıbiber tohumlarının etanollü ekstraktlarının yüksek yağlı ve kolesterollü diyetle beslenen sıçanlarda antioksidatif savunma sistemini aktive ederek oksidatif hasarın azaltılabileceğinin göstergesi olduğu ileri sürülmüştür [39].

Kırmızıbiberin, Kore'de yetiştirilen 5 türünün (*Capsicum annuum* L) plesenta, sap ve perikarp kısımlarından metanollü ekstreleri hazırlanmış ve bu ekstrelerin antioksidan özellikli fenolik bileşikleri, toplam flavonoid ve kapsaisin içeriklerinin analizleri yapılmıştır. Çalışmada bu analizlerle ilişkili olan ABTS, DPSS ve nitrik oksit (NO) serbest radikal temizleme aktiviteleri SOD enzim aktivitesi incelenmiştir. Çalışmada kullanılan biberin ayrı kısımlarıyla oluşturulan tüm ekstraklar yüksek antioksidan aktivite göstermiştir. Ayrıca antioksidan aktiviteler ile fenolik ve flavonoid bileşikler arasında pozitif yönde bir korelasyon olduğu bildirilmiştir. Özellikle kapsaisin içeriğinden dolayı kırmızıbiberin insan sağlığını iyileştirebilecek gıda maddesi olabileceği sonucuna varmışlardır [40].

Tarımsal atık olan kırmızıbiber saplarıyla yapılan bir çalışmada, kırmızıbiber saplarının biyoyararlanımı için uygun bir yöntem tasarlanarak, SOD aktivitesi ve makrofajlardaki NO üretimi üzerinde kırmızıbiber saplarının inhibitör etkisi araştırılmıştır. Çalışma sonunda, ilginçtir ki kırmızıbiberin saplarındaki fenolik, flavonoid ve kapsaisin içeriğinin perikarp ve plesanta ekstraktlarına oranla daha fazla miktarlarda tespit edilmiştir. SOD enzim aktivitesi analiz edildiğinde 100µg/mL konsantrasyonda sap, plesanta ve perikarp içeriğinin sırasıyla %52,3, %7,4 ve %10,4'lük etkinliğe sahip olduğu tespit edilmiştir. Ayrıca kırmızıbiber saplarının diğer parçalara göre çok yüksek seviyede klorojenik asit (3,82mg/gdw) ve p-kumarik asit (2,98 mg/gdw) içerik ile en güçlü antioksidan aktiviteyi göstermiştir. Bu çalışma ile kırmızıbiber tarımsal atıklarınının anti-inflamatuar ajan geliştirme fırsatı olarak kullanılabileceğini göstermiştir [41].

Bazı araştırmacılar tarafından yapılan bir çalışmada ise kırmızıbiber (*Capsicum annuum,* L.) perikarp ve tohumu ekstraktlarının bazı antioksidan aktiviteleri (DPPH radikal süpürme, süperoksit anyon radikal süpürme, hidroksil radikal süpürme, ABTS radikal süpürme, demir şelatlama aktivitesi, SOD aktivitesi ve indirgeme gücünün yanı sıra toplam fenolik ve flavonoid içeriklerinin belirlenmesi gibi) analiz edilmiştir. Çalışma sonunda tüm gruplardaki ekstrakların bütün antioksidan test yöntemlerinde göre güçlü antioksidan aktivite gösterdiği bildirilmiştir. Ayrıca bu çalışmayla kırmızıbiber perikarp ekstraktının hem hidroksil hem de DPPH radikalleri üzerinde güçlü demirli şelatlama aktivitesi ve yüksek süpürme aktivitesi gösterirken, süperoksit anyon radikaline karşı oluşan SOD aktivitesinin daha zayıf olduğu rapor edilmiştir. Ancak kırmızıbiber tohum ekstraktının ise perikarp ekstresine oranla SOD aktivitesinin daha yüksek olduğu bununla birlikte daha zayıf demirli şelatlama aktivitesi, hidroksil radikal süpürme ve DPPH aktivitesi bildirilmiştir. Sonuç olarak Kırmızıbiber tohumunun indirgeme gücü seviyesi ve ABTS radikal süpürme aktivitesinin, test edilen en yüksek konsantrasyondaki kırmızıbiber perikarpından bile daha yüksek olduğu bildirilmiştir. Diğer taraftan bu çalışmada doz miktarı arttıkça, kırmızıbiber tohumu ve kırmızıbiber perikarp ekstrelerindeki antioksidan aktivitenin de arttığı gözlenmiştir. Ancak istisnai şekilde metal şelatlama, SOD ve ABTS radikal süpürme aktivitelerinin konsantrasyon miktarının artışı ile artmadığı da rapor edilmiştir [42].

Yapılan başka bir çalışmada, *S. cerevisiae* hücrelerine radyasyon uygulanarak superoksit dismutaz enziminin koruyucu etkileri araştırılmıştır. Çalışmada, iyonize radyasyon uygulanmış yabani tip ve SOD geni delesyonlu suşlar arasındaki karşılaştırmalar sonucunda, canlılık oranları ve protein karbonil düzeyleri arasında belirgin farklılıklar belirlenmiştir [43]. H_2O_2 'nin yüksek dozlarda süperoksit dismutaz enziminin aktivitesini engellediği, süperoksit radikalinin hücre içinde birikerek katalazı inhibe ettiği rapor edilmiştir [44]. GST'nin antioksidan görevi ise; maya hücreleriyle yapılan çalışmalarda farklı besin kaynakları ve oksidatif strese karşı sentezlendiği saptanarak gösterilmiştir [45]. Bu

çalışmaların dışında maya hücrelerinde, selenyum bileşikleri, vitamin A ile vitamin E'nin ve enzimlerin koruyucu etkileri de incelenmiştir [46].
Saccharomyces cerevisiae ile yapılan bir çalışmada ise, bu mayanın ürettiği hidrojen peroksidin (H_2O_2) ekmek hamurunun fermantasyondaki etkisi incelenmiştir. Ekmek hamurunun fermantasyonunun hamur matrisinin güçlenmesine katkıda bulunduğu bilinmektedir. Ve bu etkide maya tarafından üretilen hidrojen peroksidin etkisi üzerine yapılan bu çalışmada Rezaei ve arkadaşları, hamur ve sulu fermentasyon et suyunda maya tarafından hidrojen peroksit üretimini ve etkisini incelemiştir. Çalışmanın sonunda fermente hamurda daha önceki uygulamalarda elde edilen yüksek seviyelerdeki hidrojen peroksit miktarının kullanılan potasyum dikromat / asetik asit bazlı yönteminden kaynaklandığı ifade edilmiştir. Bunu ispatlamak için Kemilüminesans HyPer Blu testini kullandıklarında fermente hamur veya et suyunda maya tarafından hidrojen peroksit üretiminin olmadığını tespit etmişlerdir. Ancak bununla birlikte düşük miktarlarda H_2O_2 oluşumunun, bulunan katalaz varlığından ve hidrojen peroksitin glüten proteinleri ile hızlı reaksiyona girmesinden kaynaklanabileceği vurgulanmıştır. Bu çalışmayla araştırıcılar fermentasyon üzerine hamur matrisindeki reolojik özelliklerin değişiminde maya tarafından üretilen H_2O_2 üretiminden kaynaklanmadığını ifade etmişlerdir [47].

S. cerevisiae suşunda ve geleneksel olmayan maya türlerinde triptofan kaynaklı sentezlenen Melatonin (N-asetil-5-metoksitriptamin) varlığı, *Saccharomyces cerevisiae*'nin antioksidan özelliklerinin kaynağı olarak düşünülmektedir. Ancak Saccharomyces dışı türler ve *S. cerevisiae*'nın diğer türleri üzerindeki olası melatoninin antioksidan etkisinin olup olmadığını anlamak için Vazquez ve arkadaşları sekiz *S. cerevisiae* suşu ve geleneksel olmayan dört maya türünde (*Torulaspora delbrueckii*, *Metschnikowia pulcherrima*, *Starmerella bacillaris* ve *Hanseniaspora uvarum*) melatoninin antioksidan kapasitesini incelemişlerdir. Bu amaçla ROS oluşumu, lipid peroksidasyonu, katalaz aktivitesi, yağ asidi bileşimi ve peroksizom proliferasyonunu analiz etmişlerdir. Çalışma sonucu daha önceki düşünceleri destekler şekilde olmuştur. Bu sonuca varılmasının nedeni, melatonin varlığının peroksizom birikimini ve kısmen de katalaz aktivitesini artırdığının tespit edilmesidir. Bu çalışma ile, melatonin varlığında büyüyen hücrelerin H_2O_2' neden olduğu oksidatif strese maruz kaldığında, uygulama yapılan bütün türlerde ROS birikiminin ve lipid peroksidasyonunun daha düşük olduğu rapor edilmiştir. Bunun sonucu olarak da oksidatif stres altında artan katalaz aktivitesinin melatonin varlığında azaldığı bildirilmiştir. Bu çalışmayla görülmüştür ki melatonin hem *S. cerevisiae* hem de Saccharomyces olmayan mayalarda bir antioksidan molekül olarak görev yapmaktadır [48].

Bütün bu çalışmalara bakıldığında, çalışılan bütün ekstrelerin antioksidan aktivitelerinin (glutatyon, SOD, peroksidaz, katalaz, ABTS, DPSS ve nitrik oksit (NO) ve DPPH serbest radikal temizleme aktiviteleri gibi) fenolik ve flavonoid bileşiklerinin miktarlarıyla pozitif yönde bir korelasyon olduğu bildirilmiştir. Bu çalışmalarla benzer şekilde özellikle domates ekstrelerinde H_2O_2 grubuna kıyasla diğer gruplarda; antioksidan etkinin göstergesi olan CAT (D1+H grubu hariç), SOD değerlerinin artış gösterdiği, bununla birlikte değerlerinin azalması olumlu olarak karşılanan MDA, SOD inhibisyon değerlerinin ise H_2O_2 grubuna kıyasla azalış göstermiştir. Kırmızıbiber çalışmamızın H_2O_2 grubuna göre karşılaştırdığımızda ise; MDA'nın bütün gruplarda azaldığı gözlendi. Bununla birlikte SOD ve SOD inhibisyon değerlerinin domatesteki gibi olumlu sonuçlar vermediği tespit edildi. Bu sonuçlar daha önce yapılan birçok çalışmayı destekler niteliktedir.

SONUÇ

Sonuç olarak elde ettiğimiz verilerin ışığında, *S. cerevisiae*'in besi ortamına eklenen domates ve kırmızıbiber bitkisinin her ikisinin ekstrelerinin eklendiği gruplarda hidrojen peroksit radikaline karşı savunma mekanizması geliştirdiği, bunula birlikte farklı bölgelerden toplanan bazı örneklerin antioksidan aktivitelerinde ufak da olsa farklılıklar gösterdiğini belirledik. MDA değerlerinin ekstre gruplarında azalma göstermesi, CAT ve SOD enzimlerinin çoğunlukla artış göstermesi bu antioksidan etkiyi desteklemekte olup, bununla birlikte SOD inhibisyon değerlerinin kırmızıbiberde domatesteki gibi olumlu sonuçlar vermediğini tespit ettik. Bu değişimlerin kullandığımız meyve ekstrelerindeki lipofilik moleküllerin değişim oranlarıyla ilişkili olduğunu düşünmekteyiz. Ancak bu farklılığa rağmen her iki bitkinin içerik ve antioksidan aktivite bakımından etkinliği göz önünde bulundurulduğunda, insan beslenmesine katkı sağlayacak bu bileşiklerin izole edilip hem gıda katkı maddesi olarak kullanılması hem de doğal olarak bu ürünlerin tüketilmesinin teşvik edilmesinin öneminin anlaşılması yolunda çalışmamızın diğer çalışmalar için faydalı olacağını ümit ediyoruz.

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EFFECT OF SOME FOOD COMPONENTS AND DIET PATTERNS ON PARKINSON'S DISEASE

ABSTRACT

Objective: Pharmacotherapies for Parkinson's disease, whose global prevalence has increased by 155% in the past 30 years, relieve symptom burden but are ineffective in stopping disease progression. A healthy diet and a variety of nutrients may protect against Parkinson's through their antioxidant and anti-inflammatory effects, as well as a balanced brain-gut microbiota system. The aim of this study was to examine the effects of food components and dietary patterns in Parkinson's disease.

Materials and Methods: Using Pubmed, Science Direct, Cochrane Library databases, articles containing the keywords “Parkinson's disease”, “diet therapy”, “Mediterranean diet”, “ketogenic diet” were examined.

Results: Dietary flavonoid and vitamin E intake and coffee consumption have been associated with a reduced risk of Parkinson's disease. It is also emphasized that vitamin B12 is protective against Parkinson's. Foods rich in polyphenols support the proliferation of bacteria such as *Flavonifractor plautii*, which are equipped with neuroprotective properties in the intestine. Olive oil is rich in hydroxytyrosol, which inhibits alpha-synuclein aggregation. Omega-3 fatty acids protect alpha-synuclein homeostasis. Omega-3, omega-6, vitamin A and E supplements have been reported to delay disease prognosis. Total dairy consumption was associated with a significantly increased risk of PD, with heterogeneity across studies. Compliance with the Mediterranean and MIND diets has been found to be effective in reducing the incidence of Parkinson's disease, improving motor/non-motor symptoms, and delaying disease progression. It has been reported that the ketogenic diet reduces non-motor symptoms more than the standard diet.

Conclusion: Intervention in dietary patterns rather than a single nutrient or nutrient element appears to be a more effective approach in preventing Parkinson's disease and alleviating

symptom burden. More randomized clinical trials are needed to better understand the role of dietary patterns in Parkinson's disease.

Keywords: Parkinson's Disease, Diet Therapy, Mediterranean Diet

PARKİNSON HASTALIĞINDA BAZI BESİN BİLEŞENLERİ VE DİYET MODELLERİNİN ETKİSİ

ÖZET

Amaç: Geçtiğimiz 30 yılda küresel prevalansı %155'lik artış gösteren Parkinson hastalığına yönelik farmakoterapiler semptom yükünü hafifletse de hastalığın ilerlemesini durdurmadaki etkisi kısıtlıdır. Sağlıklı bir diyet ve çeşitli besinler antioksidan ve antiinflamatuar etkilerinin yanı sıra dengeli bir beyin bağırsak mikrobiyota sistemi yoluyla Parkinson'a karşı koruyucu olabilir. Bu çalışmanın amacı Parkinson hastalığında besin bileşenleri ile diyet modellerinin etkisini incelemektir.

Materyal ve Yöntem: Pubmed, Science Direct, Cochrane Library veri tabanları kullanılarak "Parkinson hastalığı" "diyet terapi" "Akdeniz diyeti" "ketojenik diyet" anahtar kelimelerini içeren makaleler incelenmiştir.

Bulgular: Diyetle flavanoid, E vitamini alımı ve kahve tüketimi Parkinson riskinde azalmayla ilişkilendirilmiştir. Ayrıca B12 vitamininin Parkinson'a karşı koruyucu olduğu vurgulanmaktadır. Polifenol açısından zengin besinler bağırsakta nöroprotektif özelliklerle donatılmış *Flavonifractor plautii* gibi bakterilerin çoğalmasını desteklemektedir. Zeytinyağı alfa-sinüklein agregasyonunu inhibe eden hidroksitirosol açısından zengindir. Omega-3 yağ asitleri alfa-sinüklein homeostazını koruyucudur. Omega-3, omega-6, A ve E vitamini takviyesinin hastalık prognozunu geciktirdiği raporlanmıştır. Çalışmalar arasındaki heterojeniteyle birlikte toplam süt ürünleri tüketimi Parkinson riskinde anlamlı artışla ilişkilendirilmiştir. Akdeniz ve MIND diyetine uyumun Parkinson insidansının azaltılmasında, motor/motor dışı semptomların iyileştirilmesinde, hastalık ilerlemesinin geciktirilmesinde etkili olduğu bulunmuştur. Ketojenik diyetin standart diyete kıyasla motor dışı semptomları daha fazla azalttığı bildirilmiştir.

Sonuç: Parkinson hastalığının önlenmesinde ve semptom yükünün hafifletilmesinde tek bir besin veya besin ögesinden ziyade diyet kalıplarına müdahalenin daha etkili bir yaklaşım olduğu görülmektedir. Diyet modellerinin Parkinson hastalığındaki rolünün daha iyi anlaşılabilmesi için daha fazla randomize klinik çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Parkinson Hastalığı, Diyet Tedavisi, Akdeniz Diyeti

GİRİŞ

Son 30 yılda küresel prevalansı %155 artış gösteren Parkinson hastalığı özellikle orta ve ileri yaştaki yetişkinlerde yaygın olarak görülen nörodejeneratif bir hastalıktır (1). Parkinson hastalığı, temel olarak klasik motor semptomlara (bradikinezi, rijidite, duruş bozukluğu, tremor) yol açan dopamin eksikliği ile karakterize bir durumdur (2, 3). Motor dışı semptomlar da (konstipasyon, anksiyete, depresyon, azalmış hafıza, yorgunluk) hastalar arasında yaygındır (2, 4).

Genetik ve çevresel faktörler hastalık gelişiminde önemli bir etken olsa da kesin patogenezi halen belirsizliğini korumaktadır (1). Lewy cisimciklerindeki α-sinüklein proteininin agregasyonu ve dopaminerjik nöronların kaybı, Parkinson hastalığındaki başlıca nöropatolojik değişikliklerdir (5). Oksidatif stresin α-sinüklein agregasyonunu tetiklediği, α-sinüklein tortularının ise mikroglial hücre ve Nükleer Faktör Kabba B (NF-κB) aktivasyonu ile inflamatuar süreci başlattığı bildirilmiştir. İnflamasyon ise dopaminerjik nöron kaybını artırmaktadır (1, 5, 6). Barsak disbiyozu ve mitokondriyal fonksiyon bozukluğunun da hastalığın patogenezinde önemli bir etkiye sahip olabileceği vurgulanmaktadır (2, 7). Mitokondriyal disfonksiyon bozulmuş otofaji ile birlikte 4-hidroksinonenal gibi oksitlenmiş membran lipidlerinin toksik birikimine neden olur (2).

Parkinson hastalığının da içinde olduğu nörolojik hastalıklar dünya çapında ölümcül olmayan hastalık yükünün önde gelen nedenidir (8). Bu hastalıklar için onaylanmış ilaç tedavileri olsa da önleme stratejilerine ihtiyaç vardır (9). Parkinson hastalığına yönelik mevcut farmakoterapiler semptom yükünü hafifletse de hastalık prognozunu durdurmada etkisiz kalmaktadır (2). Sağlıklı bir diyetin teşviki yönünde yaşam tarzı müdahaleleri halk sağlığı üzerinde etkili olabilecek önemli bir yaklaşımdır (9). Bazı besinler ve diyet kalıpları antioksidan ve antiinflamatuar etkilerinin yanı sıra dengeli bir beyin bağırsak mikrobiyota sistemi oluşturulması yoluyla Parkinson hastalığının önlenmesine ve yönetimine katkıda bulunabilir (1). Bu bölümde bazı besin bileşenleri ve diyet modellerinin Parkinson hastalığına etkisi incelenecektir.

BESİN BİLEŞENLERİNİN ETKİSİ

Belirli besin ve besin bileşenlerinin Parkinson hastalığı gelişme riskini etkileyebileceği bildirilmiştir. Örneğin meyve ve sebzelerde bulunan flavanoidler oksidatif dengeyi destekleyip nöroinflamasyonu baskılayarak Parkinson riskini azaltabilir (1). Polifenol açısından zengin besinler (üzüm, zeytinyağı, kırmızı şarap, meyveler gibi) nöroprotektif özelliklerle ilişkili prevotella, bacteroides, *Flavonifractor plautii* gibi bakterilerin çoğalmasını destekler (10). Böylece beyin dokusunda patojen proteinlerin oluşumu engellenir. Zeytin ve zeytinyağı, alfa-sinüklein agregasyonunu inhibe eden ve nöronal hücre ölümünü önleyen hidroksitirosol polifenolleri açısından zengindir (1). Zerdeçalda bulunan bir polifenol olan kurkuminin Parkinson riskini azaltabileceği bildirilmiştir (11). Safranın, α-sinüklein fibrilleri oluşumuna karşı insan nöron hücre dizisi üzerinde sitoprotektif bir etkisi olduğu bulunmuştur (12). Safran ayrıca beyin dopamin konsantrasyonunu doza bağlı bir şekilde artırabilir (13). Wistar farelerinde oluşturulan deneysel Parkinson modelinde safranın biyoaktif bileşiği olan krosinin Parkinson hastalığındaki nöroinflamasyonu azalttığı bulunmuştur (14).

Otuz üç prospektif kohort çalışmanın meta analizine göre (çalışmalar arasındaki yüksek heterojeniteyle birlikte) artmış süt ve toplam süt ürünleri tüketiminin Parkinson hastalığı riskinde anlamlı artışla ilişkili olduğu bulunmuştur. Bu çalışmada kırmızı et, kanatlı eti, balık

ve yumurta tüketiminin Parkinson riskiyle anlamlı bir ilişkisi bulunmamıştır (15). Kahve tüketiminin kafeinin adenozin A1 ve A2 reseptörlerini bloke ederek merkezi sinir sistemi aktivitesini artırmasının bir sonucu olarak Parkinson hastalığı riskini azaltabileceği belirtilmektedir (3, 16). Krusifer sebzeler triptofan amino asidinin mükemmel bir kaynağıdır. Triptofan metabolitlerinin birçoğu kan-beyin bariyerini geçebilir ve astrositlerde aril hidrokarbon reseptörünü aktive edebilir. Bu süreç, NF-κB baskılanmasına yol açar. Böylece mikroglial aktivasyon ve nörotoksisite azalır (17). Diyet lifi mikrobiyota tarafından kısa zincirli yağ asitleri üretimini destekler. Kısa zincirli yağ asitlerinin G proteinine bağlı reseptörlere (GPR41, GPR43) bağlanıp düzenleyici T hücrelerini aktive ederek anti-inflamatuar etkiler uyguladığı, böylece Parkinson riskini azaltabileceği bildirilmektedir (1). Konstipasyon Parkinson hastalarında en sık görülen motor dışı semptomdur. Fonksiyonel kabızlığı olan Parkinson hastalarında 12 hafta boyunca prebiyotik inülin içeren simbiyotik tedavisinin bağırsak hareketi sayısında ve Birleşik Parkinson Hastalığı Derecelendirme Ölçeği (UPDRS) bölüm 1'de anlamlı iyileşme sağladığı bulunmuştur (18).

Çeşitli çalışmalarda bazı vitaminlerin Parkinson hastalığındaki rolü de incelenmiştir. Meta analiz çalışmasında B12 vitamininin Parkinson hastalığına karşı koruyucu olduğu bulunmuştur (8). İsveç'te 18-94 yaş arası 43865 katılımcı ile yürütülen prospektif kohort çalışmada katılımcıların çalışma başlangıcında diyette E ve C vitamini alımının 17 yıllık takip süresi sonunda Parkinson hastalığı riskiyle ters ilişkili olduğu bulunmuştur. Beta-karotenin tahmini alımıyla Parkinson hastalığı gelişme riski arasında ilişki gözlenmemiştir (3). Meta analiz çalışmasında ise diyetle C vitamini alım düzeylerinin Parkinson hastalığı ile ilişkili olmadığı ancak yüksek E vitamini alınması durumunda düşük E vitamini alımına göre Parkinson hastalığı gelişme riskinin %21 daha az olduğu bulunmuştur (19). Yapılan bir müdahale çalışmasında 40 Parkinson hastası otuz ay boyunca günlük 20 ml saf sızma zeytinyağı (kontrol grubu) veya omega-3 (EPA, DHA), omega 6 (gamma linolenik asit ve linoleik asit), A vitamini, E vitamini ve saf gamma tokoferol karışımı içeren bir ürünü tüketmiştir. Çalışma sonunda müdahale grubunda UPDRS'ye göre değerlendirilen hastalık prognozunun kontrol grubuna kıyasla önemli ölçüde geciktiği gözlenmiştir (20). Mitokondriyal disfonksiyon Parkinson hastalığı patogenezini etkileyen bir faktördür. Omega-3 yağ asitlerinin mitokondriyal fonksiyonun iyileşmesi ve alfa-sinükleinin protein homeostazını korunmasına yardımcı olduğu bildirilmiştir (1). Koenzim Q-10'un Parkinson fare modellerinde nigrostriatal dopaminerjik sistemdeki hasarı azalttığı gösterilmiştir (21).

Besin bileşenlerinin Parkinson hastalığındaki rolüne ilişkin çoğu veri hayvan çalışmaları veya hücre kültürü deneylerine dayanmaktadır (12, 14, 21). Meta analiz çalışmasında B12+folat, yüksek flavanollü içecek, omega-3+E vitamini, CoQ10+E vitamini, D vitamini, kurkumin, whey protein, bitter çikolata, üzüm suyu, düzenli kahve tüketimi gibi takviyelerin Parkinson hastalığında motor/motor olmayan semptomlar üzerine etkisi olmadığı bildirilmiştir. Besin bileşenlerinin bu hasta grubunda etkisinin daha iyi anlaşılabilmesi için klinik çalışmalara ihtiyaç vardır (1).

DİYET MODELLERİNİN ETKİSİ

Besinler arasındaki karmaşık sinerjik etkişim nörolojik hastalıklarda belirli besinleri içeren diyet modellerinin rolüne olan ilgiyi artırmıştır. Buna paralel olarak başta Akdeniz diyeti olmak üzere bazı diyet kalıpları ile Parkinson hastalığı arasındaki ilişkiyi inceleyen araştırmalar artmaktadır (1). Akdeniz diyeti yüksek miktarda sızma zeytinyağı, taze sebze, meyve, tam tahıl, kuruyemiş ve kurubaklagil, orta düzeyde balık, süt ürünü ve kırmızı şarap, az miktarda kanatlı eti, kırmızı et, yumurta ve tatlı tüketimiyle karakterizedir (22).

Hipertansiyon, tip 2 diyabet, abdominal obezite ve hiperlipideminin beyne zarar verebilecek inflamasyon ve hiperinsülinemi ile ilişkili olduğu, biyoaktif bileşenler yönünden zengin Akdeniz diyetinin metabolik parametrelerde iyileşme sağladığı bildirilmiştir (23). Ayrıca Akdeniz diyetindeki A, E, C vitamini, niasin, B12 gibi vitaminlerin dopaminerjik nöronların korunmasına, α-sinüklein agregasyonunun ve nöroinflamasyonun önlenmesine aracılık edebileceği vurgulanmaktadır (1).

Parkinson hastaları (n=70) ile yapılan bir çalışmada katılımcılar 10 hafta boyunca Akdeniz diyeti veya geleneksel İran diyeti (Akdeniz diyetine göre daha az zeytinyağı, sebze, sert kabuklu yemiş, balık ve süt ürünü; daha fazla ekmek, tahıl, kırmızı et ve şeker içerir) uygulamak üzere rastgele gruplara atanmıştır. Başlangıçta gruplar arasında serum total antioksidan kapasite ve UPDRS açısından anlamlı bir fark gözlenmemiştir. Müdahale sonunda Akdeniz diyeti uygulanan grupta serum TAC seviyelerinin anlamlı şekilde arttığı, UPDRS skorunun ise anlamlı şekilde daha düşük olduğu bulunmuştur (24). Parkinson hastalığı ve konstipasyonu olan 36 Parkinson hastasıyla yapılan randomize kontrollü çalışmada ise katılımcılar 8 hafta boyunca kabızlık için sadece standart bakım almış veya standart bakıma ek olarak Akdeniz diyeti uygulanmıştır. Çalışma sonunda konstipasyon skorundaki azalma bakımından Akdeniz diyetinin standart bakıma göre bir üstünlüğü bulunmamıştır (25). On iki çalışmanın dahil edildiği bir meta analizde Akdeniz diyetine en yüksek uyumun en düşük uyuma kıyasla %25 daha düşük Parkinson hastalığı insidansı ile ilişkili olduğu bulunmuştur (1).

Parkinson hastalığında etkisi incelenen bir diğer diyet modeli Nörodejeneratif Gecikmeye Yönelik Akdeniz-DASH Müdahalesi (MIND) diyetidir. Beyin sağlığına odaklanan ve yaşlılık döneminde beyin fonksiyonlarını korumak için özel olarak geliştirilen MIND diyeti Akdeniz ve DASH (Hipertansiyonu Durdurmaya Yönelik Diyet Yaklaşımları) diyet kalıplarının birleşimidir. Bu diyet modelinde anti-inflamatuvar, antioksidan ve nöroprotektif bileşenler açısından zengin berry grubu meyve ve yeşil yapraklı sebzelerin tüketimine özel olarak vurgu yapılmaktadır. MIND diyeti sağlıksız olduğu düşünülen hayvansal ve yüksek doymuş yağ içeren besinlerin alımını kısıtlayarak nörodejenerasyonu yavaşlatmaya odaklanır (17, 26). Yapılan bir çalışmada kadınlarda MIND diyetine uyumun en yüksek tertilinde en düşük tertiline kıyasla Parkinson hastalığı başlangıç yaşının yaklaşık 17 yıl daha geç olduğu bulunmuştur (27). Parkinsonizm olan 1205 katılımcı ile yapılan bir çalışmada MIND ve Akdeniz diyet skorunun motor, motor dışı ve toplam semptom yükündeki iyileşme ile arasındaki ilişki incelenmiştir. Her iki diyet skorundaki artışın da motor, motor dışı ve toplam semptom yükündeki iyileşme ile ilişkili olduğu ancak bir MIND diyet puanının semptom şiddetini azaltmada bir Akdeniz diyet puanının yaklaşık iki katı kadar güçlü etkiye sahip olduğu saptanmıştır. Bu çalışmada tereyağı, margarin, kırmızı et, peynir, fastfood, şekerli içecekler, hamur işleri ve tatlılar Parkinson semptomlarının şiddetli olması ile ilişkilendirilirken kuruyemiş, sebze, berry, fasulyeler ve kızartılmamış balık ise semptom şiddetinin düşüklüğü ile ilişkilendirilmiştir (4). Başlangıçta parkinsonizmi olmayan yaşları 59-97 arasında değişen 706 katılımcı ile yürütülen bir çalışmada başlangıçta daha yüksek MIND diyet puanının parkinsonizm ilerlemesinin daha yavaş bir oranı ve parkinsonizm riskinin azalmasıyla ilişkili olduğu bildirilmiştir. Bu çalışmada DASH diyet puanı iki sonuçla da (Parkinsonizm riski ve ilerlemesi) ilişkili bulunmazken Akdeniz diyet skoru sadece parkinsonizm ilerlemesinin azalmasıyla ilişkili bulunmuştur (6).

Ketojenik diyetin nörodejeneratif hastalıklarda çeşitli mekanizmalarla faydalı etkiye sahip olabileceği bildirilmiştir. Daha önce de belirtildiği gibi mitokondriyal disfonksiyon Parkinson hastalığı patogenezini etkileyen bir faktördür. Keton cisimleri varlığı

mitokondriyal enzimlerin ekspresyonunu modüle eder ve hipokampus gibi beyin bölgelerinde mitokondriyal biyogenezi artırır. Keton üretimi mitokondriyal fonksiyonu destekler. Ketojenik diyet NF-κB ekspresyonunu azaltarak N-metil-D-aspartat eksitotoksisitesinin neden olduğu nöronal hasarı hafifletebilir (16, 28). On altı Parkinson hastasıyla yapılan randomize kontrollü çalışmada katılımcılar üç hafta boyunca orta zincirli trigliserit (MCT) destekli ketojenik diyet veya standart diyet uygulamıştır. Çalışma sonunda motor dışı semptom şiddeti skoru MCT destekli ketojenik diyet uygulanan grupta standart diyet uygulanan gruba göre anlamlı şekilde daha fazla azalırken UPDRS, temel hareketlilik becerileri ve dinlenme durumu elektroensefalografisi açısından gruplar arasında anlamlı bir fark gözlenmemiştir (2).

Yapılan bir randomize kontrollü çalışmada Parkinson hastalarında (n=45) nikotin açısından zengin (20 µg/gün) diyet ve standart diyetin (1.8 µg/gün) etkileri incelenmiştir. Domates, patlıcan, patates, çay, domates salçası, kurutulmuş yeşil biber diyetteki başlıca nikotin kaynaklarıdır. Nikotinden zengin ve standart diyetler izokalorik olup makro besin ögesi bileşimleri benzerdir. On iki haftalık müdahale süresinin sonunda nikotin açısından zengin diyet grubunda standart diyet grubuna kıyasla UPDRS skoru ve serum α-sinüklein düzeyi anlamlı şekilde iyileşmiştir (29). Antioksidan ve antiinflamatuvar yolakları hedefleyerek diyet kalıplarına yapılacak müdahalenin Parkinson hastalarında hem motor hem de motor dışı semptom yükünü hafifletebileceği bildirilmiştir (7).

SONUÇ

Parkinson hastalığının artan yaygınlığı ve sağlık sistemlerine oluşturduğu yük göz önüne alındığında bu hastalığın henüz oluşmadan önlenmesine yönelik etkili stratejiler geliştirmek son derece önemlidir. Beslenmeye yönelik yaşam tarzı müdahaleleri Parkinson hastalığının patogenezine dahil olan süreçleri hedefleyerek bu alandaki boşluğu dolduran önemli bir faktör olabilir. Günümüzde Parkinson hastalığının önlenmesinde ve semptom yükünün hafifletilmesinde tek bir besin veya besin ögesinden ziyade diyet kalıplarına müdahalenin daha etkili bir yaklaşım olabileceği üzerinde durulmaktadır. Antioksidan, antiinflamatuvar besin bileşenleri açısından zengin diyetler beyindeki oksidatif stres ve nöroinflamasyonun baskılanması, barsak disbiyozisinin, mitokondriyal disfonksiyonun önlenmesi yoluyla Parkinson hastalığına karşı koruyucu bir etkiye sahip olabilir. Diyet modelleri ve Parkinson hastalığı arasındaki ilişki vaka-kontrol çalışmaları veya besin tüketiminin yalnızca bir kez değerlendirildiği kohort çalışmalara dayandırılmaktadır. Nedenselliğin ve diyet modellerinin Parkinson hastalığındaki rolünün daha iyi anlaşılabilmesi için tatmin edici örneklem büyüklükleri ile yapılacak randomize klinik çalışmalara ihtiyaç vardır.

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CURRENT DIETARY APPROACHES IN IRRITABLE BOWEL SYNDROME

ABSTRACT

Objective: Irritable Bowel Syndrome (IBS) is a disorder of gut-brain interaction characterized by recurrent abdominal pain and changes in bowel habits. With a global prevalence of 4%, it significantly reduces the quality of life for millions of people. Although its exact etiology remains unclear, the gut microbiota plays a critical role in the development of IBS. Medical nutrition therapy holds a key role in the treatment of the disease. The aim of this study is to examine the effectiveness of current dietary approaches in the treatment of IBS.

Materials and Methods: Articles containing the keywords “IBS,” “dietary treatment,” “low FODMAP diet,” “microbiota,” and “starch- and sucrose-restricted diet” were reviewed in the Science Direct, Cochrane Library, and PubMed databases.

Results: Probiotic supplementation in IBS has been shown to provide significant improvements in symptoms. However, the evidence in the literature regarding specific strains and dosages remains inconclusive. The Low FODMAP diet, which is low in fermentable oligo-, di-, and monosaccharides and polyols, is a standardized approach supported by numerous randomized controlled trials. Nevertheless, its implementation is complex and has been associated with a reduction in microbial diversity. A decrease in beneficial bacteria may negatively affect microbiota balance, posing long-term risks. Additionally, it has been associated with nutrient deficiencies, poor dietary adherence, and psychological stress. A more recent dietary approach, the starch- and sucrose-restricted diet, has demonstrated similar beneficial effects to the Low FODMAP diet. It has been found to be easier to implement, and sustainability has been achieved through the reduction of sucrose, starch, and processed carbohydrates. Another recent dietary model, the microbiota-based, artificial intelligence-supported personalized diet, has also shown positive effects on IBS. In addition to producing effects similar to those of the Low FODMAP diet in alleviating symptoms, this approach has been associated with increased alpha and beta diversity. The advantage of personalized diets in terms of sustainability has also been emphasized. Within the scope of current treatments aimed at symptom relief, the importance of a multidisciplinary approach that includes pharmacotherapy, dietary interventions, and brain-gut-focused behavioral therapies has been highlighted.

Conclusion: As alternatives to the low FODMAP diet in the current dietary treatment of IBS, the starch and sucrose restricted diet and the microbiota-based, artificial intelligence supported personalized diet have come to the forefront. Their ease of implementation and positive effects on the microbiota are promising. More comprehensive clinical studies are needed to better understand the roles of these current dietary models in the management of IBS.

Keywords: Irritable Bowel Syndrome, Dietary Treatment, Low FODMAP Diet, Starch and Sucrose Restricted Diet.

İRRİTABL BAĞIRSAK SENDROMUNDA GÜNCEL DİYET YAKLAŞIMLARI

ÖZET

Amaç: İrritabl Bağırsak Sendromu (İBS), tekrarlayan abdominal ağrı ve dışkılama alışkanlıklarında değişikliklerle karakterize bir bağırsak-beyin etkileşim bozukluğudur. Küresel prevelansı %4 olup, milyonlarca insanın yaşam kalitesini düşürmektedir. Etiyolojisi tam olarak bilinmemekle birlikte bağırsak mikrobiyotası İBS gelişiminde kritik bir öneme sahiptir. Hastalığın tedavisinde tıbbi beslenme tedavisinin rolü büyüktür. Bu çalışmanın amacı İBS tedavisine yönelik güncel diyet modellerinin etkisini incelemektir.

Materyal ve Yöntem: Science Direct, Cochrane Library ve Pubmed veri tabanlarında "İBS", "diyet tedavisi", "düşük FODMAP diyeti", "mikrobiyota", "Nişasta- sükroz kısıtlı diyet" anahtar kelimelerini içeren makaleler incelenmiştir.

Bulgular: İBS'de probiyotik takviyesinin semptomlarda anlamlı iyileşmeler sağladığı gösterilmiştir. Ancak literatürdeki tür ve doza yönelik sonuçlar net değildir. Fermente edilebilir oligo-, di-, monosakkaritler açısından düşük bir diyet olan Düşük FODMAP diyeti birçok randomize kontrollü çalışmada faydası desteklenmiş standart bir yaklaşımdır. Ancak uygulaması karmaşıktır ve mikrobiyal çeşitliliğin azalmasıyla ilişkilendirilmiştir. Yararlı bakterilerin azalmasıyla mikrobiyota dengesi olumsuz etkileneceği için uzun vadede risk teşkil etmektedir. Ayrıca besin ögesi eksiklerine, diyete uyum sorunlarına ve psikolojik strese yol açabildiği görülmüştür. Güncel bir diyet yaklaşımı olan nişasta- sükroz kısıtlı diyet, düşük FODMAP diyetine benzer olumlu etkiler göstermiştir. Uygulanması daha kolay bulunmuş, sükroz, nişasta ve işlenmiş karbonhidratların azaltılmasıyla sürdürülebilirlik sağlanmıştır. Diğer güncel bir diyet modeli olan mikrobiyota temelli yapay zeka destekli kişiselleştirilmiş diyetin de İBS üzerinde olumlu etkileri görülmüştür. Mikrobiyota temelli yapay zeka destekli kişiselleştirilmiş diyet, semptomlar üzerinde düşük FODMAP diyetiyle benzer etkiler sağlamasının yanında alfa ve beta çeşitlilikteki artışla ilişkilendirilmiştir. Kişiselleştirmiş diyetin sürdürülebilirlik bakımından avantajına dikkat çekilmiştir. Semptomların hafifletilmesine yönelik güncel tedavi kapsamında farmakoterapi, diyet ve beyin- bağırsak odaklı davranışsal tedavilerin birlikte olduğu multidisipliner yaklaşımın önemi vurgulanmıştır. **Sonuç:** İBS'nin güncel diyet tedavisinde düşük FODMAP diyetine alternatif olarak nişasta-sükroz kısıtlı diyet ve mikrobiyota temelli yapay zeka destekli kişiselleştirilmiş diyet öne çıkmaktadır. Uygulama kolaylığı ve mikrobiyota üzerine sağladığı olumlu etkiler umut vericidir. Bu güncel diyet modellerinin İBS yönetimindeki rollerinin daha iyi anlaşılabilmesi bakımından daha kapsamlı klinik çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: İrritabl Bağırsak Sendromu, Diyet Tedavisi, Düşük FODMAP Diyeti, Nişasta- Sükroz Kısıtlı Diyet.

GİRİŞ

İrritabl bağırsak sendromu (İBS) toplumun %7-16'sını etkileyen yaygın bir gastrointestinal hastalıktır. Tekrarlayan abdominal ağrı, rahatsızlık hissi, şişkinlik ve dışkılama alışkanlıklarındaki (dışkılama sıklığı ve şekli) değişim ile karakterizedir (1). 18–39 yaş aralığındaki bireylerde ve kadınlarda (erkeklere oranla 2 kat daha fazla) daha yaygındır (2). Rome-IV kriterlerine göre küresel prevelansı %4'tür. Çünkü Rome-IV kriterleri daha spesifik ve kısıtlayıcıdır. Rome IV kriterleri abdominal ağrının haftada en az bir kez tekrarlamasını ve dışkılama düzeni/formundaki değişiklikle ilişkili olmasını şart koşmaktadır (3). IBS mortaliyeti artırmamaktadır, hastalarda yaşam kalitesini azaltan bir morbidite ile ilişkilidir. Hastaların büyük bir kısmında, semptomların şiddeti günlük yaşamı ciddi şekilde kısıtlayabilmektedir. Gastroenteroloji poliklinik başvurularının %25-50'sini oluştururken işe devamsızlığın ikinci en yaygın nedeni olarak tanımlanır (4). 1885 hastayla yapılan bir anket çalışmasında IBS semptomlarının aylık 8 gün üretkenliği düşürdüğü, aylık ortalama 1.5 gün okul ya da iş kaybına neden olduğu bildirilmiştir. IBS semptomlarından bir ay süreyle kurtulma karşılığında, hastaların yarısından fazlası kafein veya alkolden, %40'ı cinsel ilişkiden,%24,5'i cep telefonundan,ve %21,5'i ise internet kullanımından bir ay boyunca vazgeçebileceğini belirtmiştir (5). Bir diğer çalışmada IBS hastalarının hastalığın kalıcı olarak iyileştirilmesi için yaşam beklentilerinden 10–15 yıl feda etmeye razı olduklarını ifade etmişlerdir (6). Aynı zamanda İBS hastaları sağlık hizmetlerini sık kullanmaktadır, bu da azımsanmayacak derecede önemli sağlık maliyetlerine yol açmaktadır (7,8). Bu nedenlerle İBS'de hastalar ve toplum için İBS yönetimi son derece önemlidir.

İBS Tanı Kriterleri ve Sınıflandırması

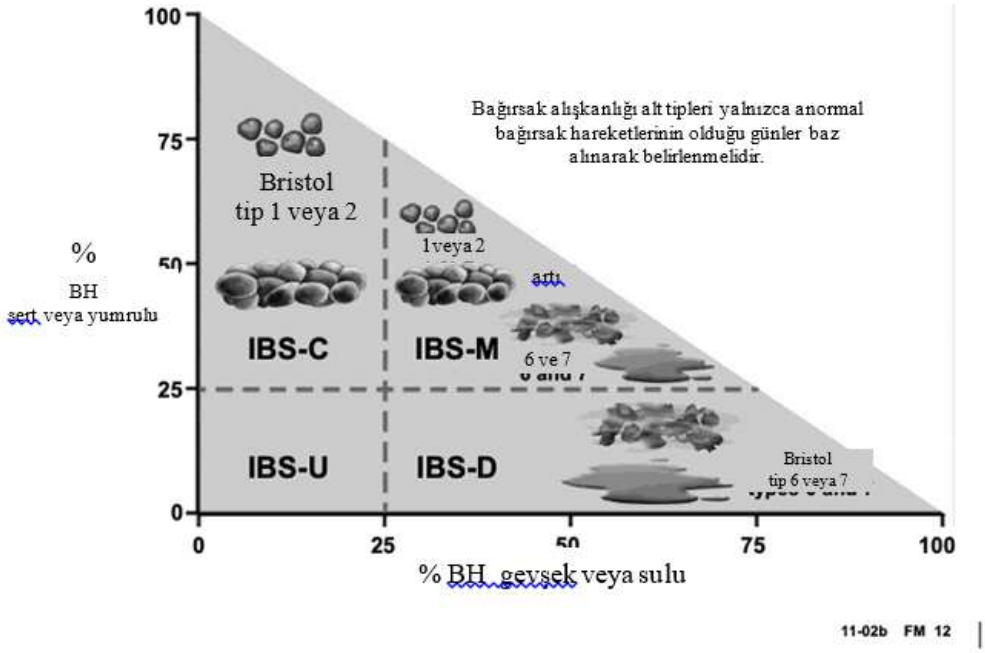
İBS tansıı semptom değerlendirmesine dayanmaktadır. Şu ana kadar güvenilir bir biyomarker bilinmemekle birlikte hastalığın tanısında Rome IV kriterleri kullanılmaktadır. Rome Rome IV'e göre IBS tanısı için semptomların başlangıcının tanıdan en az 6 ay önce olması, son 3 ay boyunca, haftada en az 1 gün karın ağrısı yaşanması, ağrının en az 2'siyle ilişkili olması: dışkılama, dışkı sıklığında değişiklik, dışkının görünümünde değişiklik gereklidir (9). Semptom baskınlığına göre IBS-C (konstipasyon baskın), IBS-D (diyare baskın), IBS-M (karışık tip), IBS-U (sınıflandırılmayan tip) olarak alt tiplere ayrılır (10). Bristol Dışkı Skalası (Bristol Stool Chart) olarak bilinen tıbbi bir sınıflandırma dışkının şeklini ve kıvamını 7 farklı tipe ayırarak bağırsak sağlığı hakkında bilgi verir. Bu skala genellikle sindirim sorunlarını tanımlamak ve bağırsak alışkanlıklarını izlemek için kullanılmaktadır. Özellikle IBS gibi durumlarda klinik değerlendirmeye yardımcı olur. Şekil 1.1'de gösterilmiştir. Tip 1: Ayrı ayrı sert topaklar şeklindedir. Kabızlık belirtisidir. Dışkı çok uzun süre bağırsakta kaldığı için fazla su emilmiş ve sertleşmiştir. Tip 2: Pütürlü bir sosis şeklindedir. Hâlâ kabızlık belirtisidir ama Tip 1'e göre biraz daha ilerlemiş bir dışkı formudur. Tip 3: Yüzeyinde çatlaklar olan sosis şeklindedir. Normal sınırların biraz dışında olup genellikle endişe verici değildir. Tip 4: Sosis veya yılan gibidir. Sağlıklı bağırsak hareketlerini göstermektedir. Tip 5: Belirgin kenarları olan yumuşak parçalardır. Hafif diyareye eğilimli olabilir. Tip 6: Pütürlü kenarları olan gevşek parçalardan oluşur, lapa gibidir. Diyare başlangıcıdır. Bağırsaklar hızlı çalışıyor olabilir. Tip 7: Tamamen sıvıdır, katı parça yoktur. Bağırsaklar çok hızlı çalışıyor ve su emilimi gerçekleşememiştir. Dehidrasyon riski vardır.

Şekil 1.1: Bristol dışkı skalası



Kaynak: (11)

Şekil 1.2: İBS alt tipleri ve Bristol skalası ile ilişkisi



Kaynak: (11)

IBS-D alt tipinde, bağırsak hareketlerinin %25'inden fazlası Bristol dışkı formu ölçeğinde tip 6 veya 7 şeklindedir ve %25'inden azı tip 1 veya 2'dir. IBS-C alt tipinde, bağırsak hareketlerinin %25'inden fazlası Bristol dışkı formu ölçeğinde tip 1 veya 2, %25'inden azı ise tip 6 veya 7'dir. IBS-M alt tipinde, bağırsak hareketlerinin %25'inden fazlası hem tip 1 veya 2 hem de tip 6 veya 7 olarak gözlenir. IBS-U alt tipinde ise hastalar IBS tanı kriterlerini karşılasa da, Bristol dışkı formu tiplerine göre bu üç alt gruptan hiçbirine net olarak uymazlar (12).

Etiyolojisi ve Patofizyolojisi

IBS sadece "fiziksel bir sindirim sistemi hastalığı" değil; sinir sistemi, bağışıklık ve mikrobiyal sistemlerin etkileşiminde ortaya çıkan bağırsak beyin etkileşim bozuklukları (DGBI) sınıfında yer alan karmaşık bir durumdur (13). İBS'nin etiyolojisi hâlâ tam olarak bilinmemekle birlikte çevresel, kalıtsal ve psikososyal faktörlerin rol oynadığı düşünülmektedir. Hastalıkla ilişkili olabileceği düşünülen pek çok mekanizma tartışılmaktadır. Bunlar arasında visseral aşırı duyarlılık, bağırsak–beyin aksının bozulması, bağırsak epitelinin geçirgenliğinde değişiklikler, bağırsak hareketliliğinin bozulması, bağışıklık sisteminin artmış aktivitesi ve bağırsak mikrobiyotasının dengesinin bozulması (disbiyozis) yer almaktadır (14,15).

Mikrobiyota, nörotransmitter üretimi, vagus sinir aktivitesi ve bağışıklık sistemi üzerinden merkezi sinir sistemini etkilemektedir. IBS hastalarında beyin-bağırsak ekseni genellikle bozulmuştur. Bu da anksiyete, depresyon ve ağrı duyarlılığıyla ilişkilidir (16). Yorgunluk, anksiyete, depresyon, uyku kalitesi hastalığın sadece eşlik eden değil merkezi bileşenleridir (13). IBS-D'li bireyler diğer alt tiplere sahip bireylerle kıyasla daha düşük bir yaşam kalitesiyle, daha yüksek bir ekonomik yükle ve depresyon/anksiyete komorbiditesiyle karşı karşıyadır (17).

Genel Tedavi Yaklaşımı

İBS tedavi stratejilerinin ana hedefi altta yatan patofizyolojik süreci ortadan kaldırmak değil, semptomları hafifletmek üzerinedir. Farmakolojik ve farmakolojik olmayan tedavi yaklaşımları mevcuttur. (18). Amerikan ve İngiliz Gastroenteroloji dernekleri farmakolojik tedavi seçenekleri arasından antispazmodikleri önermektedir. Bu ilaçların karın ağrısı ve krampları hafiflettiği düşünülmektedir (19). Trisiklik antidepresanlar norepinefrin ve dopamin reseptörleri aracılığıyla psikolojik stresi ve visseral ağrıyı azaltması yoluyla İBS semptomlarının iyileştirilmesinde kullanılabilmektedir (20). Amerikan ve İngiliz kılavuzları birinci basamak müdahale olarak farmakolojik olmayan müdahalelerden kapsamlı bir hasta eğitimi ile birlikte egzersiz, stres azaltma ve diyet değişikliği gibi yaşam tarzı değişikliklerini önermektedir (21). 14 randomize kontrollü çalışmayı içeren (683 İBS hastası) sistematik bir derlemede yoga, Tai Ji ve aerobik egzersiz gibi fiziksel aktivite müdahalelerinin gastrointestinal semptomları anlamlı şekilde iyileştirdiğini gözlenmiştir (22). Stres azaltma da İBS semptomlarının yönetiminde önemli rol oynamaktadır. Bu anlamda Bilişsel Davranışçı Terapi (BDT), Hipnoterapi gibi bağırsak–beyin psikoterapileri tedavi yaklaşımları olarak öne çıkmaktadır (23). BDT, bağırsak–beyin psikoterapileri arasında en kapsamlı şekilde incelenmiş olanıdır, 30'dan fazla randomize kontrollü çalışmayla desteklenmiştir (18). 42 randomize kontollü çslışmsyı karşılaştıran bir meta-analizde, davranışsal terapilerin İBS'de abdominal ağrıyı kontrol gruplarına göre iyileştirdiğini; ancak hiçbir müdahalenin diğerlerine göre anlamlı derecede üstün olmadığını göstermiştir (24).

Diyet Yaklaşımları

İBS'de diyet yönetimi hastalar ve sağlık hizmeti için önemlidir. Lif alımı (beslenme ve takviye) semptom şiddetini azaltmak ve genel iyilik hali için birçok kılavuzda birinci basamak tedavi olarak önerilmektedir. Uluslararası kılavuzların çoğu, İBS'nin global semptomlarının tedavisinde çözünür lifleri önerirken, çözünmeyen lifleri önermemektedir. Çözünür lifler (psyllilum, yulaf kepeği, meyve ve sebze posası) bağırsak lümeninde su tutarak kolonik geçişi iyileştirir ve özellikle İBS-C'de etkili bulunmuştur (18). 906 İBS hastasını içeren bir meta-analizde lif semptomlarda anlamlı bir fayda sağlamıştır. Ancak bu fayda yalnızca çözünür lif için geçerli bulunmuş, çözünmeyen lif için böyle bir etki saptanmamıştır (25). Amerikan Gastroenteroloji Derneği, günde yaklaşık 25–35 gram lif alımını, gaz ve şişkinliği önlemek için yavaş artışla birlikte önermektedir (26).

Yapılan bir ankette IBS hastalarının %80'inden fazlası besinle ilişkili semptomlar bildirmiş ve daha şiddetli semptomları olan hastaların, sorumlu tuttukları besinlerin sayısını daha fazladır. Bu nedenle, eliminasyon diyetleri sıkça denenmektedir (27). Yüksek fermente edilebilir oligosakkaritler, disakkaritler, monosakkaritler ve polioller (FODMAP'lar) içeren gıdaların kısıtlanmasını içeren düşük FODMAP diyeti İBS için en çok araştırılmış diyet müdahalelerinden biridir (25).

Düşük FODMAP Diyeti

Bu diyet fermente olabilen kısa zincirli karbonhidratlar olan oligosakkaritler, disakkaritler, monosakkaritler ve pololler açısından zengin gıdaların kısıtlanmasını içerir. Bunlar bazı meyveler (armut, elma), bazı sebzeler (sarımsak, soğan), süt ürünleri (süt, yumuşak peynirler) ve baklagillerdir. Bu besinlerin, bağırsakta daha fazla substrat ve su birikimine neden olarak bağırsak lümeninde distansiyon oluşturduğu, bunun da IBS hastalarında ağrıyı tetiklediği düşünülmektedir (28).

Düşük FODMAP diyeti kısıtlama, yeniden tanıtma ve kişiselleştirme olmak üzere 3 aşamada uygulanır. İlk aşamadan (genellikle 2–6 hafta süresince), FODMAP içeriği yüksek olan besinler diyetten çıkarılarak semptomlarda iyileşme olup olmadığı değerlendirilir. İyileşme sağlanırsa diyet uygulanmaya devam eder; sağlanmazsa diyetin etkisiz olduğu düşünülerek bırakılır. Semptom iyileşmesi gözlenen hastalarda ikinci aşamada genellikle 6–10 hafta süren kademeli yeniden tanıtma süreci başlar. Bu aşamada, bir gıda grubu kademeli olarak eklenir ve hastanın tepkilerine göre düzenlemeler yapılır. Son aşamada ise hastanın tolere edebildiği besinleri içeren, kişiselleştirilmiş bir diyet planı oluşturulur. Hasta bu planı dilediği kadar esnetebilir ve kendi semptom kontrolüne göre ayarlayabilir (29). Sistematik derlemeler ve meta-analizler bu diyetin, standart diyet önerileriyle karşılaştırıldığında semptom iyileşmesini desteklediğini ortaya koymaktadır. Özellikle İBS-D alt tipinde sonuçlar belirgindir (30,31,32). 13 randomize kontrollü çalışmayı inceleyen bir sistematik derlemede, düşük FODMAP diyetinin alışılmış beslenme ve diğer tüm diyet müdahalelerinden üstün olduğu sonucuna ulaşılmıştır (33). Birinci basamak sağlık hizmetlerinde yapılan randomize kontrollü bir çalışmada, düşük FODMAP diyetinin antispazmodiklere göre daha etkili bulunmuş ve bu sonuçlar 4 haftadan itibaren ortaya çıkmış, 16 haftalık takipte devam etmiştir (34). Yakın zamanlı bir meta-analizin sonuçlarına göre ise düşük FODMAP diyeti hem kontrollü hem de gerçek yaşam verilerinde İBS semptomlarını azaltmış, yaşam kalitesinde artış sağlamıştır (35).

Güncel Yaklaşımlar

Düşük FODMAP diyeti kısa vadeli etki üretirken uzun vadeli uygulamada besin eksiklikleri, psikolojik stres, diyet uyum sorunları oluşabilmektedir (36). Bazı hastalar, düşük FODMAP diyeti önerilerinin karmaşıklığından ve diyetin kişiselleştirilmesindeki zorluklardan şikayetçi olduklarını bildirmiştir (37). Aynı zamanda İBS hastalarının %25–50'si düşük FODMAP diyeti sırasında hâlâ semptomlar yaşamaktadır. Bu gibi sebepler bireyleri yeni yaklaşımlara itmiştir (38). Yeni yaklaşımlardan biri nişasta-sükroz azaltılmış diyettir. Bu diyet sakaroz, nişasta ve eklenmiş şekerlerin azaltılmasına odaklanır. Düşük FODMAP diyetiyle arasındaki en büyük fark fruktan, fruktoz, laktoz ve tatlandırıcıların alımına izin vermesi; düşük FODMAP diyetinin ise nişasta açısından daha az kısıtlayıcı olmasıdır (38,39). Yapılan çalışmalarda nişasta ve sükroz azaltılmış diyet belirgin semptom iyileşmesi sağlamıştır (40,41). *Roth B ve ark. Yaptığı bir* çalışmada 155 İBS hastası (Rome IV kriterlerine göre) düşük FODMAP ve nişasta sükroz azaltılmış grup olmak üzere 2 gruba ayrıldı. 2 grupta da benzer semtomlarda iyileşme görülürken 6. ayda katılımcıların %64,7'si nişasta-sükroz azaltılmış diyeti daha uygulanabilir ve etkili buldu. Bu diyet düşük FODMAP diyeti kadar etkili ve daha az karmaşık olduğu için uygunluk oranı yüksek bulunmuştur (42). 14 randomize kontrollü çalışmanın dahil edildiği meta-analizde ise düşük FODMAP ve nişasta sükroz azaltılmış diyetlerin İBS semptomlarını azaltmada etkili olduğu gösterilmiştir (43).

Düşük FODMAP diyetinin 4 haftalık uygulama sonrası bifidobakterium gibi yararlı bak. belirgin azalma görülürken Firmicutes/Bacteriodetes oranında değişiklik gözlenmiştir. Bu durum mikrobiyota dengesini olumsuz etkileyebilmektedir (36). Bu anlamda yeni bir yaklaşım olan mikrobiyota temelli ya kişileştirmiş diyet ortaya çıkmaktadır. Tunali ve ark. 121 İBS (Rome IV kriterlerine göre) hastasını içeren randomize çift körlü 6 hafta süren bir çalışma yapmıştır. Bir grup mikrobiyom analizi sonucu yapay zeka destekli kişileştirilmiş diyet planı alırken diğer grup Düşük FODMAP diyeti almıştır. Her iki grupta da abdominal ağrı, şişkinlik ve yaşam kalitesinde anlamlı iyileşme gözlenirken mikrobiyota temelli yapay zeka destekli kişiselleştirilmiş diyet grubunda alfa–beta çeşitlilik artarken katılımcıların çoğu bu diyeti daha uygulanabilir buldu. Bu yaklaşımı, semptom iyileşmesinin ötesinde, mikrobiyotanın çeşitliliğini artırarak uzun vadeli bağırsak sağlığına katkı sağlayabilir sonucuna ulaşıldı (44).

Mikrobiyota temelli yaklaşımların rolünü inceleyen yakın zamanlı bir derlemede; probiyotikler, prebiyotikler, simbiyotikler ve fekal mikrobiyota transplantasyonunun (FMT) İBS semptomları üzerindeki etkisini araştırmıştır. Karışım probiyotikler en etkili sonucu verirken simbiyotik ve prebiyotiklerde anlamlı fark bulunamamıştır (45). IBS tedavisinde sinbiyotiklerin etkinliğini değerlendiren 8 randomize, çift kör, plasebo kontrollü klinik çalışmayı kapsayan bir derlemede sinbiyotikler özellikle çok suşlu preparatların genel olarak IBS semptomlarını iyileştirme potansiyeli gösterse de her çalışmada aynı güçlü etki gözlenmemiş (46). 12 randomize kontrollü çalışmayı içeren FMT'nin IBS tedavisindeki etkinliğini ve güvenliğini sistematik olarak incelemeyi amaçlayan derlemede endoskopik veya rektal uygulamalarda umut vaat etmekle birlikte oral kapsül uygulamaları etkisiz görülmüştür (47).

SONUÇ VE ÖNERİLER

İBS semptomlarını yönetmede diyet temelli yaklaşımlar, farmakolojik olmayan etkili stratejiler arasında yer almaktadır. Düşük FODMAP diyeti, özellikle IBS-D alt tipinde güçlü semptomatik iyileşmeler sağlamakta; ancak uzun vadede mikrobiyota çeşitliliğinde azalma,

psikolojik zorluklar ve besin yetersizlikleri gibi potansiyel riskler barındırmaktadır. Nişasta ve sükroz azaltılmış diyet, düşük FODMAP diyetine benzer etkinliğe sahip olup, katılımcılar tarafından daha uygulanabilir bulunmuştur. Mikrobiyom-temelli, yapay zekâ destekli kişiselleştirilmiş diyet uygulamaları, hem semptom kontrolü hem de mikrobiyota çeşitliliği açısından umut verici sonuçlar göstermektedir. Ancak kısıtlayıcı diyetler kısa süreli uygulanmalı ve diyetisyen kontrolünde kişiye özel olarak planlanmalıdır. İBS'ye özgü güncel diyet yaklaşımlarının kısa ve uzun vadedeki etkilerini inceleyen daha kapsamlı çalışmalara ihtiyaç vardır.

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EFFECTS OF RADIOFREQUENCY RADIATION ON OXIDATIVE STRESS AND HISTOPATHOLOGICAL CHANGES IN LIVER TISSUE: AN EVALUATION OF CURRENT FINDINGS

ABSTRACT

Objective

This study aims to evaluate the potential oxidative stress effects of increased radiofrequency (RF) radiation exposure on liver tissue in light of current literature findings, particularly in the context of the growing prevalence of mobile communication technologies. Specifically, the study examines how RF exposure—depending on frequency, exposure duration, specific absorption rate (SAR), and the developmental stage of the organism—affects biochemical and histopathological changes in the liver.

Methods

In this review, recent experimental studies investigating the effects of RF radiation on liver tissue were systematically analyzed. Evaluations were based on oxidative stress parameters such as malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as observed histopathological changes. The results were compared considering the exposure frequency, SAR value, duration, and modulation characteristics.

*Results*The findings from the literature demonstrate that RF radiation exposure in animal models leads to reductions in antioxidant enzyme activities, increases in lipid peroxidation products, and structural alterations in liver histology. However, some studies reported no significant changes in oxidative stress parameters following low SAR exposure or short-term exposure. Moreover, it has been suggested that the oxidative effects of RF radiation may vary depending on the existing cellular stress status and interactions with environmental factors.

Conclusion

RF radiation appears to induce oxidative stress responses in liver tissue, with the severity of these effects being highly dependent on multiple variables, including exposure duration, dose, frequency, and the biological condition of the organism. Future studies with standardized, long-term, and comprehensive designs are needed to more clearly elucidate the biological impacts of RF exposure.

Keywords: Radiofrequency radiation, oxidative stress, liver tissue.

INTRODUCTION

Exposure to electromagnetic fields has become an increasingly significant environmental concern due to the widespread use of mobile communication technologies and wireless devices. Radiofrequency (RF) radiation, covering the frequency range of 3 kHz to 300 GHz, constitutes a major part of the electromagnetic spectrum encountered in daily life [1]. The World Health Organization (WHO) and the International Agency for Research on Cancer (IARC) have classified RF radiation as a Group 2B agent—possibly carcinogenic to humans—emphasizing the need for more detailed investigations into its potential biological effects [2].

RF radiation affects living organisms through both thermal and non-thermal mechanisms. Thermal effects are associated with tissue heating due to energy absorption, while non-thermal effects involve oxidative stress, inflammation, DNA damage, and alterations in cellular signaling pathways—all of which may occur without a measurable increase in tissue temperature [3]. While thermal effects lead to an increase in tissue temperature, non-thermal effects encompass a range of biochemical and molecular alterations, including oxidative stress, inflammation, DNA damage, and disruptions in cellular signaling pathways [4]. In particular, oxidative stress and inflammatory responses are considered key mechanisms through which RF radiation may induce pathological alterations in target organs [5].

RF electromagnetic waves can be absorbed by various body tissues, such as the liver and brain, depending on the location where the mobile phone is carried [6]. The conductivity and dielectric properties of different tissues influence the rate at which electromagnetic waves are absorbed. Conductivity, in particular, is dependent on tissue density, which varies across different organs [7]. The absorption of RFR within tissues is directly related to their dielectric properties and electrical conductivity. Apart from the brain, tissues with high water content—such as the liver, lungs, and kidneys—exhibit significantly higher conductivity compared to low-water-content tissues like bone and adipose tissue. For instance, at a frequency of 1 GHz, the conductivity of liver tissue (0.98 S/m) is nearly twenty times greater than that of bone tissue (0.05 S/m) [8]. Understanding the potential biological effects of such exposure—particularly in terms of oxidative stress parameters in liver tissue—is of critical importance. Several animal studies have demonstrated that exposure to RF radiation at frequencies of 900, 1800, and 2100 MHz can induce oxidative stress in the livers of rats [9-11], In fact, some studies have also shown that such exposure may lead to DNA damage [12]. Ruediger (2009) conducted a comprehensive review of one hundred studies examining the genotoxicity of RF electromagnetic fields in both in vivo and in vitro settings. He concluded that cells are highly sensitive to electromagnetic exposure and that weak fields, such as those generated by RF radiation, may accelerate electron transfer and thereby destabilize hydrogen bonds within cellular macromolecules. Although the energy of weak fields like RF is insufficient to directly break chemical bonds in DNA, genotoxic effects may still occur through indirect mechanisms such as microthermal processes, the generation of reactive oxygen species (ROS), or interference with DNA repair systems [13]. Trošić et al. (2011) demonstrated that exposure to RF radiation at 915 MHz with Global System for Mobile Communications (GSM) signal modulation (2.4 W/m² power density, SAR: 0.6 W/kg) may induce DNA strand breaks in kidney and liver cells of rats [12]. Electromagnetic wave exposure affects the liver in a manner similar to other toxic agents; the ROS generated by electromagnetic waves are primarily detoxified in the liver, which may lead to hepatotoxicity [14].

As the metabolic center of the body, the liver is highly susceptible to processes such as oxidative stress and inflammation. However, studies investigating the effects of RF exposure on liver tissue are relatively limited in the literature, and their findings vary significantly depending on factors such as exposure duration, frequency, and SAR [15]. This review addresses the potential biological effects of RF radiation on liver tissue, with a particular focus on oxidative stress and histopathological alterations, as interpreted in light of current findings.

FINDINGS

In recent years, the oxidative stress mechanisms induced by radiofrequency (RF) radiation in biological tissues have been extensively investigated. The liver stands out as one of the primary organs in which these effects can be clearly observed, due to its central role in metabolism and detoxification. In a study conducted by Özgür et al. (2010), rats were exposed to RF radiation at a frequency of 1800 MHz with a SAR value of 0.38 W/kg. Following daily exposures of 10 and 20 minutes, oxidative damage was observed in all groups, with severity increasing in relation to exposure duration [16]. Similarly, Salah et al. (2013) reported that exposure to RF radiation at 2.45 GHz for one hour daily over a period of 21 days led to a reduction in key antioxidant enzyme activities—such as glutathione peroxidase (GSH-Px), catalase (CAT), and superoxide dismutase (SOD)—in liver and kidney tissues, while causing a significant increase in MDA levels [17]. These findings suggest that RF exposure disrupts oxidative balance and promotes an increase in free radical production. In another study conducted by Fahmy and Mohammed (2021), rats continuously exposed to Wi-Fi–derived RF radiation at 2.45 GHz with a low SAR value (0.01 W/kg) for 40 days exhibited a marked decrease in GSH and SOD activities, along with a significant increase in MDA levels. Furthermore, this study identified cellular-level structural alterations in liver tissue, indicating that RF radiation can cause damage not only at the biochemical level but also at the histological level Focusing on the effects of chronic exposure, Berköz et al. (2018) reported that exposure to RF radiation at 1800 MHz for two hours daily over a period of eight weeks resulted in increased levels of malondialdehyde (MDA) and nitric oxide (NO) in various organs, including the liver, while leading to decreased activities of antioxidant enzymes such as CAT, GSH, and SOD [18]. These results suggest that long-term RF exposure may contribute to the development of systemic oxidative stress. In another study conducted by Koyu et al. (2009), exposure of rats to 1800 MHz RF radiation resulted in a significant increase in MDA levels, accompanied by a decrease in the activities of antioxidant enzymes such as SOD and GSH-Px. Moreover, the study demonstrated that the administration of caffeic acid phenethyl ester (CAPE), a compound with antioxidant properties similar to resveratrol, provided a protective effect against oxidative stress by mitigating damage in liver tissue [6]. This finding suggests that the use of antioxidants following RF exposure may have the potential to prevent oxidative damage in liver tissue. In a study conducted by Kumari et al. (2012), rats exposed to cell phone–derived RF radiation at 2.45 GHz for two hours daily over a period of 35 days exhibited a decrease in SOD and GPx levels, an increase in CAT activity, and elevated MDA levels. Furthermore, impairments in liver function tests were also reported in this study, indicating that RF exposure may directly impact liver function [19]. Similarly, Eşmekaya et al. (2011) demonstrated that exposure of rats to pulse-modulated RF radiation at 900 MHz with a SAR value of 1.20 W/kg for 20 minutes daily over a period of three weeks resulted in increased levels of MDA and nitric oxide (NO) in liver tissue, along with a reduction in GSH levels [9].

In a study conducted by Eid et al. (2015), oxidative stress– and inflammation-associated liver damage was observed in albino rats exposed to electromagnetic radiation emitted from mobile phones at 900 MHz. However, it was reported that supplementation with vitamin E and silymarin was able to mitigate these adverse effects [20]. These findings suggest that RF exposure may modulate oxidative stress responses depending on the frequency and modulation characteristics of the radiation. Overall, the accumulated evidence indicates that RF radiation can trigger oxidative stress responses in liver tissue, leading to damage at both biochemical and histological levels. Furthermore, it is understood that the weakening of antioxidant defense mechanisms and processes such as lipid peroxidation are exacerbated in relation to the duration, frequency, and SAR value of RF exposure.

In recent years, the effects of RF radiation exposure during pregnancy and the postnatal period on antioxidant defense mechanisms have also become an area of interest. In a study conducted by Salameh et al. (2022), rats continuously exposed to 900 MHz RF radiation from the beginning of pregnancy until postnatal day 21 showed age-dependent variations in the activity and expression levels of catalase (CAT), cytoplasmic superoxide dismutase (cytoSOD), and mitochondrial superoxide dismutase (mitoSOD) enzymes in liver tissue. In the neonatal period (postnatal day 1, PND1), a decrease was observed in both the activity and expression levels of CAT. During early development (PND9), cytoSOD levels were found to increase.

Conversely, a reduction in mitoSOD activity was noted at PND21, while an increasing trend was observed at other developmental stages. These findings suggest that RF exposure may induce developmental stage–specific adaptive responses in the antioxidant system [21]. Similarly, in another study conducted by Okatan et al. (2019), the oxidative stress parameters and histopathological effects of 900 MHz RF radiation on liver tissue were evaluated in rats during adolescence (postnatal days 35–59). Following daily exposure for one hour, significant decreases were observed in 8-hydroxy-2'-deoxyguanosine (8-OHdG) and SOD levels. However, no statistically significant changes were noted in other parameters such as MDA, total antioxidant status (TAS), total oxidant status (TOS), and oxidative stress index (OSI). Histopathological examination revealed structural abnormalities, including disorganization of hepatocyte alignment, cytoplasmic vacuolization, and sinusoidal dilation. These findings suggest that RF exposure during adolescence may lead to both microscopic structural damage and functional impairments in specific antioxidant systems within the liver [22].

In light of all these findings, it is understood that the effects of RFR exposure on oxidative stress and antioxidant defense systems vary not only according to frequency and SAR values, but also depending on exposure duration, dose, and the developmental stage of the organism. The literature suggests that low-level RF radiation exposure may trigger cellular adaptive responses that exert a regulatory effect on antioxidant systems; however, this effect tends to become more pronounced in the presence of additional antioxidant support [23]. Moreover, it has been noted that moderate levels of ROS may stimulate an increase in antioxidant enzyme activities, whereas excessive ROS production can suppress antioxidant defense systems and exacerbate cellular damage [24].

Although previous findings have demonstrated that RFR exposure can disrupt oxidative balance, it is noteworthy that the effects are not always consistent, and different outcomes have been reported in the literature. In a study conducted by Özgür et al. (2015), exposure of guinea pigs to GSM-modulated 900 MHz RFR (0.4 W/kg, 10 or 20 minutes daily for 7

days) resulted in a significant decrease in SOD activity in liver tissue, whereas no notable changes were observed in protein oxidation levels [25]. However, some studies have reported that within certain SAR ranges (0.3–2.0 W/kg), RFR does not exert a significant effect on cellular ROS levels [26-28]. However, it has been shown that when the SAR value exceeds 2 W/kg, intracellular ROS production increases significantly [29]. Zmyślony et al. (2004) reported that RFR alone did not increase ROS production; however, when combined with iron ($FeCl_2$), a significant increase in ROS levels was observed. This finding suggests that the potential of RFR to induce oxidative responses may be modulated through interactions with other oxidative agents present in the environment [30].

The contradictory results regarding the effects of RFR exposure on antioxidant systems highlight the influence of numerous variables in this field, including frequency, SAR value, exposure duration, modulation type, biological model, and accompanying environmental factors. In a study by Kamali et al. (2018), long-term exposure of rats to Wi-Fi–derived RFR at 2.45 GHz (24 hours per day for 10 weeks) led to significant decreases in the activities of antioxidant enzymes such as CAT, SOD, GSH-Px, and GSH, while an increase in GST activity was observed. However, no statistically significant changes were reported in MDA and GSH levels [31]. Similarly, in a study conducted by Borzoueisileh et al. (2020), exposure to RFR at 900 MHz and 2.4 GHz for four hours daily over a period of seven days did not result in a significant change in MDA levels. However, it was suggested that compared to ionizing radiation, RFR might have the potential to suppress oxidative responses [32]. Zong et al. (2015) similarly reported that exposure to 900 MHz RFR alone did not alter liver MDA levels in rats; however, under oxidative stress conditions induced by bleomycin, RFR exposure was found to reduce MDA levels, suggesting a potential protective effect. [33]. Additionally, another study conducted by Bodera et al. (2015) indicated that short-term RFR exposure had no significant effect on MDA levels in the liver [34].

Overall, these findings suggest that the effects of RFR on oxidative stress are not solely dependent on exposure parameters, but may also vary based on the existing level of cellular stress and environmental factors.

CONCLUSION

The findings presented in this review indicate that RF radiation can trigger oxidative stress responses in liver tissue, and that the extent of these effects varies depending on several factors, including the frequency, duration, dose (SAR value) of exposure, and the developmental stage of the organism. Various studies have demonstrated that RF exposure can weaken antioxidant defense mechanisms and increase lipid peroxidation, ultimately leading to biochemical and histopathological damage. However, some investigations have also reported that under certain SAR ranges or specific environmental conditions, RF radiation may suppress oxidative responses or exert no significant effect. It is therefore understood that the biological impact of RF radiation is shaped not only by direct exposure parameters but also by the existing oxidative burden and adaptive cellular responses.

Consequently, there is a need for more comprehensive and standardized studies that consider not only exposure parameters but also the biological status of the system and environmental interactions when evaluating the effects of RF exposure. Future research will be essential to better elucidate the long-term impacts of RF radiation and to identify potential protective strategies, thereby contributing valuable insights to public health.

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THE RELATIONSHIP BETWEEN MACRONUTRIENT INTAKE and DIETARY GLYCEMIC LOAD in CARDIOVASCULAR PATIENTS

ABSTRACT

Objective: Recently, the relationship between chronic diseases and dietary glycemic load (GL) has been a frequently discussed issue. This study was designed and conducted to examine the relationship between macronutrient intake and dietary glycemic load in patients with cardiovascular disease.

Materials and Methods: The study was carried out with 92 volunteer individuals diagnosed with cardiovascular disease, aged between 40 and 70, who were receiving treatment at Kayseri Erciyes University Training and Research Hospital. Patients' general demographic characteristics and three-day food consumption records were obtained through face-to-face interviews by the researcher. The glycemic index (GI) of foods was determined based on the study by Foster-Powell et al. Dietary GL was calculated by multiplying the total carbohydrate amount by the GI of the diet and dividing by 100. Diets with a GL value below 120 were considered low-to-moderate, while those above 120 were classified as high GL.

Results: The glycemic load of the diets of the women in the study was low-to-moderate (116.1 ±41.0), whereas for men, it was high (139.57±49.4). Among the participants, 37% of women and 61.7% of men had a high glycemic load. The average total carbohydrate intake for those with a low GL diet was 145.34±42.2 g, while for those with a high GL diet, it was 180.42±82.0 g (p0.05). A positive correlation was observed between daily carbohydrate intake and GL, while a negative correlation was found between fat intake and GL ($p<0.001$).

Conclusion: The glycemic load of the diets of cardiovascular patients, particularly men, was higher, and it was influenced by the macronutrient composition of the diet. Conducting intervention studies that implement low glycemic load diets without increasing fat content could be beneficial for cardiovascular patients.

Keywords: Glycemic load, cardiovascular disease, macronutrients

KALP-DAMAR HASTALARINDA MAKRO BESİN ÖĞELERİ ALIMI VE DİYETİN GLİSEMİK YÜKÜ ARASINDAKİ İLİŞKİ

ÖZET

Amaç: Son zamanlarda kronik hastalıklarla diyetin glisemik yükü arasındaki ilişki sıkça tartışılan konular arasında yer almaktadır. Bu çalışma, kalp-damar hastalarında makro besin öğelerinin alımı ile diyetin glisemik yükü (GY) arasındaki ilişkiyi incelemek amacıyla planlanıp yürütülmüştür.

Materyal ve Yöntem: Çalışma, Kayseri Erciyes Üniversitesi Eğitim ve Araştırma Hastanesinde tedavi gören, kalp damar hastalığı tanısı konulmuş, yaşları 40-70 yaş arası olan 92 gönüllü kişi üzerinde yürütülmüştür. Hastaların genel demografik özellikleri ve üç günlük besin tüketim kayıtları araştırmacı tarafından yüz yüze görüşme yöntemi ile elde edilmiştir. Besinlerin glisemik indeksi (Gİ) Foster-Powell ve arkadaşlarının yaptıkları çalışma esas arak belirlenmiştir. Hastaların diyetlerinin GY hesaplaması ise; diyetin Gİ nin toplam karbonhidrat miktarıyla çarpılarak 100'e bölünmesiyle hesaplanmıştır. Diyetin GY değeri <120'in altında olanlar düşük-orta, üzerinde olanlar ise yüksek GY olarak kabul edilmiştir.

Bulgular: Araştırmaya katılan kadınların diyetlerinin glisemik yükü düşük-orta (116,1 ±41,0), erkeklerin ise yüksek (139,57±49,4) olup kadınların %37'sinin erkeklerin ise %61,7'sinin glisemik yükü yüksektir. Diyetin glisemik yükü düşük olanların ortalama toplam karbonhidrat alımı 145,34±42,2g, yüksek olanların ise 180,42±82,0g'dır ($p<0,05$). Günlük CHO gereksinimini karşılama oranı ise sırasıyla %59,2±19,04 ve %71,19±29,8'dir ($p<0,05$). Hem kadınların hem de erkeklerin polisakkarit ve nişasta alımı yüksek GY olan grupta daha fazla, posa tüketimi daha düşüktür ($p<0,05$). GY gruplarına göre protein ve yağ alımı miktarı ile bunların günlük gereksinimlerine göre karşılanma oranları arasında istatistiksel olarak önemli bir fark bulunmamıştır ($p>0,05$). Günlük alınan karbonhidrat miktarı ile GY arasında pozitif, yağ alımı ile negatif korelasyon saptanmıştır ($p<0,001$).

Sonuç: Kalp damar hastalarının diyetlerinin glisemik yükü özellikle erkeklerde daha yüksek olup diyetin makro besin öğeleri içeriğinden etkilenmektedir. Kalp damar hastalarında diyetin yağ oranını yükseltmeden düşük glisemik yük içeren diyetlerin uygulandığı müdahale çalışmalarının yapılması yararlı olacaktır.

Anahtar Kelimeler: Glisemik yük, Kalp-damar hastalığı, Makro besin öğeleri

Giriş

Kardiyovasküler hastalıklar (KVH), dünya genelinde en yaygın ölüm nedenlerinden biri olup, her yıl yaklaşık 17,9 milyon insan bu hastalıklar nedeniyle hayatını kaybetmektedir. Bu, tüm küresel ölümlerin yaklaşık %32'sini oluşturmaktadır. Dünya Sağlık Örgütü verilerine göre bu ölümlerin %85'i kalp krizi ve inmeden kaynaklanmakta olup, dörtte üçü düşük ve orta gelirli ülkelerde görülmektedir.[1] Türkiye İstatistik Kurumu'nun 2023 yılı verileri de benzer bir tabloyu yansıtmaktadır; dolaşım sistemi hastalıkları, %33,4 ile ülkemizdeki başlıca ölüm nedenidir ve bu ölümlerin %42,4'ü iskemik kalp hastalıklarından kaynaklanmaktadır.[2]

KVH'nin gelişiminde davranışsal risk faktörleri önemli rol oynamaktadır. Sağlıksız beslenme, fiziksel hareketsizlik, tütün kullanımı ve zararlı alkol tüketimi bu risk faktörlerinin başında gelmektedir.[3] Son yıllarda glisemik indeks (GI) ve glisemik yük (GY) gibi beslenme ile ilişkili kavramların KVH üzerindeki potansiyel etkileri giderek daha fazla araştırılmaktadır. Yüksek GI ve GY içeren diyetlerin, özellikle koroner kalp hastalığı (KKH) riskini artırabileceğine dair çeşitli epidemiyolojik kanıtlar mevcuttur.[4]

Yüksek karbonhidrat alımı, plazma trigliserid düzeylerini artırırken yüksek yoğunluklu lipoprotein (HDL) kolesterol düzeylerini azaltmakta, ayrıca kan şekeri ve insülin düzeylerini yükselterek KVH riskini artırıcı bir metabolik profil oluşturabilmektedir.[5] Bu bağlamda, postprandiyal (öğün sonrası) glisemi düzeyinin hem diyabetik hem de diyabetik olmayan bireylerde bağımsız bir KVH risk faktörü olduğu belirtilmektedir.[6]

Glisemik yük kavramı, hem karbonhidratın kalitesini (GI) hem de miktarını dikkate alarak, bir besinin insülin yanıtı üzerindeki etkisini daha gerçekçi şekilde yansıtmaktadır.[7] Dolayısıyla, glisemik yükün KVH ile ilişkisini değerlendirmek, hastalığın önlenmesi ve yönetimi açısından büyük önem taşımaktadır.

Mevcut epidemiyolojik kanıtlardan yola çıkarak bu çalışma, kardiyovasküler hastalığı olan bireylerde makro besin öğeleri alımı ile diyetin glisemik yükü arasındaki ilişkiyi incelemek amacıyla planlanmıştır.

Materyal ve Yöntem:

Bu tanımlayıcı araştırma, Kayseri Erciyes Üniversitesi Eğitim ve Araştırma Hastanesi'nde, en az bir yıl önce kardiyovasküler hastalık tanısı almış, yaşları 40 ile 70 arasında değişen 45 kadın ve 47 erkek olmak üzere toplam 92 gönüllü birey ile yürütülmüştür. Katılımcıların diyabet, böbrek hastalığı veya kanser gibi eşlik eden başka bir kronik hastalığa sahip olmaması çalışma kriteri olarak belirlenmiştir.

Katılımcıların demografik özellikleri ve üç günlük besin tüketim kayıtları, araştırmacı tarafından yüz yüze görüşme yöntemiyle toplanmıştır. Veri toplama sürecinde porsiyon tahmininde doğruluk sağlamak amacıyla "Yemek ve Besin Fotoğraf Kataloğu" kullanılmıştır.[8] Tüketilen yemeklerin bileşimleri, "Standart Yemek Tarifeleri"[9] ve "Beslenme"[10] kitaplarına göre hesaplanmıştır. Enerji ve besin öğesi içerikleri, Bilgisayar Destekli Beslenme Programı (BEBİS 8.1) ile analiz edilmiş ve elde edilen veriler Türkiye Beslenme Rehberi 2022 doğrultusunda değerlendirilmiştir.[11]

Besinlerin glisemik indeks (GI) değerleri, Foster-Powell ve arkadaşlarının yayımladığı uluslararası tablo temel alınarak belirlenmiştir.[7] Diyetlerin glisemik yük (GY) hesaplaması, toplam karbonhidrat miktarının GI değeri ile çarpılıp 100'e bölünmesiyle yapılmıştır. GY

değeri 120'nin altında olanlar "düşük-orta", 120 ve üzeri olanlar ise "yüksek glisemik yük" olarak sınıflandırılmıştır.

Araştırma verilerinin analizi için **SPSS 16.0 (Statistical Package for the Social Sciences)** programı kullanılmıştır. Sürekli değişkenlerin normal dağılım durumu Kolmogorov-Smirnov testi ile değerlendirilmiştir. Normal dağılım gösteren değişkenler ortalama ± standart sapma ile, normal dağılmayan değişkenler ise medyan (alt–üst değerler) ile tanımlanmıştır. Gruplar arası karşılaştırmalarda, normal dağılım göstermeyen veriler için **Mann-Whitney U testi**, niteliksel değişkenler için **Ki-Kare testi** uygulanmıştır. Sürekli değişkenler arasındaki ilişkiler, dağılım durumuna göre **Spearman** veya **Pearson korelasyon katsayısı** ile analiz edilmiştir. Tüm testlerde anlamlılık düzeyi **p<0,05** olarak kabul edilmiştir.[12]

Araştırma için etik onay, Erciyes Üniversitesi Tıp Fakültesi Tıbbi Araştırmalar Etik Kurulu tarafından 96681246-2017 sayılı karar ile verilmiştir.

Bulgular:

Araştırmaya katılan kadınların diyetlerinin glisemik yükü düşük-orta (116,1 ±41,0), erkeklerin ise yüksek (139,57±49,4) olup kadınların %37'sinin erkeklerin ise %61,7'sinin glisemik yükü yüksektir. Tablo1'de katılımcıların diyetinin glisemik yüküne göre enerji ve besin ögeleri tüketimi ile günlük gereksinmenin karşılanma oranı görülmektedir. Buna göre Diyetin glisemik yükü düşük olanların ortalama toplam karbonhidrat alımı 145,34±42,2g, yüksek olanların ise 180,42±82,0g'dır (p<0,05). Günlük CHO gereksinimini karşılama oranı ise sırasıyla %59,2±19,04 ve %71,19±29,8'dir (p<0,05). GY gruplarına göre protein ve yağ alımı miktarı ile bunların günlük gereksinimlerine göre karşılanma oranları arasında istatistiksel olarak önemli bir fark bulunmamıştır (p>0,05).

Tablo 1. Katılımcıların diyetinin glisemik yüküne göre enerji ve besin ögeleri tüketimi ile günlük gereksinmenin karşılanma oranı

	Düşük GY	**Yüksek GY**	**Toplam GY**	**P**
	x̄±SS	**x̄±SS**	**x̄±SS**	
Günlük Alınan	**Medyan(Alt-Üst)**	**Medyan(Alt-Üst)**	**Medyan(Alt-Üst)**	
Enerji (kal)	1382,83±409,95	1523,73±572,67	1459,41±507,23	0,186
	1342,2(665-2876)	1380,5(696,7-3565)	1359,5(665-3565)	0,391
Protein (g)	60,71±26,76	60,74±23,12	60,72±24,71	0,995
	57,8(27-178)	55(29,9-138)	57(27-178)	0,928
Yağ (g)	61,76±25,66	60,08±25,64	60,85±25,53	0,755
	62,5(23-168)	56,1(20-131)	59,9(20-168)	0,616
Karbonhidrat (g)	145,34±42,25	180,42±82,01	164,4±68,81	**0,010**
	137(65,3-243,6)	157,9(63,1-563)	150(63,1-563)	**0,026**
Enerjinin Karşılanma Oranı (%)	77,31±23,57	82,4±29,27	80,08±26,8	0,367
	75(33-126)	76,5(33-166)	75,5(33-166)	0,655
Karbonhidrat Karşılanma Oranı (%)	59,24±19,04	71,18±29,8	65,73±26,02	**0,022**
	58(20-101)	68(22-184)	62,5(20-184)	**0,043**
Protein Karşılanma Oranı (%)	90,07±38,1	87,82±32,28	88,85±34,87	0,760
	86(29-251)	80,5(35-163)	84(29-251)	0,799
Yağ Karşılanma Oranı (%)	103,45±41,02	97,62±40,04	100,28±40,37	0,493
	102(40-221)	98(21-202)	101,5(21-221)	0,490

*p<0,05

Tablo2'de katılımcıların cinsiyete ve glisemik yüke göre karbonhidrat tüketim miktarları görülmektedir. Hem kadınların hem de erkeklerin polisakkarit ve nişasta alımı yüksek GY olan grupta daha fazla, posa tüketimi daha düşüktür (p<0,05).

Tablo 2. Katılımcıların cinsiyete ve glisemik yüke göre karbonhidrat tüketimleri

	Kadın(n:45)			Erkek (n:47)		
	Düşük GY	Yüksek GY	p	Düşük GY	Yüksek GY	p
	x̄±SS	x̄±SS		x̄±SS	x̄±SS	
	Medyan(Alt-Üst)	Medyan (Alt-Üst)		Medyan (Alt-Üst)	Medyan (Alt-Üst)	
CHO (%)	41,45±8,38	49,3±6,6	0,060	41,82±8,04	46,52±7,62	0,055
	41,83(27,79-53,12)	48,3(35,58-60,4)	**0,020**	41,03(29,45-57,38)	47,1(34,9-63,21)	0,073
Glukoz (g)	6,97±4,22	8±2,96	0,377	7,64±5,11	9,03±5,86	0,104
	6,5(2-17,9)	7,8(3,5-14,3)	0,453	6,9(0,4-16,9)	6,8(1,2-18,5)	0,069
Fruktoz (g)	6,95±4,46	9,7±5,09	0,143	8,2±6,26	10,6±7,62	0,102
	4,8(0,9-16,7)	8,5(2,8-18,3)	0,381	6,8(0,2-24,4)	10,8(0,8-22,9)	0,074
Galaktoz (g)	2,98±1,71	3,35±2,04	0,143	3,56±2,03	3,2±182	0,781
	3(0,4-6,3)	2,95(0,4-6,8)	0,208	3,5(0,7-7,5)	3(0,75-7-6)	0,818
Polisakkarit (g)	82,65±2,56	113±47,3	**p<0,001**	94,55±4,54	120,94±62	**0,050**
	74,6(50-139,1)	102(62-224,2)	**0,000**	82,6(33,5-174,6	108(35,4-290,3)	**0,007**
Monosakkarit (g)	17,08±7,02	22,49±6,27	0,082	18,01±11,5	24,83±21,8	0,101
	16,2(7,5-30)	21,65(15,6-32,6)	0,133	17,2(2,1-46)	18,6(2,1-99,4)	0,094
Sakkoroz (g)	12,58±8,4	20,2±1,26	0,138	20,2±13,6	31,25±35,2	0,291
	11,6(1,8-38,6)	15,45(7,3-39,4)	0,107	18,6(1,6-41,7)	19,9(1,2-143,5)	0,701
Nişasta (g)	74,9±3,11	104,7±5,2	**p<0,001**	87,56±45,1	120±64,5	**0,003**
	67,9(17,8-139,1	90,85(56,5-224,2)	**0,000**	76(35,4-174,6)	122,9(35,4-290,3)	**0,004**
Posa (g)	18,71±5,31	14,82±2,97	**0,004**	19,52±5,59	16,07±3,69	**0,014**
	18,70(9-31,2)	15,70(9,2-19,1)	**0,010**	18,95(11,6-33,3)	15,4(9,7-21,9)	0,050

*p<0,05

Tablo3'de katılımcıların diyetlerinin glisemik yükü ile günlük tükettikleri enerji ve besin öğeleri arasındaki ilişki görülmektedir. Buna göre günlük alınan karbonhidrat miktarı ile GY arasında pozitif, yağ alımı ile negatif korelasyon saptanmıştır (p<0,001).

Tablo 3. Katılımcıların diyetlerinin glisemik yükü ile günlük tükettikleri enerji ve besin öğeleri arasındaki ilişki

	Glisemik Yük		
	r	p	N
Enerji	0,182	0,083	92
Karbonhidrat	**0,349**	**0,001**	92
Yağ	**-0,354**	**0,001**	92
Protein	-0,132	0,211	92

*p<0,05

Tartışma:

Bu çalışma, kardiyovasküler hastalığı olan bireylerde diyetin glisemik yükü (GY) ile makro besin öğeleri alımı arasındaki ilişkiyi incelemiştir. Bulgular, erkek bireylerin diyetlerinde glisemik yükün kadınlara kıyasla daha yüksek olduğunu göstermektedir. Benzer şekilde Yumuk'un çalışmasında da erkeklerin %88,1'inin, kadınların ise %60,6'sının yüksek glisemik yüke sahip diyetler tükettiği bildirilmiştir[13]. Bu durum, erkek bireylerde daha

yüksek miktarda kompleks karbonhidrat veya nişasta içeren besin tüketiminin glisemik yükü artırabileceğini düşündürmektedir.

Çalışmada glisemik yük düzeyi ile toplam karbonhidrat alımı arasında pozitif bir ilişki bulunmuş, glisemik yük yükseldikçe posa alımının ise azaldığı gözlemlenmiştir. Bu bulgular, Görez'in çalışmasıyla paralellik göstermektedir[14]. Posa alımının azalması, glisemik yükün yükselmesinde etkili olabilecek önemli bir faktördür; çünkü posa, mide boşalmasını geciktirerek glikoz emilimini yavaşlatmakta ve insülin yanıtını dengelemektedir[15].

Ayrıca, monosakkarit ve sakkaroz tüketiminin de yüksek GY grubunda daha fazla olduğu gözlenmiştir. Her ne kadar bu fark istatistiksel olarak anlamlı olmasa da, dikkat çekici bir eğilim olarak değerlendirilmiştir. Bu bulgu, basit şekerlerin yüksek GY'ye katkıda bulunabileceğini ve özellikle rafine karbonhidrat içeren besinlerin diyetteki glisemik yükü artırabileceğini düşündürmektedir. Rafine şekerlerin hızlı emilimi nedeniyle postprandiyal glisemiyi yükselttiği ve uzun vadede glukoz metabolizmasını olumsuz etkileyebileceği literatürde de bildirilmektedir[16,17.]

Çalışmamızda, nişasta ve polisakkarit alımlarının yüksek GY grubunda daha fazla olduğu görülmüştür. Nişasta içeriği yüksek besinlerin türüne ve pişirme şekline göre glisemik indeksleri değişebilmekte, bu da GY'yi doğrudan etkilemektedir. Özellikle rafine karbonhidrat kaynakları (örneğin beyaz ekmek, patates püresi) yüksek Gİ ve GY'ye sahiptir[18]. Bu bağlamda, sadece miktarın değil karbonhidratın kalitesinin de göz önünde bulundurulması gereklidir.

Glisemik yükün kardiyovasküler risk ile ilişkisi birçok çalışmada ortaya konmuştur. EPICOR çalışmasında Sieri ve arkadaşları, yüksek GY içeren diyetlerin kadınlarda koroner kalp hastalığı riskini anlamlı ölçüde artırdığını bildirmiştir[19]. Benzer şekilde, Halton ve arkadaşları da kadınlarda yüksek glisemik yükün kardiyovasküler hastalık riskini %90 oranında artırdığını göstermiştir[20]. Bu sonuçlar, çalışmamızın bulgularını desteklemekte ve glisemik yükün cinsiyet temelli farklılıklarla da ilişkili olabileceğini düşündürmektedir.

Çalışmamızda, GY ile karbonhidrat alımı arasında pozitif, yağ alımı ile negatif bir korelasyon gözlenmiştir. Bu durum, diyet bileşenleri arasında bir yer değiştirme etkisi olabileceğini düşündürmektedir. Yani, karbonhidrat ağırlıklı diyetlerde yağ tüketimi nispeten azalmakta ve bu dengenin glisemik yük üzerine doğrudan etkisi olmaktadır. Protein alımı ise GY ile anlamlı bir ilişki göstermemiştir. Ancak bazı literatürlerde protein içeren öğünlerin insülin yanıtını artırabildiği ve karbonhidratlarla birlikte tüketildiğinde sinerjik etki gösterebildiği belirtilmektedir[21].

Glisemik yük yalnızca metabolik etkiler değil, aynı zamanda inflamasyon, oksidatif stres ve endotel fonksiyonları ile de ilişkilidir. Yüksek GY'li diyetler, postprandiyal hiperglisemiye neden olarak reaktif oksijen türlerinin artışına ve inflamatuar sürecin tetiklenmesine yol açmaktadır[22]. Bu mekanizma, ateroskleroz ve insülin direnci başta olmak üzere birçok kronik hastalığın gelişiminde önemli rol oynamaktadır.

Çalışmamızın bulguları, glisemik yükü azaltmaya yönelik beslenme müdahalelerinin özellikle kalp damar hastalığı olan bireylerde önemli olabileceğini göstermektedir. Ancak bu sonuçlar, farklı yaş grupları, sosyoekonomik düzeyler ve diyet alışkanlıkları göz önünde bulundurularak yapılacak daha geniş ölçekli ve prospektif çalışmalarla desteklenmelidir.

Sonuç:

Bu çalışmada, kardiyovasküler hastalığı olan bireylerin diyetlerinin glisemik yük düzeyinin özellikle erkeklerde daha yüksek olduğu ve glisemik yükün, diyetin makro besin öğesi bileşiminden etkilendiği belirlenmiştir. Glisemik yük düzeyi arttıkça toplam karbonhidrat alımının arttığı, posa ve yağ alımının ise azaldığı gözlenmiştir.

Bu bulgular doğrultusunda, kalp damar hastalarının beslenme planlamasında glisemik yük düzeyi dikkate alınmalı; yağ oranı yükseltilmeden, düşük glisemik yük içeren dengeli diyetlerin uygulanmasına yönelik müdahale çalışmalarına ihtiyaç duyulmaktadır. Bu tür müdahaleler, kardiyovasküler risk faktörlerinin yönetiminde etkili olabilir.

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DIETARY CARCINOGENS

ABSTRACT

Objective: The rapid increase in the burden of cancer has become a major challenge for public health and health systems globally, ranking second among causes of death. While 10 million new cancer cases were diagnosed in 2023, studies show that a healthy diet can reduce cancer risk by 30-50%. In this review, dietary carcinogens, which have an important role in cancer prevention, are discussed.

Materials and Methods: In this review, studies published between 2015 and 2025 were examined and evaluated with a qualitative analysis method. WoS, PubMed and Scopus databases and the terms “cancer”, ‘nutrition’ and “dietary carcinogens” were used as keywords. The selection of studies was based on publication in peer-reviewed journals in SCI-Expanded and recognized field indexes.

Results: Dietary carcinogens were basically categorized into four groups.

1.Naturally Occurring Carcinogens: Aflatoxin produced by aspergillus found mostly in nuts such as corn, peanuts, walnuts, etc., fumonisin produced by fusarium found in corn, and aristolochic acid found in aristolochia genus plants are included in this group.

2.Carcinogens Found in Processed Foods: Processed meat (Group1) and red meat (Group2A), which are in the class of carcinogens formed during the processing or cooking process of foods, are in this group. Every 50 g of processed meat consumed daily increases the risk of colorectal cancer by about 16%. The formation of heterocyclic amines and polycyclic aromatic hydrocarbons when meat is cooked or smoked at high temperatures and oxidative damage caused by iron-catalyzed N-nitrozo compounds increase cell proliferation in the mucosa and cause carcinogenesis.

3.Obesity: Obesity, which has the potential to cause cancer at different levels with its many types, is the third leading cause of cancer after tobacco and infection. The risk increases in the elderly compared to the young, in women compared to men and especially in the android type. Obesity shows this effect by increasing the release of adipokines, inflammatory cytokines, insulin, growth factor and steroid hormones.

4. Alcohol: Alcohol consumption is responsible for 13.9% of cancer deaths between 30-34 years of age and exerts its effect by metabolizing ethanol to the carcinogenic metabolite

acetaldehyde, DNA methylation and increasing endogenous estrogen levels, especially in people with low folate intake.

Conclusion: Healthy eating and reduction of dietary carcinogens is an important strategy to reduce diet-related cancers.

Keywords: Nutrition, Dietary Carcinogens, Cancer

DİYET KANSEROJENLERİ

ÖZET

Amaç: Kanser yükünün hızlı artışı, küresel düzeyde halk sağlığı ve sağlık sistemleri için önemli bir sorun haline gelerek ölüm nedenleri içinde ikinci sıradadır. 2023 yılında 10 milyon yeni kanser vakası teşhis edilmiş olmakla beraber çalışmalar sağlıklı beslenmenin kanser riskini %30-50 oranında azaltabileceğini göstermektedir. Bu derlemede kanserin önlenmesinde önemli bir yere sahip olan diyet kanserojenleri ele alınmıştır.

Materyal ve Yöntem: Derlemede, 2015-2025 yılları arasında yayımlanan araştırmalar incelenerek niteliksel bir analiz yöntemi ile değerlendirilmiştir. Araştırmada başlıca WoS, PubMed ve Scopus veritabanları ile "kanser", "beslenme" ve "diyet kanserojenleri" terimleri anahtar kelime olarak kullanılmıştır. Araştırmaların seçiminde SCI-Expanded ve tanınmış alan indekslerdeki hakemli dergilerde yayımlanma şartı aranmıştır.

Bulgular: Diyet kanserojenleri temel olarak dört gruba ayırılmıştır.

1.Doğal Olarak Oluşan Kanserojenler: Çoğunlukla mısır, yer fıstığı, ceviz vb kuruyemişlerde bulunan aspergillusun ürettiği aflatoksin, mısırda bulunan fusariumun ürettiği fumonisin ve aristolochia cinsi bitkilerde bulunan aristoloşik asit bu grupta yer almaktadır.

2.İşlenmiş Besinlerde Bulunan Kanserojenler: Besinlerin işleme ya da pişirme sürecinde oluşan kanserojen sınıfında yer alan işlenmiş et (Grup1) ve kırmızı et (Grup2A) bu gruptadır. Günlük tüketilen her 50 g işlenmiş et kolorektal kanser riskini yaklaşık %16 artırmaktadır. Etin yüksek sıcaklıkta pişirilmesi veya tütsülenmesi ile heterosiklik aminler ve polisiklik aromatik hidrokarbonların oluşması ve hem demir ile katalize edilen N-nitrozo bileşiklerden kaynaklanan oksidatif hasar mukozadaki hücre proliferasyonunu arttırarak karsinogeneze neden olmaktadır.

3.Obezite: Birçok türüyle farklı düzeylerde kanser oluşturma potansiyeli olan obezite, tütün ve enfeksiyondan sonra kansere neden olan üçüncü etmendir. Gençlere göre yaşlılarda, erkeklere göre kadınlarda ve özellikle android tipte risk artmaktadır. Obezite bu etkisini adipokin, inflamatuar sitokinler, insülin, büyüme faktörü, streoid hormonların salınımını artırarak göstermektedir.

4. Alkol: Alkol tüketimi 30-34 yaş arasında kanser ölümlerinin %13.9'undan sorumlu olup etkisini etanolün kanserojenik metabolit asetaldehide metabolize olması, özellikle folat alımı düşük olan kişilerde DNA metilasyonu ve endojen östrojen seviyelerini artırarak gerçekleştirmektedir.

Sonuç: Sağlıklı beslenme ve diyet kanserojenlerinin azaltılması özellikle diyetle ilişkili kanserlerin azaltılmasında önemli bir stratejidir.

Anahtar Kelimeler: Beslenme, Diyet Kanserojenleri, Kanser

GİRİŞ

Kanser, vücudun hemen hemen her organında veya dokusunda, anormal hücrelerin kontrolsüz bir şekilde çoğalması, normal sınırlarını aşarak vücudun diğer bölgelerine yayılması ve/veya diğer organlara metastaz yapmasıyla ortaya çıkan geniş bir hastalık grubudur. Dünya genelinde 2018 yılında 18 milyondan fazla kanser vakası bildirilirken aynı yıl kanser nedeniyle 9,5 milyondan fazla ve 2020 yılında yaklaşık 10 milyon insan hayatını kaybetmiştir. Erken yaşta ölümlerin (30-69 yaş) %29,7'si kansere atfedilmekte ve kanser, 134 ülkede erken yaşta ölümlerin birinci veya ikinci nedeni arasında yer almaktadır (WHO, 2020).

Tüm kanser türlerinin yaklaşık %5-10'unu genetik bozukluklardan kaynaklanırken %90-95'i ise beslenme (%30-35), sigara kullanımı (%25-30) ve alkol tüketiminden (%4-6) kaynaklanmaktadır (Anand vd., 2008). Çoğu solid tümör, hangi organ sisteminde geliştiğinden bağımsız olarak, yaklaşık 15-25 yıllık bir biyolojik gelişim süreciyle evrilmektedir. Diyetle alınan kanserojenler bağlamında değerlendirildiğinde, günümüzde tanısı konulan birçok tümörün etiyolojik kökenlerinin 1975–1995 yılları arasına uzandığı varsayılmaktadır. Dolayısıyla, 20-40 yıl önceki diyet kaynaklı kanserojen etmenlerin, önümüzdeki 20–40 yıl içinde tanısı konulacak kanserler için risk faktörü olmaya devam edip etmeyeceği, halen önemli bir sorundur (Fitzmaurice vd., 2018).

Çeşitli besinlerin ve beslenme modellerinin kanser riskini artırdığına dair kanıtlar artmakla beraber bu etki kısmen, gıda mutajenlerinin tüketiminden kaynaklanmaktadır. Bu mutajenler, besinin ağza alınmasından sindirim sürecine kadar maruz kalma yolu boyunca (ağız boşluğu, yemek borusu, gastrointestinal sistem) ve karaciğer gibi bu yol dışındaki organlarda kanser gelişimine katkıda bulunmaktadırlar (Khambete ve Kumar, 2014).

Besinlerdeki kanserojen maddelerin çeşitli kaynakları vardır. Bu maddeler fiziksel ortamda doğal olarak ve insan beslenmesinin bir parçası olan çok sayıda bitki, mantar ve mikroorganizmada bulunmaktadır. Bazı kanserojenler besinlerin geleneksel pişirme, işleme ve depolama yöntemleri sonucu oluşabilirken sanayileşmenin artmasıyla pestisit, endüstriyel atıklar, ilaçlar vb. kanserojen çevre kirleticilerin besinlerde bulunması da söz konusudur (Prieto vd., 2023).

Uluslararası Kanser Araştırma Ajansı (IARC), insanlar için kanserojen tehlike oluşturan kimyasalları; insanlar için kanserojen (Grup 1), insanlar için muhtemelen kanserojen (Grup 2A), insanlar için olası kanserojen (Grup 2B) ve insanlar için kanserojenliği sınıflandırılamayan (Grup 3) olmak üzere dört ana grupta incelemektedir (IARC, 2012).

Doğal Olarak Oluşan Kanserojenler

Doğal olarak oluşan kanserojenler, besinlerin bir parçası olan bitkiler gibi doğal bileşenleri ve mantar veya mikroorganizmalar tarafından üretilen doğal bileşik veya toksinleri içermektedir. Bu grupta yer alan başlıca kanserojenler aflatoksin, aristoloşik asit ve fumonisinlerdir. Bu kanserojen maddelerin ortak özelliği dünya genelinde yaygın olarak tüketilen temel tahıllar ve gıda maddeleri aracılığıyla maruziyetin gerçekleşmesidir. Bu nedenle, etkili bir korunma stratejisi; kaynak azaltımını, birincil ve ikincil korunma yaklaşımlarını ve ticaret ile pazarlamada uygun düzenleyici sınırların belirlenmesini içermelidir (Fitzmaurice vd., 2018).

Tablo 1. Bitki, mantar ve mikroorganizmalarda bulunan doğal olarak oluşan kanserojen maddeler (Prieto vd., 2023)

Kanserojen madde	IARC grubu	Bulunduğu besinler
Bitkiler		
Areka cevizi	1	Çiğnenmiş betel palmiye meyvesi
Aristolosik asit	1	Geleneksel Çin bitkisel tedavisi
8-Metoksipsoralen (artı ultraviyole A)	1	Kereviz, maydanoz, havuç, portakal, limon vb.
Sikasin	2B	Tohumlar
Metil öjenol	2B	Karanfil yağı, fesleğen, hindistan cevizi, tarçın, zencefil vb.
Pirolizidin alkaloidler: Lasiokarpin, monokrotalin ve riddellin	2B	Bal, çay, bitki çayları ve gıda takviyeleri
Mantar ve mikroorganizmalar		
Aflatoksin (B1, B2, B2A, G1, G2, G2A)	1	Tahıllar, yağlı tohumlar, meyveler, sebzeler, kuruyemişler, kuru meyveler, kahve çekirdekleri, kakao çekirdekleri ve baharatlar
Aflatoksin M1	2B	
Fumonisin	2B	
Mikrosistin-LR	2B	Balık, yumuşakçalar ve sebzeler
Okratoksin A	2B	Tahıllar, yağlı tohumlar, meyveler, sebzeler, kuruyemişler, kuru meyveler, kahve çekirdekleri, kakao çekirdekleri ve baharatlar
Sterigmatosistin	2B	Tahıllar, hayvan yemi, sert peynir, ceviz ve yeşil kahve çekirdekleri

Aflatoksin

1970'li yılların başından bu yana aflatoksin, insan kanserojeni olarak defalarca incelenmiş ve nihayetinde IARC Monografileri Cilt 56'da insanlar için kanserojen (Grup 1) olarak sınıflandırılmıştır (WHO, 2017).

Aflatoksin, çeşitli araştırmalarda farklı kanser türleri ile ilişkilendirilmektedir. Safra kesesi kanseri ve safra taşı olan hastalarla safra taşı olmayan kanserli hastalar arasında gerçekleştirilen çalışmada aflatoksin maruziyetinin safra kesesi kanseri ile ilişkili olduğu bulunmuştur (Koshiol vd., 2017). Tümör başlatıcı hücreler olarak bilinen kanser kök hücrelerinin incelenmesiyle gerçekleştirilen çalışmada aflatoksin B1 kaynaklı mutasyonun hepatik kanser oluşumuna yol açtığı saptanmıştır (Ju vd., 2016). İran'da gerçekleştirilen

araştırmada ise buğday ununun aflatoksin ile kontaminasyonunun özofagus kanseri riskini artırdığı sonucuna ulaşılmıştır (Ghasemi-Kebria vd., 2013).

Aristoloşik asit

Aristoloşik asit, temel tahılların tarla koşullarında büyüme sürecinde *Aristolochia* bitkilerinin tarlalara yayılması sonucu bu tahılların kazara kontaminasyona uğramasıyla diyetle alınan bir kanserojen olarak öne çıkmıştır. Hasat sırasında, bu bitkiler buğday gibi gıda ürünleriyle birlikte toplanmaktadır. Ayrıca, insan maruziyetine yol açan bir diğer yaygın kaynak, bu bileşik grubuyla kontamine olduğu gösterilmiş olan bazı bitkisel ilaçlardır. Son 25 yıl içerisinde aristoloşik asidin insanlar için kanserojen olarak sınıflandırılmasını destekleyecek yeterli kanıt birikmiş ve IARC Monografileri Cilt 100A'da insanlar için kanserojen (Grup 1) olarak sınıflandırılmıştır (Burrnett vd., 2018).

Aristoloşik asit çeşitli araştırmalarda farklı kanser türleriyle ilişkilendirilmektedir. Tayvan'da tip 2 diyabetli hastalarla yürütülen kohort çalışmasında aristoloşik asit maruziyetinin doza bağlı olarak diyabetli hastalarda böbrek, mesane, pelvis, üreter, karaciğer, kolorektum ve prostat kanseri riskini artırdığı ve 500 mg'dan fazla dozlarda aristoloşik asit maruziyetinin kadınlarda ekstrahepatik safra kanalı kanseri riskini artırdığı bulunmuştur (Chen vd., 2022). Reçeteli olarak satılan ve aristoloşik asit içeren Çin bitkisel ürünleri ile idrar yolu kanseri riski arasındaki ilişkinin incelendiği araştırmada; aristoloşik asit içeren Çin bitkisel ürünlerinin tüketimi, arsenik maruziyetinden bağımsız olarak ve doza bağlı olarak idrar yolu kanseri riskinin artmasıyla ilişkilendirilmiştir (Lai vd., 2010).

Fumonisin

Fumonisinlerin insan kanserinde rol oynadığına dair ilk bulgular, 1988 yılında Güney Afrika'nın Transkei bölgesinde yaşayan bireylerde yüksek özofagus kanseri insidansı ile ilişkilendirilmiştir. Fumonisin, sfingolipid metabolizmasında görevli olan seramid sentaz enziminin inhibisyonu yoluyla toksik etki göstermektedir (IARC, 2016).

Fumonisin, çeşitli araştırmalarda farklı kanser türleriyle ilişkilendirilmektedir. Yu vd. (2021), fumonisin B1'e maruz kalmanın özofagus kanseri ile ilişkili olduğunu bulmuşlardır. Çin'de hasat edilen mısırların incelendiği çalışmada ise fumonisinlerin primer karaciğer kanseri için risk faktörü olduğu sonucuna ulaşılmıştır (Ueno vd., 1997).

İşlenmiş Besinlerde Bulunan Kanserojenler

Besin hazırlama/işleme sürecinde uygulanan bir dizi prosedür, gıda zincirinde ve yerel çevrede kanserojen madde oluşumuna yol açabilmektedir. Bu prosedürler arasında tuzlama veya tütsüleme yoluyla et ve balıkların korunması, etlerin ızgara veya fırında pişirilmesi ve bitkisel yağlarda pişirilmesi, şeker içeriği yüksek besinlerin kızartılması, kavrulması ve pişirilmesi, hatta gıda fermantasyonu da yer almaktadır. Besinlerin işleme ya da pişirme sürecinde oluşan kanserojen sınıfında yer alan işlenmiş et (Grup1) ve kırmızı et (Grup2A) bu grupta yer almaktadır ve günlük tüketilen her 50 g işlenmiş et kolorektal kanser riskini yaklaşık %16 artırmaktadır (Prieto vd., 2023).

Et ve balıkların tütsülenerek ya da ızgarada pişirilerek saklanması, polisiklik aromatik hidrokarbonların (PAH'lar) oluşumuna neden olabilmektedir. PAH'lar, eksik yanma veya piroliz süreçleri sonucunda meydana gelir ve genellikle karmaşık karışımlar hâlinde bulunurlar. Hem kanserojen hem de kanserojen olmayan bileşikler tanımlanmış olmakla birlikte, en fazla endişe yaratan PAH'lar genotoksik ve kanserojen özellikte olanlardır. Sigara içmeyen bireyler için PAH maruziyetinin en önemli kaynağı besinlerdir (Anderson ve Philips, 2013).

Etin yüksek sıcaklıkta pişirilmesi veya tütsülenmesi ile heterosiklik aminler ve polisiklik aromatik hidrokarbonların oluşması ve hem demir ile katalize edilen N-nitrozo bileşiklerden kaynaklanan oksidatif hasar mukozadaki hücre proliferasyonunu arttırarak karsinogeneze neden olmaktadır (Fitzmaurice vd., 2018). Bu bağlamda gerçekleştirilen araştırmalar, işlenmiş et ve et ürünleri tüketiminin mide, kolon, rektum, pankreas, akciğer, prostat, testis, böbrek ve mesane kanseri ve lösemi riskiyle önemli ölçüde ilişkili olduğunu göstermektedir (De Stefani vd., 2009; Hu vd., 2011; Lin vd., 2015).

Besinleri pişirme esnasında ısıtılan yağ, PAH'lar da dahil olmak üzere bir dizi kanserojen kimyasal madde üretebilmektedir. Ancak, üretilen bileşiklerin çoğu uçucudur ve bu nedenle besini tüketenden çok besini pişiren için daha fazla risk oluşturabilmektedir. IARC, yüksek sıcaklıkta kızartma işleminden kaynaklanan emisyonları 2A grubunda sınıflandırmaktadır (Anderson ve Marrs, 2017).

Tablo 2. Besin işleme sonucu ortaya çıkan kanserojenler (Prieto vd., 2023)

Kanserojen madde	IARC grubu	Bulunduğu besinler
Heterosiklik aminler	2A/2B	Izgara balık ve et, et özleri, domuz pastırması, kızartılmış veya tavada pişirilmiş et, kazein pirolizatı ve proteinlerin pirolizi ile elde edilen ürünler
N-Nitrozo bileşikleri: N-Nitrozaminler ve nitrozamitler	2A/2B	Tütsülenmiş balık ve et, jambon, sosisli sandviç, pastırma, sosis, sığır eti vb.
Polisiklik aromatik hidrokarbonlar (PAHS)	2A/2B	Etler (ızgara, mangal, tütsülenmiş), balık (konserve, işlenmiş, tütsülenmiş), kahve, tahıllar vb.
Akrilamid	2A	Patates (özellikle patates kızartması ve patates cipsi), tahıl ürünleri (kahvaltılık gevrek, kurabiye ve tost gibi), kahve
Etil karbamat (üretan)	2A	Alkollü içecekler, şarap, bira, ekmek, soya sosu ve yoğurt
Furan ve metilfuranlar	2B	Hazır yemekler, kavrulmuş kahve, kızarmış ekmek

Obezite

Obezite, Dünya Sağlık Örgütü tarafından vücutta sağlık açısından risk oluşturacak şekilde aşırı veya anormal yağ birikimi olarak tanımlanmaktadır (WHO, 2024). Yetişkin kadınlarda vücut ağırlığının ortalama %25-30'unu yetişkin erkeklerde ise ortalama %15-20'sini yağ dokusu oluşturmaktadır ve bu oranın kadınlarda %30, erkeklerde ise %25'in üzerinde olması obezite olarak tanımlanmaktadır. Bunun yanında vücut ağırlığının (kg) boy uzunluğunun (m) karesine bölünmesiyle elde edilen beden kütle indeksi 30 ve üzerinde olan bireyler obez olarak kabul edilmektedir (T.C. Sağlık Bakanlığı, 2017). Obezite hem bağımsız olarak hem de diğer hastalıklarla ilişkili olarak birçok sağlık sorununa neden olmakta veya mevcut sağlık sorununun şiddetini artırmaktadır ve bu nedenle halk sağlığı sorunlarının başında gelmektedir (Kopelman, 2000). 2019 yılında optimumdan yüksek BKİ'nin kardiyovasküler hastalıklar, diyabet, kanser, nörolojik bozukluklar, kronik solunum yolu hastalıkları ve sindirim bozuklukları gibi bulaşıcı olmayan hastalıklardan dolayı yaklaşık 5 milyon ölüme neden olduğu tahmin edilmektedir (Murray vd., 2020). Tüm bu olumsuz sağlık sonuçlarına rağmen dünya genelinde yetişkinlerde görülen obezite oranı iki kattan fazla artış gösterirken ergenlik dönemindeki bireylerde bu oran 4 kat artmıştır (WHO, 2024). Bu hızlı artışın önüne geçilebilmesi için obezitenin nedenlerinin araştırılması ve bu nedenlerin önlenmesine yönelik eylem planlarının oluşturulması elzemdir.

Küresel ölçekte, fazla kilo ve obeziteye atfedilebilecek kanserlerin medyan oranı, kanser türüne ve ülkeye bağlı olarak %1-9,5 arasında değişmektedir (Arnold vd., 2016). En yüksek oranlar Kuzey Amerika, Orta Doğu ve Avrupa'da görülmekte; Sahra Altı Afrika ve Asya'da ise daha düşük oranlar gözlemlenmektedir. Bu durum, bu bölgelerdeki obezite prevalansıyla uyumludur. Bu nüfus atfedilebilirlik oranları genellikle kadınlar ve erkekler için benzerdir; ancak, belirli kanser türleri için obeziteye bağlı riskler ve bu topluluklardaki obezite prevalansına bağlı olarak cinsiyete göre farklılıklar ortaya çıkabilmektedir. Küresel düzeyde, obezite; atfedilebilir oranlar açısından değerlendirildiğinde sigara kullanımı ve enfeksiyonların ardından kanser için en önemli üçüncü risk faktörü olarak sıralanmaktadır (Renehan ve Soerjomataram, 2016).

Obezitenin kanser etiyopatogenezindeki rolü tam olarak aydınlatılamamış olsa da; hiperinsülinemi/insülin direnci ve insülin benzeri büyüme faktörü-I (IGF-I) sisteminde ve sinyal iletiminde görülen anormallikler, cinsiyet hormonlarının biyosentezi ve ilgili biyokimyasal yollar, subklinik düzeydeki kronik düşük dereceli inflamasyon ve oksidatif stres, adipositokin fizyopatolojisinde meydana gelen bozulmalar, ektopik yağ birikiminden kaynaklanan faktörler, mikroçevreye ve hücresel düzeye ait bozulmalar, sirkadiyen ritmin bozulması ve diyetle alınan besin öğeleri gibi hem obeziteye hem de kansere neden olan faktörler, bağırsak mikrobiyotasında meydana gelen değişiklikler aracılığıyla obezite ve kanserin ilişkili olduğu düşünülmektedir (Avgerinos vd., 2019; Renehan vd., 2015).

Obezite, çeşitli çalışmalarda farklı kanser türleriyle ilişkilendirilmektedir. Wei vd. (2025), çalışmalarında obezite ile akciğer kanserinin ilişkili olduğu, bu ilişkiye inflamasyonun aracılık ettiği ve bu ilişkinin kadınlarda daha belirgin olduğu sonucuna ulaşmışlardır. İsveç'te gerçekleştirilen kohort çalışmasında baş ve boyun, gastrointestinal sistem, malign melanom, genital organlar, endokrin organlar, bağ dokusu ve hematolojik maligniteler başta olmak üzere erkeklerde 15, kadınlarda 16, toplamda ise 18 kanser türü ile obezitenin ilişkili olduğu bulunmuştur (Sun vd., 2024). Pankreas kanseri olan hastalarla gerçekleştirilen çalışmada obezitenin ve özellikle deri altı dokusunda yağ dağılımı olmak üzere yağ dokusunun pankreas kanseri olan hastalarda sağ kalım ile ilişkili olduğu ve obezitenin

kanserin etiyopatogenezinde rol oynamasının dışında kanser hastalarında sağ kalım ile de ilişkili olduğu sonucuna ulaşılmıştır (Lee vd., 2025). Meme kanseri hastalarında gerçekleştirilen çalışmada ise yüksek BKİ'ye veya abdominal obeziteye sahip olmak felç dahil olmak üzere kardiyovasküler hastalık riskinde artış ile ilişkilendirilmiştir (Kim vd., 2025).

Alkol

IARC, alkol tüketimini insanlar için karsinojen (Grup 1) olarak sınıflandırmıştır. Alkollü içecekler çok sayıda karsinojenik bileşik içermekle birlikte, alkol tüketimi ile kanser gelişimi riski arasındaki ilişkinin büyük çoğunluğu etanolden kaynaklanmaktadır (Pflaum vd., 2016). Alkol ile kanser gelişimi riski ilişkisinin mekanizması tam olarak aydınlatılamamış olsa da etanolün varsayılan başlıca karsinojenik mekanizmaları arasında; etanolün, karsinojenik bir metabolit olan asetaldehite metabolize edilmesi, tek karbon metabolizması yolunun ve DNA metilasyonunun inhibisyonu (özellikle düşük folat alımına sahip bireylerde), endojen östrojen düzeylerini artırması, reaktif oksijen türleri ve polar metabolitlerin üretimi, etanol metabolizması yoluyla prokarsinojenlerin aktif karsinojenlere dönüşümü, lipid peroksidasyonu, prostoglandin üretimi, insülin benzeri büyüme faktörü 1 (IGF-1) yolunun değişimi ve tütün gibi çevresel karsinojenlerin hücre içine geçişi için çözücü görevi görmesi yer almaktadır (WCRF/AICR, 2018).

Alkol tüketimi 30-34 yaş arasında kanser ölümlerinin %13.9'undan sorumludur. Epidemiyolojik çalışmalar kronik alkol tüketiminin orofarenks, gırtlak, yemek borusu ve karaciğer kanseri başta olmak üzere üst sindirim sistemi kanseri için oldukça önemli bir risk faktörü olduğunu göstermektedir (Pöschl ve Seitz, 2004). Alkol ile kanser ilişkisinde doz-yanıt ilişkisi gözlenmekte ve bu ilişki neredeyse doğrusal bir artış göstermektedir. Alkolün kanser riskinde artışa neden olmadığı herhangi bir güvenli alt eşik düzeyi bulunmamaktadır (Bagnardi vd., 2015).

Alkol, kanser gelişim riskiyle ilişkilendirilse de böbrek kanseri riskini azaltıcı etki gösterdiğine dair kanıtlar mevcuttur. Bu durum, hafif ve orta düzeyde alkol tüketiminin insülin duyarlılığını artırması, kan lipid profilini iyileştirmesi ve adiponektin düzeylerini yükseltmesi ile açıklanmaktadır (WCRF/AICR, 2018). Benzer şekilde kırmızı şarabın resveratrol içeriği nedeniyle antikarsinojenik etki gösterebileceği düşünülse de bulgular, kırmızı şaraptaki resveratrolün önleyebileceği her bir kanser vakasına karşılık, etanol nedeniyle 100.000 kanser vakasının meydana geldiğini göstermektedir (Rehm vd., 2017).

Dünya Kanser Araştırma Fonu (WCRF) ve Amerikan Kanser Araştırma Enstitüsü'nün (AICR) kanser ve birçok kronik hastalığın önlenmesine yönelik önerileri

Sağlıklı vücut ağırlığında olun: Hayatınız boyunca vücut ağırlığınızı, sağlıklı yetişkin BKİ aralığında (18,5–24,9 kg/m²) kalmanızı sağlayacak şekilde korumaya çalışın.

Fiziksel olarak aktif olun: Hareketsiz kalmanıza yol açan alışkanlıklarınızdan uzaklaşın ve en az orta düzeyde aktif olun. Bu konuda ulusal kılavuzları takip edin.

Tam tahıllar, sebzeler, meyveler ve baklagiller açısından zengin bir diyet modeli benimseyin: Diyetle günde en az 30 g posa almaya özen gösterin. Öğünlerinizde sıklıkla tam tahıllar, nişastasız sebzeler, meyveler ve fasulye ve mercimek gibi baklagillere yer verin. Her gün en az 5 porsiyon nişastalı olmayan sebze ve meyve tüketin. Nişastalı kök ve yumruları temel besin olarak tüketiyorsanız, mümkünse nişastalı olmayan sebzeleri, meyveleri ve baklagilleri de düzenli olarak tüketin.

Fast food ve yağ, nişasta veya şeker içeriği yüksek diğer işlenmiş besinlerin tüketimini sınırlayın: Yağ, nişasta veya şeker içeriği yüksek işlenmiş besinlerin tüketimini sınırlayın. Bunlar arasında fast food (enerji yoğunluğu yüksek, sıklıkla ve büyük porsiyonlarda tüketilen hazır gıdalar), birçok hazır yemek, atıştırmalık, unlu mamuller ve tatlılar ile şekerlemeler (şeker) bulunmaktadır.

Kırmızı et ve işlenmiş et tüketimini sınırlayın: Kırmızı et tüketiyorsanız, tüketimini haftada 3 porsiyondan fazla olmamak üzere sınırlayın. Tuzlama, kurutma, fermantasyon, tütsüleme veya lezzeti artırmak ya da saklanabilirliğini iyileştirmek için diğer işlemlerden geçirilmiş et olan işlenmiş eti çok az tüketin veya hiç tüketmeyin.

Şekerli içeceklerin tüketimini sınırlayın: Su ve şekersiz içecekleri tüketmeyi tercih edin.

Alkol tüketimini sınırlayın: Alkollü içecek tüketimi birçok kanser türünün nedenidir. Kanseri önlemek açısından alkol tüketmemek en iyisidir. Kanser gelişme riskinin artışına neden olmayan bir alkol tüketim sınırı bulunmamaktadır.

Kanserden korunmak amacıyla takviye kullanmayın: Besin takviyesi, diyetle tek başına elde edilebilecek miktarın ötesinde mikro besinler veya diğer besin bileşenlerinin tüketim düzeylerine ulaşmak amacıyla “besin bileşeni” içeren, sindirim için tasarlanmış bir üründür. Çoğu insan için doğru besin ve içecek seçimi, besin takviyelerine karşı daha fazla koruma sağlamaktadır. Yüksek dozda besin takviyelerinin kanserin önlenmesi amacıyla kullanılması önerilmez; enerji, makro ve mikro besin ögesi gereksinimlerinizi diyetle karşılayın.

Anneler için; mümkünse bebeğinizi emzirin: Dünya Sağlık Örgütü tavsiyesine uygun olarak bebeğinizi mümkünse ilk 6 ay yalnızca anne sütü, 2 yaşına kadar uygun tamamlayıcı gıdalarla birlikte anne sütü ile besleyin.

Kanser teşhisi konulduktan sonra; mümkünse önerileri uygulayın: Tüm kanser hastaları, eğitimli uzmanlardan beslenme tedavisi ve fiziksel aktivite konusunda rehberlik almalıdır. Aksi tavsiye edilmedikçe ve mümkünse, tüm kanser hastalarının akut tedavi aşamasından sonra mümkün olduğunca kanserden korunmaya yönelik önerilere uymaları önerilmektedir (Clinton vd., 2020).

SONUÇ

Diyet kanserojenleri, çeşitli kanser türleriyle ilişkilendirilmektedir. Sağlıklı beslenme, yemek hazırlarken uygun hazırlama, pişirme ve depolama yöntemlerini kullanma, sağlıklı vücut ağırlığını koruma ve diyet kanserojenlerinin azaltılması özellikle diyetle ilişkili kanserlerin azaltılmasında önemli bir stratejidir.

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THE IMPACT OF NUTRITION ON NEURODEVELOPMENTAL AND PSYCHOSOCIAL HEALTH IN EARLY CHILDHOOD

ABSTRACT

Objective: Early childhood, encompassing the period from birth to approximately six years of age, represents one of the most critical and sensitive phases of human development. A significant portion of brain development is completed during the early years of life. Inadequate nutrition during this period can lead to permanent developmental delays. This study aims to emphasize the importance of this issue.

Materials and Methods: This study is based on a review of articles obtained from national and international databases such as Google Scholar, PubMed, Web of Science, and Google Academic. Articles published in Turkish and English that address issues related to "nutrition", "early childhood", "neurodevelopment" and "psychosocial health" were examined using both Turkish and English keywords.

Results: During early childhood, nutrition is closely associated with caregiving. Effective feeding supports both the growth and development of children at all ages. Supporting development requires not only the consumption of appropriate nutrients essential for the central nervous system but also effective communication during mealtimes. Healthy neurodevelopment depends on factors such as socioeconomic status, interpersonal relationships, and nutrition. It has been shown that stress, emotional deprivation, and inflammation contribute to impaired brain development. Early manifestations of these adverse effects include medical and psychosocial problems, reduced academic achievement and productivity, and the potential transmission of these issues to future generations. The proper functioning of brain chemicals (neurotransmitters) depends on essential nutrients. Deficiencies in iron (Fe), zinc (Zn), and omega-3 fatty acids have been associated with restlessness, aggression, anxiety, and attention difficulties. Children with balanced nutrition tend to be calmer, more cooperative, and socially engaged.

Conclusion: Healthy nutrition in early childhood forms the foundation of both cognitive and social development and is directly linked to long-term outcomes such as quality of life, academic success, and mental health. In this context, public awareness should be raised through a multidisciplinary approach involving families, educational institutions, and healthcare providers working in collaboration.

Keywords: Nutrition, early childhood, neurodevelopment, psychosocial health

BESLENMENIN ERKEN ÇOCUKLUK DÖNEMINDE NÖROGELIŞIMSEL VE PSIKOSOSYAL SAĞLIĞA ETKILERI

ÖZET

Amaç: Erken çocukluk, çocuğun doğumdan itibaren yaklaşık 6 yaşına kadar olan dönemi kapsayan, gelişim açısından en kritik ve hassas dönemleri barındıran evredir. Beyin gelişiminin önemli bir kısmı yaşamın ilk yıllarında tamamlanır. Bu dönemde yetersiz beslenme, kalıcı gelişimsel gecikmelere sebep olabilir. Çalışmada bu konunun önemine vurgu yapılması amaçlanmıştır.

Materyal ve Yöntem: Çalışmada "Google Scholar", "Pubmed", "Web of Science", "Google Akademik" gibi ulusal ve uluslararası veri tabanları taranarak ulaşılan makalelerden yararlanılmıştır. Araştırmada "beslenme", "erken çocukluk dönemi", "nörogelişim", "psikososyal sağlık", Türkçe ve İngilizce anahtar kelimeleriyle sorunlara ilişkin verileri içeren, yayın dili Türkçe ve İngilizce olan, makaleler incelenmiştir.

Bulgular: Bu dönemde beslenme, çocuklar için bakım ile aynı anlamı taşır. Etkili bir besleme her yaşta çocuğun hem büyümesini hem de gelişimini destekler. Gelişimin desteklenmesi sadece doğru besinlerin, merkezi sinir sisteminin gereksinimi olan besinlerin tüketilmesi yolu ile değil, aynı zamanda beslenme zamanlarındaki doğru iletişim ile mümkündür.

Nörogelişimin sağlıklı bir şekilde sürdürülmesi sosyoekonomik durum, kişiler arası ilişkiler ve beslenme faktörüne bağlıdır. Stres, emosyonel yoksunluk, inflamasyonun beynin az gelişmesinde etkili olduğu gösterilmiştir. Bu etkilerin erken belirtileri tıbbi ve psikososyal problemler, akademik başarı, üretkenlik kaybı ve bunlarında gelecek nesle aktarılması şeklinde görülmektedir. Beyin kimyasallarının (nörotransmitterler) sağlıklı ve dengeli çalışması için besin öğelerine ihtiyaç vardır. Yetersiz demir (Fe), çinko (Zn) ve omega 3 yağ asidi eksiklikleri; huzursuzluk, saldırganlık, anksiyete ve dikkat dağınıklığı ile ilişkilidir. Dengeli beslenen çocuklar daha sakin, uyumlu ve sosyal olarak katılımcı olma eğilimindedir.

Sonuç: Erken yaşta sağlıklı beslenme, hem bilişsel, hem sosyal gelişimin temeli olup, uzun vadede yaşam kalitesi, okul başarısı ve ruh sağlığıyla doğrudan bağlantılıdır. Bu konu bağlamında multidisipliner iletişimlerle ailenin, eğitim ve sağlık kurumlarının işbirliği içinde olduğu bir yaklaşım ile toplumun bilinçlendirilmesi büyük önem taşımaktadır.

Anahtar Kelimeler: Beslenme, erken çocukluk dönemi, nörogelişim, psikososyal sağlık

GİRİŞ

Erken çocukluk, doğumdan itibaren yaklaşık altı yaşına kadar süren ve gelişimsel açıdan kritik bir dönemi kapsayan bir evredir. Bu dönem, beynin gelişiminin büyük ölçüde tamamlandığı, çocuğun bilişsel, duyuşsal ve sosyal becerilerinin temellerinin atıldığı hassas bir zaman aralığıdır.

Bu süreçte çocuk, çevresindeki uyaranları anlamlandırma çabası içerisindedir ve dış dünyaya yoğun bir ilgi gösterir. Bu nedenle, erken çocukluk döneminde edinilen deneyimler, alınan eğitim ve benimsenen beslenme biçimleri bireyin tüm yaşamını etkileyebilecek düzeyde önem taşımaktadır[1-3]. Nitekim bu dönemdeki gelişimsel desteklerin birey ve toplum üzerindeki etkileri literatürde sıkça vurgulanmıştır.

Tablo I. Gelişen beyni etkileyen bazı çevresel faktörler

Normal gelişim için gerekli olanlar	Normal gelişim için zararlı olanlar
Sağlıklı gebelik ve doğum	Prenatal enfeksiyonlar
Oksijen	Alkol
Yeterli protein ve enerji	Sigara
Mikronütrientler (demir, çinko, gibi)	Kurşun
İyot	Poliklorinated bifenil (PCB)
Tiroid hormonu	İyonizan radyasyon
Folik asit	Kokain
Esansiyel yağ asitleri	Metabolik bozukluklar (fenilkefonuri, hiperamonemi gibi)
Duyusal uyarı	Alüminyum
Aktivite	Metilcıva
Sosyal ilişki	Kronik stres

Tablo 1'de görüldüğü üzere, erken dönemde beyin gelişimini etkileyen çevresel ve biyolojik faktörler iki grupta değerlendirilmektedir[4]. Beslenme, bu faktörler arasında özel bir yere sahiptir. Yeterli ve dengeli beslenme yalnızca büyüme ve nöromotor gelişimi değil; bağışıklık sistemi yanıtlarını, yaşlanma sürecinin yavaşlamasını ve çeşitli kronik hastalıkların (örneğin aterosklerotik hastalıklar, katarakt, maküla dejenerasyonu ve bazı kanser türleri) önlenmesini de doğrudan etkilemektedir.

Erken çocukluk döneminde uygulanacak gelişim destekleyici müdahalelerin önemi, yalnızca bireysel kazanımlarla sınırlı değildir. Bu müdahaleler, aynı zamanda çocukların gelişim hakkını güvence altına almak ve toplumsal refah düzeyini artırmak açısından da büyük önem arz etmektedir. Beyin gelişimi döllenme ile başlamakta ve kısa süre içinde hızla ilerleyerek adölesan döneme kadar devam etmektedir. Bu hızlı gelişim prenatal dönemden başlayıp okul çağına kadar geçen süreçte, çeşitli evreleri kapsayan çok aşamalı bir yapı sergilemektedir. Nöronların oluşum süreci; nörülasyon ve nörogenez evrelerini içerir. Oluşan nöronların uygun anatomik konumlarına yerleşmeleri migrasyonla sağlanır. Ardından, nöronlar arası iletişimin temelini oluşturan akson ve dendritlerin gelişimi, nöronal diferensiyasyon ve yol bulma (pathfinding) mekanizmaları aracılığıyla gerçekleşir. Sinaptik bağlantıların oluşumu sinaptogenez olarak adlandırılırken, bu bağlantıların seçilerek rafine edilmesi ve fonksiyonel olarak güçlendirilmesi sinaptik olgunlaşma sürecini oluşturur. Süreç sonunda, nöronların çevresinde destekleyici hücresel yapılar (glial hücreler) ve etkili sinir iletimini sağlayan miyelin kılıfların oluşumu gliagenez ve miyelinizasyon yoluyla tamamlanır[4-6].

Beyin, yüksek düzeyde enerji ve besin ihtiyacına sahip bir organdır. Ortalama olarak, toplam günlük enerji alımının yaklaşık %20'sini -yaklaşık 400 kilokalori- tüketir. Kütlesinin yaklaşık %60'ı lipitlerden oluşur ve yapısında yüksek oranda kolesterol ile çoklu doymamış yağ asitleri (PUFA'lar), özellikle Omega-3 yağ asitleri, bulunur.

Serotonin, norepinefrin ve dopamin gibi monoamin nörotransmitterlerin biyosentezi, ilgili amino asit öncüllerinin yeterliliğine ve mineral bağımlı kofaktörlerin varlığına bağlıdır. Bu süreçte, metilasyon döngüsü kritik bir rol oynar; söz konusu döngü, monoamin nörotransmitter sentezinde önemli bir kofaktör olan tetrahidrobiopterin'in (BH_4) üretimi açısından elzemdir. Folat ve çeşitli B vitaminleri, metilasyon döngüsünün sağlıklı işleyişi için gereklidir. Bu döngünün etkin çalışması, kardiyovasküler hastalıklar ve majör depresyon ile ilişkili yüksek homosistein düzeylerini de düşürür.

Omega-3 çoklu doymamış yağ asitleri (PUFA'lar), nöronal hücre zarlarının yapısal bütünlüğü açısından vazgeçilmez bileşenlerdir ve merkezi sinir sisteminde çok sayıda temel biyolojik süreci modüle ederler. Özellikle, nörotransmisyonun düzenlenmesinde, gen ekspresyonunun kontrolünde, nörogenez ve nöronal hayatta kalma mekanizmalarının desteklenmesinde doğrudan rol oynarlar. Bunun yanı sıra, antioksidan etkileri vardır ve anti-inflamatuar özellikler sergilerler [7-10].

Psikososyal Gelişim

Gelişim, döllenme ile başlayıp yaşam boyu devam eden; bireyin bilişsel, dilsel, sosyal, duygusal ve fiziksel alanlardaki deneyimlerinin tamamını kapsayan dinamik ve bütüncül bir süreçtir. Erken çocukluk döneminden itibaren insan gelişimini açıklamaya yönelik pek çok kuramsal yaklaşım geliştirilmiştir. Bu kuramlardan biri olan psikososyal gelişim kuramı, bireyin gelişimini sosyal ilişkiler bağlamında ele alır.

Psikososyal gelişim kuramının öncüsü Erik Erikson, bireyin yaşamı boyunca sekiz evreden geçtiğini öne sürer ve her bir evrenin belirli bir psikososyal çatışma içerdiğini belirtir. Erikson'a göre, bu çatışmaların başarılı bir şekilde çözülmesi, bireyin bir sonraki gelişim dönemine sağlıklı bir temel ile geçmesini sağlar. Söz konusu gelişim evreleri sırasıyla şu şekildedir[11]:

1. Temel güvene karşı güvensizlik
2. Özerkliğe karşı utanç ve kuşku
3. Girişimciliğe karşı suçluluk
4. Başarıya karşı aşağılık duygusu
5. Kimlik kazanmaya karşı rol karmaşası
6. Yakınlık kurmaya karşı yalnızlık
7. Üretkenliğe karşı duraklama
8. Benlik bütünlüğüne karşı umutsuzluk[11].

Erikson, gelişimi yaşam boyu süren sosyal bir süreç olarak ele alarak, bireyin bu kritik evrelerde hangi ihtiyaçlara sahip olabileceğine dikkat çeker. Her dönemde karşılaşılan çatışmaların başarıyla aşılmaması durumunda, bu çözülmemiş problemler sonraki gelişim evrelerini olumsuz yönde etkileyebilir ve bireyin yaşamında kalıcı sorunlara yol açabilir[12].

Çocuğun Psikososyal Gelişimini Destekleme Sürecinde Yoksulluk ve Ebeveyn Ruh Sağlığı Faktörleri

Çocuğun Psikososyal Gelişimini Destekleme (ÇPGD) programında dikkate alınan önemli etmenlerden biri de yoksulluktur. Yoksulluk; yetersiz besin alımı, elverişsiz fiziksel yaşam koşulları, çevresel toksinlere maruz kalma, annede depresyon, anne sütüyle beslenmenin azalması ya da tamamen kesilmesi, madde kullanımı, çocuğun ihmal ve istismar riskinin artması, aile içi çatışmalar, günlük bakımın yetersizliği ve çeşitli sağlık problemleri gibi birçok olumsuz duruma neden olabilmektedir.

Ebeveynlerin ruh sağlığı da çocuğun gelişimi açısından kritik öneme sahiptir. Ruhsal sorunlar, özellikle de ağır psikiyatrik bozukluklar, çocukta ihmal ve istismar riskini artıran önemli bir faktör olarak değerlendirilmektedir. Beardslee ve arkadaşlarının (1983) bulgularına göre, depresyon tanısı konmuş ebeveynlerin çocuklarında psikopatolojik bozuklukların ortaya çıkma olasılığı anlamlı düzeyde yüksektir[13]. Postpartum dönemde depresyon yaşayan annelerin ise bebeklerine karşı daha olumsuz tutumlar sergilediği ve bebekleriyle olumlu etkileşim kurma sıklığının azaldığı belirtilmektedir[14].

Bu nedenle, çocuğun psikososyal gelişimini destekleme görüşmeleri sırasında ebeveynlerin depresyon ve anksiyete düzeyleri değerlendirilmekte, ayrıca şizofreni, entelektüel yetersizlik (mental retardasyon) gibi çocuğun psikososyal gelişimini doğrudan olumsuz etkileyebilecek ciddi psikiyatrik rahatsızlıkların varlığı gözlemlenmektedir. Bu tür ruhsal bozukluklar, ebeveyn-çocuk etkileşimini sekteye uğratarak çocuğun sağlıklı gelişimini tehdit edebilir[15].

Erken Çocukluk Döneminde Çevresel ve Sosyal Faktörlerin Gelişime Etkisi

Erken çocukluk dönemi, bireyin çevresel uyarıcılara en duyarlı olduğu ve çevresinden en yoğun şekilde etkilendiği kritik bir gelişim evresidir. Bu dönemde çocuğun maruz kaldığı sosyal ve çevresel faktörler, fiziksel ve bilişsel gelişimini doğrudan ve orantılı şekilde etkilemektedir. Destekleyici olmayan çevresel koşullar; yetersiz beslenme, olumsuz sosyal ilişkiler, düşük uyarıcı ortamlar ve ihmal gibi risk faktörleri, çocuğun psiko-sosyal gelişiminde duraklamalara ve sapmalara yol açabilir.

Buna karşın, gelişimi destekleyen bir çevrede bulunan, yeterli ve dengeli beslenme ile sağlıklı yaşam koşullarına sahip olan çocuklar, bu dönemde gelişimsel açıdan güçlü bir temel oluşturma şansına sahiptir. Bu nedenle, erken müdahale yaklaşımları büyük önem taşır. Olumsuz çevresel faktörlerin erken tespit edilerek ortadan kaldırılması, çocuğun sağlıklı gelişim sürecinin sürdürülmesine katkı sağlamakta ve ileriki yaşantısında karşılaşabileceği gelişimsel riskleri en aza indirmektedir[16].

SONUÇ

Erken yaşlarda sağlıklı ve dengeli beslenme, çocuğun hem bilişsel işlevlerinin gelişimi hem de sosyal becerilerinin güçlenmesi açısından kritik bir öneme sahiptir. Bu dönemde yeterli besin alımı, sinir sistemi gelişimini destekleyerek öğrenme, dikkat, problem çözme gibi bilişsel süreçlerin sağlıklı biçimde yapılandırılmasına katkı sağlar. Aynı zamanda, sosyal etkileşimlerde bulunabilme, duygusal düzenleme ve dış dünyayla sağlıklı ilişkiler kurabilme kapasitesi üzerinde de belirleyici bir rol oynar.

Sağlıklı beslenmenin yalnızca fiziksel büyümeye değil, aynı zamanda uzun vadede yaşam kalitesine, okul başarısına ve ruh sağlığına doğrudan etkisi olduğu, çok sayıda bilimsel çalışma ile ortaya konmuştur. Bu nedenle erken yaşlardan itibaren çocukların beslenme ihtiyaçlarının karşılanması, gelişimsel gecikmelerin ve psikososyal sorunların önlenmesi açısından öncelikli bir müdahale alanı olarak ele alınmalıdır.

Bu sürecin etkili biçimde yürütülebilmesi, yalnızca bir alanın değil; ailenin, sağlık sisteminin ve eğitim kurumlarının iş birliği içinde hareket ettiği çok disiplinli bir yaklaşımı gerektirmektedir. Ancak bu bütüncül yaklaşım sayesinde, çocukların sağlıklı gelişimi güvence altına alınabilir ve yaşamlarının ilerleyen dönemlerinde karşılaşabilecekleri riskler en aza indirilebilir.

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THE IMPACT OF SENSORY PLAY ON THE IMMUNE SYSTEM AND PSYCHOLOGICAL HEALTH IN THE PRESCHOOL PERIOD

ABSTRACT

Objective: The significance of studies on early childhood is increasingly recognized. However, research investigating the effects of sensory play on the immune system and psychological health during early childhood remains scarce. This study aims to explore the impact of sensory play on immune function and psychological well-being in early childhood.

Material and methods: This review study will examine the effects of sensory play on the immune system and psychological health during early childhood by synthesizing data from existing biochemical and metabolic literature. Early childhood, defined as the 0–6 age range, is known to be the period of most rapid cognitive, social, emotional, and physical development. Studies indicate that 50% of cognitive development is completed by age 4 and an additional 30% between ages 4 and 8. Furthermore, approximately 33% of academic success is associated with the education received during the 0–6 age period.

Results: It is emphasized that environmental stimuli enriched through sensory play can enhance T-cell activity, thereby strengthening the immune system. Additionally, an increase in antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx) is expected, contributing to the regulation of immune responses via NF-κB signaling pathways. Literature also suggests that stress can suppress and destabilize both innate and adaptive immune responses.

Conclusion: This study investigates various sensory play activities that may help minimize stress factors in children, highlighting the importance of tactile stimulation in maintaining active neural connections. In addition to promoting sensory development, the psychological effects of sensory play on children have also been examined. Future in-depth studies are encouraged to further elaborate on this topic and contribute meaningfully to the existing literature.

Keywords: Sensory Games, Child Psychology, Immune System, Oxidative Stress, Cytokine Balance

Introduction

Child development is used to refer to the changes that occur in children as they grow up in terms of being physically healthy, mentally alert, emotionally balanced, socially competent and academically ready to learn. Early childhood years (0-6 years), which are characterised as pre-school period, are considered as critical period in terms of all stages of development. The fact that it is characterised as a critical period is considered in terms of the period when development is the fastest. In addition, the acquisition and development of developmentally basic features also takes place during this period. In this period when the growth and development of the child is witnessed most concretely, there is the acquisition of developmental equipment in brain development areas, especially physical development. Early childhood years, which have a very important place in the general development of the child, are also very important in terms of brain development. The brain capacity and power of children largely depend on how they realise their brain development until the age of three. The period from 0-3 years of age to six years of age, when this very rapid brain development takes place, is of critical importance in terms of brain development compared to other life periods. In particular, the development of the brain in early childhood provides the shaping of cognitive features characterised as executive functions. These executive functions continue their effects in terms of intellectual, language, emotional and social development throughout life.

In this context, in this article, the definition, characteristics, developmental contributions of play, sensory games, the effects of play on reducing stress, the effects of stress on growth hormones, happiness hormones, sexual personality formation, mental development as a result of negative effects on developmental retardation, speech difficulties, sexual identity confusion and communication skills will be revealed by reviewing the literature. Play also has a therapeutic function for children. Through play, children experience relaxation by expressing the fears, anxieties and conflicts in their inner worlds. They face their fears in play and gain the ability to cope with them. They reach a sense of satisfaction by realising their desires in play. Based on this fact, psychologists have used the healing power of play since the 1900s, and as a result, a very wide field of science called Play Therapy has emerged. The aim of this review study is to examine the effects of sensory play on child development from a multidimensional perspective and to examine the contributions of these games on neurological, psychosocial and academic development in the light of the findings in the literature. The educational and developmental role of sensory play in early childhood will be emphasised.

Early Childhood Development

Early childhood is one of the critical periods in development. This period forms the basis for the child's learning experiences, well-being and productivity in the later years of life. During this period, children grow and develop faster than in any other period of their lives. Children develop in four areas: motor, cognitive, social-emotional and language. Since there are individual differences in development, no two children have the same rate of development in any of these areas of development. In addition, each child's family, cultural and life history is different from each other. Child development is used to refer to the changes that occur in children as they grow up in terms of being physically healthy, mentally alert, emotionally balanced, socially competent and academically ready to learn. Early childhood years (0-6 years), which are characterised as pre-school period, are considered as critical period in terms of all stages of development. The fact that it is characterised as a critical period is

considered in terms of the period when development is the fastest. In addition, the acquisition and development of developmentally basic features also takes place during this period. In this period when the growth and development of the child is witnessed most concretely, there is the acquisition of developmental equipment in brain development areas, especially physical development. Early childhood years, which have a very important place in the general development of the child, are also very important in terms of brain development. When this period is managed in a healthy way, we think that children will be able to reveal their potential in a comfortable way.

Sensory Games

Play is one of the basic building blocks of children's learning, discovery and development processes. Sensory games are one of the types of games in which children gain experience by interacting with the environment, especially in early childhood. Sensory games are games in which basic senses such as touch, sight, hearing, smell and taste are used effectively and children get to know the environment through sensory experiences. These types of games support the child's motor skills, cognitive flexibility, attention span and problem solving abilities, as well as contributing to the sensory integration process. It also calms children, reduces stress levels and improves self-regulation skills. Research shows that sensory play positively affects both neurological and psychosocial development of children. Play also has a therapeutic function for children. Through play, children experience relaxation by releasing the fears, anxieties and conflicts in their inner world. They face their fears in play and gain the ability to cope with them. During the play process, children use all their bodies and mental activities effectively and get involved in the game.

- It is a type of game that appeals to sensory games, touching, hearing, seeing, smelling and tasting emotions play an active role, exploring, experiencing and learning, emotional play aims to support emotional integrity, balance developmental areas, reduce stress and encourage regulation, increase curiosity and desire to learn.

- Sensory games have a great contribution to cognitive motor emotional social development areas as a list of attention, memory, problem solving, motor skills, hand-eye coordination, muscle development, emotional relaxation, helping to cope with stress, social cooperation, sharing, empathy.

- Example sensory games can be playing with kinetic sand finger painting textured material boxes water sound light tables nature walks.

- Sensory games are games that enable children to explore the environment by using their five senses of sight, hearing, touch, smell and taste. These games are very important in supporting the physical, cognitive and emotional development of children, especially in the preschool period.

- Recognising the environment through the senses, developing fine motor skills, problem solving and establishing cause and effect relationships, reducing stress, providing a relaxing effect, supporting social communication and language development.

Benefits of Sensory Games for Immune System

The immune system (Immune System) is a complex interaction between cells and molecules that act to protect the organism against possible microorganism invasions, prevent disease, repair or destroy cells that have lost their function and provide wound healing. Early

childhood period is the fastest period of development and change in the whole human life in terms of maturation of the body and nervous system in general, increase in mobility, skills and communication capacity, and rapid change in interests and abilities (Kılıçgün, 2012). Preschool period has a very important place in human development and education. In this period, emotional, social, cognitive, language and sexual identity development continues in addition to the physical development of the child. Early childhood period is accepted as a period in which skills are easily acquired and brain development is also very fast.

Sedentary life and malnutrition, as the most important factors other than biological, genetic and environmental factors, are the reasons for the onset of chronic diseases from a very young age (Ministry of Health, 2014). Having good eating habits is another healthy living behaviour that can protect individuals from diseases and improve their quality of life. We think that individuals who have good eating habits and who have received adequate attention and emotional contact from their parents or caregivers may be more easily protected from diseases. We are continuing our research on the fact that children who have sufficient physical contact with their mothers during infancy and early childhood may have an advantage in their later life.

Effects of Play on Stress Reduction and Oxidative Stress

Physical movement helps to relieve stress active games reduce cortisol levels in the body moving also increases happiness hormones such as endorphins serotonin allows the expression of emotions play allows children to express their emotions such as fear anger anxiety in symbolic ways, especially role-playing games are important. It gives a sense of control During the game, the child is in an environment where he/she can control events and objects, this makes him/her feel safe in the face of stress and at the same time provides social support The games he/she plays with his/her friends strengthen the child's social ties, cooperation, sharing and trust relationship and also provide emotional relief The game provides a trust area for the child with its familiar and repetitive structure: Object loss refers to traumatic separation from important objects of attachment. It is thought that as a result of the rupture of love ties in the early period of life, a predisposition to depression develops, and the losses experienced in adulthood trigger depressive periods by revitalising the traumatic loss in childhood. According to Freud; while mourning is a reaction to the loss of an external entity, in the melancholic patient, the object of love has been lost even if the object is not really dead. Bowlby stated that the bonds that the child establishes with the mother or mother substitutes during the development of the child are the precursors of the bonds that will be established with other bonds of love in the later years of life (Aşkın, 1999). Loss of self-esteem: Fenichel argued that the depressed individual perpetuates the narcissistic abuse experienced in early childhood (not receiving enough love from parents), thus considering self-esteem and love as the same things and that depression is an attempt to repair the self.

Bibring stated that unsatisfied narcissistic desires in different psychosexual developmental stages lead to different depressive symptoms (Aşkın, 1999; Özmen, 2001). Major depressive disorder (MDD) is a chronic, recurrent psychiatric disorder with a high mortality rate and a lifetime prevalence of 3.6-8.5% (Gold et al., 2015; Marneros, 2006). In addition to environmental and genetic factors, irregularities between neurotransmitters and neuroendocrine dysregulation are important in its aetiology (Chiriţa et al., 2015). Oxidative stress is also known to be effective in the pathophysiology of MDD (Palta et al., 2014). There is a balance between oxidative and antioxidative systems in the organism under

physiological conditions. Disruption of this balance causes many neuropsychiatric disorders including MDD. Oxidative stress negatively affects neuronal signal transduction, cellular plasticity and neuronal plasticity and causes disruptions in critical brain circuits that regulate temperament and motor behaviour. These factors are thought to play a role in the development of symptoms associated with depression (Liu et al., 2015; Vaváková et al., 2015). These studies contribute to the hypothesis that bonds established with children in early childhood may prevent serious traumas such as major depressive disorder (MDD). It has been shown that oxidation metabolites are high and antioxidation metabolite levels are low in adults with MDD (Maes et al., 2011). Total oxidant status (TOS) and oxidative stress index (OSI) levels were found to be high and total antioxidant status (TAS) levels were found to be low in patients with depressive episodes (Galecki et al., 2009). Malondialdehyde (MDA), one of the lipid peroxidation products, has been investigated as an index of oxidative damage in adult MDD (Jordan et al., 2018). Superoxide dismutase (SOD) levels, one of the antioxidant defence system enzymes, have been shown to be low in adults with MDD (Siwek et al., 2013). Adolescents with unipolar depression have been reported to have higher TOS, OSI and MDA values and lower TAS compared to their healthy peers (Bilginer et al., 2021). The recurrent nature of MDD and its consequences that may result in suicide in adolescents show the necessity of early detection of this disorder and the importance of monitoring treatment response. Therefore, it seems that we need biomarkers that can be predictive for MDD. There are very few studies investigating oxidative stress parameters in paediatric and adolescent MDD patients. In this study, our primary aim was to compare oxidative stress parameters in early childhood with those of healthy children. However, there are almost no studies in this field in the literature. However, the above-mentioned studies suggest that establishing a healthy bond with children in early childhood will form important foundations for their future. Therefore, it is very important to determine the relationship between sensory games and immune system and oxidative stress parameters and clinical variables such as gender, height, weight, body mass index (BMI), blood pressure and severity of depressive symptoms. There is a great need for scientific research in this field in the future.

The Immune System and Cytokines in Early Childhood

Cytokines, which play a fundamental role in the body's defense responses, may vary in children depending on the activity of the immune system and various environmental, physiological or pathological factors. Therefore, cytokines, which are important molecules that provide communication between immune cells, can directly affect many conditions in childhood. Infections are among the conditions that most frequently cause changes in cytokine levels in children. Viral, bacterial, fungal or parasitic infections stimulate the immune system and cause an increase in many proinflammatory cytokines, especially IL-6, TNF-α and IL-1β. In some cases, such as severe viral infections, excessive cytokine release called a cytokine storm can be observed. This can lead to severe clinical conditions in children. In conditions such as asthma, allergic rhinitis and atopic dermatitis, the Th2 type immune response becomes dominant and an increase in the levels of cytokines such as IL-4, IL-5 and IL-13 is observed accordingly. Autoimmune diseases and chronic inflammatory conditions also significantly affect cytokine balance in children. Juvenile idiopathic arthritis is one of the most common autoimmune diseases in childhood, and it is known that proinflammatory cytokines such as IL-6, TNF-α and IL-17 are significantly increased in this disease. Nutritional status is another important factor that has indirect effects on the immune system. Conditions such as inadequate protein intake, vitamin and mineral deficiencies can weaken the immune response and reduce cytokine production. On the other hand, conditions related to overnutrition such as obesity can cause low-grade chronic inflammation, leading

to an increase in cytokines such as IL-6 and TNF-α. In addition, immunity can be suppressed due to an increase in cortisol levels, especially in chronic stress situations, and this can cause an increase or decrease in the levels of some cytokines.

Considering that IFN-gamma has various effects on the brain and is shown to be associated with other psychiatric diseases in the literature, it is thought that it may also be related to studies on early childhood. One of these effects is the effect of IFN-gamma on the tryptophan-kynurenine pathway, which has been suggested to play a role in studies on early childhood and other psychiatric disorders (Oades et al., 2010; Jemli et al., 2017; Evangelisti et al., 2017). When cytokines are activated, they convert tryptophan into kynurenine instead of serotonin and contribute to the decrease of serotonin (Dantzer et al., 2008). According to this information, increased IFN-gamma levels may play a role in the pathogenesis of early childhood by increasing synaptic pruning or affecting neurogenesis. Although there are studies in the literature on the effects of early childhood sensory games on the immune system and psychological health, studies in general support the assumption that there may be a relationship with IL-10 levels in children with attention deficit hyperactivity disorder (Oades et al., 2010; Verlaet et al., 2019). In a study conducted by Donfrancesco et al. in 2016, significantly higher serum IL-10 levels were detected in patients diagnosed with attention deficit hyperactivity disorder who were positive for Purkinje cell antibodies, and it was associated with reducing cerebellum damage, assuming that increased IL-10 levels play a protective role (Donfrancesco et al., 2016). IL-10 prevents the killing of cortical and cerebellar neurons by inhibiting the death of astrocytes caused by TNF-alpha and NMDA-induced excitotoxicity (Pahan et al., 2000; Grilli et al., 2000; Bachis et al., 2001). Although cytokines such as TNF-alpha, IL-1, IL-6 have been shown to have neuroprotective effects on dopaminergic neurons by inhibiting the production of reactive oxygen species and NO in glial cells in vivo and in vitro, there is also evidence that altered functionality of IL-10 may affect dopamine balance (Molina-Holgado et al., 2001; Arimoto et al., 2007; Platzer et al., 2000). According to the literature, it is reported that cytokines in children vary depending on many environmental and physiological factors such as infection, allergic reactions, autoimmune diseases, nutritional status and stress. It is understood that the balance between proinflammatory cytokines (IL-6, TNF-α, IL-1β) and anti-inflammatory cytokines (IL-10) in particular is decisive on both peripheral immune responses and the central nervous system. It is seen that the interaction between the immune system and the nervous system in early childhood is bidirectional and dynamic, and cytokines, especially IFN-γ, IL-6 and TNF-α, can play both physiological and pathological roles in processes such as neurodevelopment, synaptogenesis and neuronal survival. However, the limited number of studies in the current literature that directly reveal these relationships indicates that the subject needs further research. In general, the text evaluates the effects of childhood immune responses on neurodevelopmental processes with a multidimensional approach and provides important clues about the potential roles of cytokines in these processes. These findings are particularly noteworthy for understanding the contribution of the immune system to attention deficit hyperactivity disorder and other neurodevelopmental disorders, and are valuable for developing prospective biomarker-based diagnostic and therapeutic approaches. In conclusion, cytokine levels in children are affected by a wide range of factors, and these levels can provide important information about the current status of the child's immune system. Therefore, measuring cytokine levels in clinical trials and disease follow-up can be an important assessment tool for child health.

Conclusion

We believe that play is one of the ways that children can easily express themselves at any age, with any material they can access in any environment. Elements that will activate their different senses that they can come into contact with during play are important. Children need loving contact from their parents and caregivers. One of the studies that have been conducted on the vital importance of contact for children is René Spitz's experiment, an important psychological study examining how babies' development is affected when they experience emotional deprivation. Spitz compared babies in prison who had regular contact with their mothers with babies growing up in an orphanage but were deprived of sufficient emotional interaction. The results were quite striking: Despite their basic needs being met, babies in the orphanage experienced serious developmental disorders and high mortality rates were observed. This experiment is considered an important study that emphasizes the critical role of love and attention in child development.

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NEUROFILAMENT LIGHT CHAIN (NFL): AN EMERGING BIOMARKER FOR EARLY DETECTION OF ACUTE NEUROLOGICAL INJURY IN THE EMERGENCY DEPARTMENT

ABSTRACT

Objective: Acute neurological conditions such as sudden changes in consciousness, stroke, head trauma, encephalopathy and epileptic seizures are clinical conditions requiring rapid diagnosis and effective intervention. Although the diagnosis in the management of these conditions is mostly based on clinical examination and imaging methods, the lack of objective and quantitative biomarkers creates an important gap. The aim of this study was to evaluate the usability of neurofilament light chain (NfL) protein, a biomarker reflecting neuroaxonal damage, in the diagnosis and prognosis of acute neurological conditions.

Materials and Methods: In this study, recent publications analysing the relationship of NfL with central nervous system damage, measurement techniques and its place in clinical practice were reviewed. Scientific data on NfL levels, which are thought to reflect central nervous system damage during acute neurological diseases, were evaluated. In addition to the diagnostic value of NfL, the evaluation processes of NfL in plasma and serum by modern measurement techniques were analysed. In particular, original studies and systematic reviews examining the relationship between NfL levels and acute neurological pictures in patients admitted to the emergency department were included in the study.

Results: NfL is a protein found in the axonal structure of neurons and released into the circulation in case of damage. Its levels increase significantly in conditions such as stroke, head trauma, epileptic seizures and encephalopathy and parallel with the severity of the disease. Thanks to advanced measurement techniques, especially ultrasensitive methods such as Simoa, the levels of NfL in the blood can be reliably determined, expanding its clinical application.

Conclusion: NfL is a promising biomarker for early diagnosis and prognosis prediction in acute neurological conditions encountered in emergency departments. Its integration into clinical decision-making processes may support more effective patient management. In addition, measurement of NfL levels, which has the potential to be a biochemical biomarker, may provide important information on the prognosis of various diseases, especially traumas. In this context, more clinical studies are needed for the widespread use of NfL.

Keywords: NfL; Emergency neurological conditions; Biomarker; Simoa; Prognosis

Introduction

In patients presenting to emergency services, acute neurological conditions such as sudden changes in consciousness, stroke, head trauma, encephalopathy and epileptic seizures are among the life-threatening clinical conditions that require rapid diagnosis and urgent intervention. These conditions are characterized by sudden and temporary or permanent deterioration of brain functions, and determining the underlying cause in a short time is critical for the success of treatment. Especially during the initial evaluation, effective use of vital signs, neurological examination and imaging methods are decisive in shaping the treatment plan. In addition, since many of these conditions can lead to irreversible damage, a multidisciplinary approach and time management are of great importance. Urgent neurological conditions are serious clinical conditions that affect the central nervous system and require rapid intervention. These conditions include a wide spectrum such as changes in consciousness, acute ischemic stroke, hemorrhagic stroke, epileptic seizures, status epilepticus, head trauma, meningitis, encephalitis and metabolic encephalopathies. These conditions may present with sudden onset neurological symptoms and may cause permanent neurological damage, disability or death if left untreated. Rapid neurological assessment, laboratory tests and effective use of imaging methods are of great importance in diagnosis. While early diagnosis and appropriate treatment positively affect the patient's prognosis, delays may lead to irreversible consequences. The use of objective and quantitative biomarkers in the early diagnosis and differential diagnosis of emergency neurological conditions has become increasingly important in recent years. Especially in cases such as traumatic brain injury, stroke, encephalopathy and epileptic seizures, markers that can be measured in peripheral blood or cerebrospinal fluid (CSF) are useful in rapid diagnosis and prognosis. S100B, glial fibrillary acidic protein (GFAP), neuron specific enolase (NSE), brain-derived neurotrophic factor (BDNF) and Ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) can provide quantitative information about the severity of brain damage. In addition, indicators reflecting systemic response such as oxidative stress markers (e.g. MDA, SOD, GPx) and inflammatory cytokines (IL-6, TNF-α) are also helpful markers in the evaluation of some neurological conditions. Making these biomarkers applicable in the emergency department with rapid and reliable measurement methods will make significant contributions to clinical decision-making processes. However, more research is needed on the standardization, sensitivity, specificity and place of these biomarkers in clinical practice. There are limited studies evaluating the usability of neurofilament light chain (NfL) protein, a biomarker reflecting neuroaxonal damage, in the diagnosis and prognosis of acute neurological conditions. Neurofilament Light Chain (NfL) is one of the intermediate filaments that provide structural support in the axons of neuronal cells and stands out especially as an indicator of neuroaxonal damage. NfL reaches measurable levels in cerebrospinal fluid (CSF) and peripheral blood with central nervous system damage, and thanks to this feature, it is considered an important biomarker in the diagnosis and prognosis of various acute neurological diseases.

Neurofilament Light Chain (NFL)

Significant increases in NfL levels have been detected in conditions such as traumatic brain injury, ischemic and hemorrhagic stroke, status epilepticus, hypoxic encephalopathy and inflammatory encephalopathies. Especially with the development of high-sensitivity immunoassay methods (e.g. Simoa technology), NfL levels in serum and plasma can be measured reliably non-invasively (1). This can contribute to clinical decision support processes by providing rapid and objective assessment in emergency department conditions.

Findings in the literature show that NfL levels correlate with the severity of the disease, degree of neuronal loss and long-term neurological outcomes. In addition, it has been reported that increased NfL levels have a predictive value in terms of prognosis; for example, it is associated with poor clinical outcomes in stroke patients. However, the specificity of NfL may be limited because its levels can increase in many different neurological pathologies. Therefore, NfL should generally be interpreted together with clinical findings, imaging methods and other biomarkers (2). Neurofilament light chain (NfL) is said to be a prognostic blood biomarker in various neurological diseases, with blood levels of NfL indicating disease severity and/or progression in Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS) (1). Neurofilaments are structural proteins released following axonal damage that occurs during neuronal degeneration. Today, especially the NfL subtype of these proteins can be detected both in the cerebrospinal fluid (CSF) and in the blood thanks to advanced high-sensitivity tests. These properties have made NfL a sensitive biomarker for neurodegenerative disorders (3). In the first of three new studies, Ming-Jang Chiu and colleagues examined the link of NfL levels in plasma with motor and cognitive impairments in Parkinson's disease (PD). Of the 178 participants, 116 were diagnosed with PD, 22 with multiple system atrophy (MSA), and the remaining 40 were healthy controls. Participants' plasma NfL levels were measured at baseline and then their motor and cognitive function was monitored for an average of three years (1). The follow-up data obtained revealed that higher baseline plasma NfL levels in PD patients were associated with more rapid motor and cognitive deterioration over three years. These findings suggest that NfL is an indicator that can predict disease progression. "Determination of NfL level from blood samples may help early identification of PD patients with a progressive course," Chiu said . It is also thought that this marker could be used to monitor therapeutic responses in future treatment trials (1).

The second study focussed on ALS disease , where NfL had previously only been analysed in CSF. Eric Thouvenot and colleagues evaluated this biomarker to investigate the extent to which serum NfLlevels at the time of diagnosis are associated with the course of the disease (4). The study included 207 ALS patients and 21 healthy individuals. The researchers used multivariate analysis and Cox regression modelling to assess the prognostic power of serum NfL levels. High levels of NfL detected at the time of diagnosis were identified as an independent factor that increased the risk of death over the course of the disease. ‘NfL levels obtained by a simple blood test provide more information about ALS prognosis than clinical indicators used so far,’ Thouvenot said (4). In the last study, the team led by Robert Zivadinov investigated the relationships between serum NfL levels and magnetic resonance imaging (MRI) findings in multiple sclerosis (MS) patients. The study included 120 people with relapsing-remitting or progressive MS and a group of 47 healthy individuals (5). At baseline and during five years of follow-up, brain lesion volumes and volumes of various brain regions were measured by MRI; serum NfL levels were also assessed. In MS patients, NfL levels measured at baseline were significantly associated with T1 and T2 lesion volumes and gadolinium-enhancing lesions. In addition, high initial serum NfL levels were found to be associated with increased atrophy in the whole brain volume, grey matter and deep grey matter nuclei in the following years (1).

The Place of NFL in Clinical Applications

Neurofilament light chain (NfL) is a structural component of neuronal axons and stands out as a quantitative biomarker of neuroaxonal damage by reaching measurable levels in cerebrospinal fluid (CSF) and peripheral blood after central nervous system (CNS) injury.

Recent studies have shown that NfL is a potential tool in the diagnosis, prognosis and monitoring of treatment response in various acute and chronic neurological diseases.

Measurement Techniques

NfL can be measured in both CSF and serum/plasma samples. High-sensitivity immunoassay methods developed in recent years, especially Single Molecule Array (Simoa) technology, provide non-invasive and reliable measurement of NfL levels in serum and plasma. These techniques allow for more widespread use of NfL in clinical applications.

The clinical application of NfL has been investigated in studies conducted in various neurological diseases: Multiple Sclerosis (MS): A meta-analysis in MS patients showed that blood NfL levels were significantly higher in MS patients compared to controls and that these levels were associated with disease activity and prognosis. Amyotrophic Lateral Sclerosis (ALS): In ALS patients, serum and CSF NfL levels were found to correlate with the rate of disease progression and that higher NfL levels were associated with worse prognosis. Neurological Outcomes After Cardiac Arrest: A meta-analysis after cardiac arrest showed that serum NfL levels had high sensitivity and specificity in predicting neurological outcomes.

Increased NFL in Acute Neurological Disorders

Stroke: In patients with acute ischemic stroke, NfL levels begin to rise early and this increase correlates with infarct volume. In addition, NfL levels are significantly higher in cases with poor prognosis. Increased NfL can also be used as a potential biomarker in the assessment of response to reperfusion treatments (thrombolytic therapy or thrombectomy).

Traumatic Brain Injury (TBI): sNfL levels after head trauma are directly related to the severity of the injury. Significant increases in sNfL levels have been observed even in mild TBI cases, and this increase can continue for days or even weeks. The fact that NfL remains stable during this period indicates that it may have diagnostic value in the late period.

Epilepsy and Status Epilepticus: Increased NfL levels after prolong seizures reflect axonal damage caused by recurrent seizures. Especially in cases such as status epilepticus, NfL elevation can provide information about the duration and severity of neuronal damage.

Encephalopathy: NfL levels increase significantly, especially in hypoxic-ischemic encephalopathy and metabolic encephalopathies, and this increase is parallel to clinical improvement or deterioration.

Conclusion

NfL is a promising biomarker that can be used in early diagnosis and prognosis prediction in acute neurological conditions encountered in emergency departments. Its integration into clinical decision-making processes may support more effective patient management. In addition, measurement of NfL levels, which has the potential to be a biochemical biomarker, may provide important information about the prognosis of various diseases, especially traumas. In this context, more clinical studies are needed for the widespread use of NfL.

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BIOCHEMICAL CAUSES OF PHOSPHORYLATED TAU INCREASE: CRITICAL CLUES FOR ALZHEIMER'S

ABSTRACT

Objective: Alzheimer's disease (AD) is a multifactorial neurodegenerative disorder characterised by progressive cognitive loss. In addition to amyloid-β deposition, abnormal increase in phosphorylated tau (p-tau) protein plays an important role in the pathogenesis of the disease. The aim of this study is to address the biochemical mechanisms underlying p-tau accumulation from a holistic perspective and to examine how the factors leading to the increase in phosphorylated tau may shed new light on Alzheimer's research.

Materials and Methods: In this study, the biochemical origins of p-tau accumulation in the pathogenesis of Alzheimer's disease were investigated in detail. It is supported by the literature that tau protein normally regulates microtubule stability and provides synaptic communication between neurons, but when it is excessively phosphorylated, it loses its structural function and tends to aggregate. The role of factors such as imbalances between protein kinases (GSK-3β, CDK5) and phosphatases (PP2A), oxidative stress and neuroinflammation in the phosphorylation process was evaluated.

Results: Studies reveal that the mechanisms directly affecting the increase of p-tau are of great importance for the early diagnosis and treatment of Alzheimer's disease. In particular, disruption of the balance between protein kinases and phosphatases, oxidative stress and neuroinflammation are important biochemical determinants of p-tau accumulation. Furthermore, indirect effects of amyloid-β on p-tau play an important role in the progression of the disease.

Conclusion: Our study integrates the current literature on the increase of phosphorylated tau protein and sheds light on new approaches in Alzheimer's research. These findings emphasise the importance of biochemical biomarkers in the early diagnosis of Alzheimer's disease and the development of treatment strategies. Furthermore, therapeutic approaches targeting the reduction of phosphorylated tau have the potential to slow the progression of Alzheimer's disease and may guide future research.

Keywords: p-tau; Alzheimer's disease; Biochemical mechanisms; Protein kinases and phosphatases; Neuroinflammation and oxidative stress

Introduction

The better understanding of Alzheimer's Disease (AD) and its consequences in the scientific world has increased the studies on the treatment of the disease. Although many studies have been conducted on the pathogenesis of AD, research on this subject is still ongoing. Amyloid beta (Aβ) peptide, neurofibrillary tangles (NFN) and hyperphosphorylated Tau protein are considered to be the most important pathological findings of the disease. In addition, factors such as inflammation, oxidative damage, glutamate excitotoxicity, insulin resistance, cholinergic loss and synapse-neuron loss are thought to contribute to this neurodegeneration (1). In AD, there are characteristic abnormal protein aggregates, including hyperphosphorylated Tau in NFM and Aβ peptide in senile plaques, and progressive brain atrophy. In recent studies on AD, it has been shown that many factors affect the risk and expression of the disease. It has been reported that tumour necrosis factor-alpha (TNF-α), IL-1 (especially IL-1β) and IL-6, which are proinflammatory cytokines formed due to inflammation in AD, are increased in CSF. It is thought that increased TNF-α is involved in endothelial and microvascular dysfunction and this is thought to lead to amyloid plaque formation (2).

The relationship between cognitive impairment in the early stage of AD and insulin resistance is related to the increase in Aβ. Insulin is secreted from beta cells of the pancreas to maintain glucose homeostasis in the periphery. It is also known that insulin has an important role on metabolism and cognitive functions in the brain (3). Insulin affects Aβ production via MEK-ERK pathway. For example, ApoE directly regulates the degradation and binding of Aβ and decreases insulin signalling and glucose in the brain (4). In the hippocampus, the ERK cascade has been shown to be necessary for the induction and maintenance of long-term potentiation (LTP) and memory enhancement. Because the ERK cascade enables the convergence of a large number of signalling cascades including CaMKII, PKA and PKC and is activated by a large number of receptors and secondary messengers involving cell homeostasis (4). Due to the accumulation of beta amyloid, intercellular communication is disrupted, cell death increases and ultimately the tissue (or organ) becomes unable to function. Among Aβs, Aβ40 and Aβ42 are the most common forms and the ratio of Aβ42 to Aβ40 is thought to be important. Although this ratio is not an important criterion for the onset of AD, it may cause interindividual variations in total amyloid load. Although both forms are toxic, Aβ42 is insoluble and accumulates in amyloid plaques, leading to early dendritic and synaptic damage and thus neurodegeneration in the brain due to neuronal cytotoxicity (5). Aβ40 has even been shown to inhibit Aβ42 oligomerisation. Therefore, according to the amyloid cascade hypothesis, it is predicted that the increase in Aβ42 level is more parallel with the onset of AD. In Tg2576 mice, when the relationship between the ratio of Aβ42 to Aβ40 and Morris Water Maze (MWM, memory-learning test) or Novel Object Recognition (NOR, novel object recognition test) tests was examined, it was shown that there was a linear relationship between problems in spatial functions and memory and Aβ ratios (6). However, some authors emphasise that there are problems in the amyloid cascade hypothesis and claim that Aβ42 is not a factor causing the onset of AD (7).

Aβ and tau in AD

AD is a complex neurodegenerative disease characterised by multiple pathogenic mechanisms, among which the amyloid cascade and tau hyperphosphorylation hypothesis are widely accepted as central paradigms explaining its progression (8-10). The amyloid

cascade hypothesis postulates that neurodegeneration in AD results from the abnormal deposition of Aβ plaques in specific brain regions (10). This pathological accumulation triggers a cascade of events, including neuritic injury, synaptic dysfunction and the formation of neurofibrillary tangles (NFTs) through tau protein aggregation, ultimately resulting in neuronal dysfunction and cell death (8,10).

In contrast, the tau hyperphosphorylation hypothesis emphasises the pathological role of abnormally phosphorylated tau protein. In this model, excessive tau phosphorylation leads to the formation of NFTs within neurons (8,9). This process disrupts the normal association of tau with microtubules and thus impairs microtubule stability and neuronal plasticity. Accumulation and aggregation of hyperphosphorylated tau exacerbates neuronal damage and contributes to the progression of AD pathology (11).

Tau Pathology

Alzheimer's disease (AD) is the most common cause of dementia worldwide, poses major social and economic challenges, and disproportionately affects older adults (12,13). AD is characterised by progressive memory loss, cognitive decline and eventually impairment of behaviour, speech and motor systems (14). The pathogenesis of AD is complex and involves multiple interconnected pathways; its hallmark pathological features are the accumulation of extracellular beta-amyloid (Aβ) plaques and intracellular neurofibrillary tangles composed of hyperphosphorylated tau protein (15). Given the complexity and burden of AD, developing effective treatment options has been a central focus of research. Until recently, the Food and Drug Administration had approved only a limited number of treatments, including cholinesterase inhibitors (e.g., donepezil, galantamine, and rivastigmine) and an N-methyl-D-aspartate (NMDA) receptor antagonist (e.g., memantine) (16). However, recent developments have led to the approval of Aβ-targeted drugs such as aducanumab and lecanemab, which aim to slow the progression of AD (16,17). This marks a significant shift towards therapies targeting pathological proteins such as Aβ and tau, reflecting an evolving approach to the management of this challenging disease. Several genetically modified rat models have been used to elucidate mutated forms of human Tau protein. The mutated Tau protein causes the development of neurofibrillary disruption. This is because rats, like humans, carry 6 Tau isoforms. This has led to the creation of rat models of Tau pathology. Overexpression of truncated, unmutated human Tau protein in neurons causes both hyperphosphorylation of Tau and the development of neurofibrillary disruption as in AD. Behavioural analyses elucidate both progressive cognitive decline and impairments in sensorimotor and reflex responses. These impairments have been shown to be directly proportional to the continuous accumulation of NFY and the mature Tau complex and to excessive axonal damage in the brainstem and spinal cord. Although excessively phosphorylated Tau is observed in the cortex and hippocampus, there is no loss of neurons in the brain. In addition, these impairments were found to cause a shortened life span (18). The first rat model provided an understanding of NFY formation in the cortex and truncated, unmutated human Tau protein. While progressive neurofibrillary deterioration was observed in these rats up to 9 months, surprisingly, no neuronal death was observed in the cortex, in the region where the tangle was over-accumulated or in the region where the expression of human Tau protein was highest. However, the life span of these rats was shortened. It is aimed to study more Tau gene transfer models in the coming years (19).

Overview of P-Tau Types

Tau protein has more than 30-40 potential phosphorylation sites. Some of these can be detected by specific immunological tests and certain p-tau species are particularly prominent in the diagnosis and staging of Alzheimer's disease.

p-tau181:

P-tau181 is the oldest and most widely used biomarker for the diagnosis of AD in both CSF (cerebrospinal fluid) and blood (20). It was widely used in early studies because it is relatively easy to detect. New technologies enable more specific and sensitive measurements in blood (21,22). However, some studies have shown the existence of p-tau species with greater diagnostic value than p-tau181 (23,24).

p-tau231:

p-tau231 may be more sensitive for the diagnosis of AD, especially in the early stages of the disease (preclinical and prodromal stages) (25,26). This form has been shown to be elevated at an earlier stage than p-tau181 and to have higher AD specificity. However, its levels in the blood are low and therefore detection is more difficult.

p-tau217:

p-tau217 is one of the most promising AD biomarkers. In individuals with AD, it shows a higher fold change (up to 4-fold) than p-tau181 (27). p-tau217 has been shown to be more specific in differentiating AD from control groups in CSF and blood and more successful in differentiating from other neurodegenerative diseases (28,29). Although its level in blood is low, this problem has been overcome with high-sensitivity measurement techniques. Furthermore, p-tau217 has been shown to be more specifically associated with Aβ plaques and not elevated in other tauopathies (e.g. PSP, CBD) (30).

Clinical Use of p-tau Biomarkers

In recent years, the importance of plasma phosphorylated tau (p-tau) proteins among biomarkers of Alzheimer's disease (AD) has increased. Various immunological assays have been developed for different phospho-epitopes (e.g. p-tau181, p-tau217 and p-tau231) and these assays are used both in the diagnosis of the disease and in the detection of early stages. However, the performance of these analyses may vary depending on the platform used, antibody types and technical details.

Plasma p-tau231 analysis shows strong associations with early stages of Alzheimer's disease, especially when applied on the UGot Simoa platform. This analysis revealed low Aβ PET signals and higher correlations with biomarkers in cognitively intact individuals. These features make it a promising candidate for the detection of preclinical Alzheimer's disease (31,32).

However, the p-tau181 assay used in the ADx Simoa platform showed stronger performance in terms of specificity and positive predictive value. This test offers high accuracy in recognising symptomatic and preclinical Alzheimer's disease and can give more successful results than previous p-tau181 tests using AT270 antibody (32).

p-tau217 test has also gained an important place in clinical research. Especially the p-tau217 test developed on the Lilly MSD platform offers high specificity in differentiating

Alzheimer's disease from other neurodegenerative diseases, and can better predict longitudinal tau accumulation and cognitive decline. For preclinical diagnosis of Alzheimer's disease, this test is reported to show higher sensitivity than both p-tau181 and p-tau231 analyses (31,32).

In addition, similarities and consistencies have been observed between p-tau217 assays developed on different platforms. For example, p-tau217 assays developed on Janssen Simoa and Lilly MSD platforms provided similar accuracy levels in many criteria such as cognitive impairment and Alzheimer's diagnosis. The results of these tests show a high level of agreement with each other in both cross-sectional and longitudinal cohorts (32).

In conclusion, p-tau biomarkers have an important potential in the detection of different stages of Alzheimer's disease. p-tau231 is particularly prominent in early stage detection, while p-tau217 is considered as a strong biomarker both diagnostically and prognostically. p-tau181, on the other hand, offers high specificity when used in appropriate analysis platforms, making it preferable in clinical studies (31,32).

Role of PP2 A/PTEN/GSK3β Axis in AD

Protein phosphatase 2A (PP2A) plays an important role in the pathogenesis of Alzheimer's disease (AD). PP2A shows neuroprotective effects by suppressing hyperphosphorylation of tau protein and amyloidogenesis processes (33). However, in AD, the catalytic activity and methylation of PP2A are decreased and the expression of its regulatory subunits is impaired (34). These disorders increase the hyperphosphorylation of tau protein and microtubule destabilisation and negatively affect synaptic plasticity (35).

ApoE4 allele suppresses the expression of PPP2R5E, a subunit of PP2A, which may contribute to tau pathology (34). Furthermore, PP2A inhibitor proteins (I1PP2A and I2PP2A) and impairments in PTPA expression increase PP2A inactivation in AD (36).

On the other hand, astrocytic lactoferrin expression may decrease Aβ production via APP dephosphorylation by increasing PP2A activity and this is considered as a potential therapeutic strategy against AD (37). GSK3β and other protein kinases have also been shown to contribute to PP2A inactivation (38). However, the exact mechanisms of these complex PP2A-related signalling pathways in AD pathogenesis are still unclear.

Biochemical Causes of Increased Phosphorylated Tau

Tau protein is a microtubule-associated protein involved in the stabilisation of microtubules. In Alzheimer's disease and other tauopathies, tau protein is abnormally hyperphosphorylated, leading to disruption of microtubule structure, synaptic dysfunction and neuronal degeneration. Hyperphosphorylation of tau is associated with increased activity of protein kinases, particularly glycogen synthase kinase-3β (GSK-3β), CDK5, MAPK and PKA. At the same time, the decrease in phosphatases such as protein phosphatase 2A (PP2A) increases this imbalance. Cellular stress factors such as oxidative stress, mitochondrial dysfunction and inflammation disrupt this kinase/phosphatase balance, promoting pathological phosphorylation of tau. These biochemical changes play a critical role in the neurodegenerative process by causing tau to lose its normal function and form toxic aggregates.

Conclusion

In conclusion, phosphorylated tau protein accumulation in Alzheimer's disease is one of the main determinants in the pathogenesis of the disease, and a detailed understanding of the biochemical mechanisms governing this process is of great importance. In particular, decreased activity and disturbances in the regulation of phosphatases responsible for tau dephosphorylation, such as PP2A, play a critical role in the progression of tau pathology. Numerous factors, such as loss of balance between protein kinases (e.g. GSK-3β and CDK5) and phosphatases, oxidative stress, disturbances in glucose metabolism and neuroinflammatory responses, trigger phosphorylation imbalance and predispose to the formation of neurotoxic tau aggregates. Understanding these complex biochemical interactions has great potential for both the development of biomarkers for early diagnosis and the identification of effective treatment strategies for the disease.

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EVALUATING THE CYTOTOXIC AND PROLIFERATIVE EFFECTS OF BEE VENOM ON PROSTATE CANCER CELLS: INSIGHTS FROM LNCAP CELLS

ABSTRACT

Prostate cancer is one of the most prevalent malignancies among men and poses ongoing challenges due to therapy resistance and recurrence. Bee venom (BV), a natural compound derived from *Apis mellifera*, has demonstrated potential anticancer properties, but its effects appear to be dose-dependent and context-specific. This study investigated BV's cytotoxic and proliferative effects on androgen-sensitive LNCaP prostate cancer cells. LNCaP cells were exposed to a range of BV concentrations (0.312–20 µg/mL), and cell viability was assessed using the MTT assay. A wound healing assay was also performed with selected doses (0.625–15 µg/mL) to evaluate cell migration. High-performance liquid chromatography (HPLC) confirmed the presence of melittin (70.98%), phospholipase A2 (14.36%), and apamin (4.05%) as major BV components. The results revealed a biphasic response: cell viability decreased significantly at 5 µg/mL, peaked at 10 µg/mL, and declined again at higher concentrations. While 10 µg/mL did not differ significantly from the control, it showed a significant increase compared to 5 µg/mL. In the wound healing assay, only the 10 µg/mL and control groups achieved complete closure within 24 hours, while other concentrations required up to 30 hours. These findings indicate that BV exerts both cytotoxic and proliferative effects on LNCaP cells in a dose-dependent manner. The proliferative response at 10 µg/mL suggests a narrow therapeutic window, underscoring the importance of precise dosing in potential clinical applications.

Keywords: Bee venom, Honeybee, LNCaP, Prostate cancer

1. Introduction

Prostate cancer is recognized as the second most commonly diagnosed malignancy among men and a leading cause of cancer-related mortality globally, posing significant challenges in treatment due to factors such as high recurrence rates and the development of resistance to therapies (Badawi, 2021; Park et al., 2010). The progression of prostate cancer correlates strongly with age; thus, with an aging global population, the incidence is expected to rise substantially soon (Badawi, 2021). Current treatment modalities, including radical prostatectomy, radiotherapy, androgen deprivation therapy (ADT), and chemotherapy, each have distinct drawbacks, underscoring the critical need for effective and innovative therapeutic strategies that are both safe and affordable (Badawi, 2021; Oršolić, 2011).

Recent research has focused on natural compounds for potential therapeutic applications, particularly animal venoms. Bee venom (BV) from the honeybee Apis mellifera exemplifies this interest, showcasing diverse bioactivities in cancer treatment (Badawi, 2021; Małek et al., 2023). The complexity of BV, which contains active peptides such as melittin, phospholipase A2, and apamin, contributes to its multifaceted pharmacological potential. Preclinical studies illustrate BV's capability to induce cytotoxicity, apoptosis, and anti-inflammatory effects across various cancer types, including prostate cancer (Elfiky et al., 2019). Notably, melittin stands out as a primary component linked to membrane disruption, NF-κB signaling inhibition, and apoptotic pathway induction (Badawi, 202; Park et al., 2010; Małek et al., 2023).

However, the cytotoxic properties of BV reveal an intriguing biphasic behavior. Research indicates that lower concentrations may potentially stimulate cellular proliferation and migration (Elfiky et al., 2019). This observation emphasizes the importance of determining optimal dosing and understanding the context-dependent roles of BV in cancer therapy (Zade, 2024). Evidence supports that BV can selectively target cancer cells while sparing normal cells, presenting a promising avenue for future therapeutic applications (Elfiky et al., 2019; Małek et al., 2023). The antagonistic effects of BV's components necessitate careful exploration, especially in the context of the estrogen-sensitive LNCaP prostate cancer cell line, which represents a valuable model for investigating hormonal influences on cancer treatment efficacy Park et al., 2010; Małek et al., 2023).

In the current study, the aim is to evaluate how BV impacts LNCaP prostate cancer cells, focusing on its cytotoxic and proliferative effects across varying concentrations. The hypothesis posits that while high concentrations of BV will demonstrate cytotoxic effects, lower doses could promote proliferation or migration. Through assessing cell viability and wound healing following BV exposure, the research intends to contribute valuable insights into the dose-dependent effects of bee venom on androgen-regulated prostate cancer cells, furthering understanding of its potential role in therapeutic and regenerative medicine approaches (Oršolić, 2011; Park et al., 2010; Małek et al., 2023).

2. Material and Methods

2.1. Bee Venom Collection, Preparation, and Analysis

Bee venom used in this study was collected in September 2021 from *Apis mellifera anatoliaca* colonies located in Muğla, Turkey. The venom was harvested using a Beesas bee venom collector system (BeeSas Beekeeping, Turkey). During collection, bees were stimulated to release venom onto sterile glass plates. Once dried, the venom residues were carefully scraped off using a sterile lancet. The collected material was then lyophilized and stored at –20 °C until further use.

The biochemical composition of the bee venom was characterized at the Food Analysis Application and Research Center of Muğla Sıtkı Koçman University. Component profiling was conducted via high-performance liquid chromatography (HPLC) using an Agilent 1260 analytical system, which included a binary pump, degasser, autosampler, column oven, and variable wavelength detector (VWD). A Poroshell C18 analytical column was employed to achieve separation of major bioactive components such as apamin, phospholipase A2 (PLA2), and melittin. Chromatographic separation was performed at a column temperature of 20 °C with a flow rate of 1 mL/min, and absorbance was monitored at 218 nm.

2.2. Cell Viability Assay

The cytotoxic effects of bee venom on LNCaP prostate cancer cells were evaluated using the methyl thiazolyl tetrazolium (MTT) assay. LNCaP cells were seeded into 96-well plates at a density of 1×10^4 cells per well and allowed to adhere for 24 hours under standard culture conditions. A bee venom stock solution (10 mg/mL) was prepared in phosphate-buffered saline (PBS) and sterilized using a 0.22 µm membrane filter. Cells were treated with a series of bee venom concentrations, including 0.312 µg/mL, 0.625 µg/mL, 1.25 µg/mL, 2.5 µg/mL, 5 µg/mL, 7.5 µg/mL, 9 µg/mL, 10 µg/mL, 12 µg/mL, 15 µg/mL, 18 µg/mL, and 20 µg/mL, for 24 hours.

After treatment, 100 µL of MTT solution (5 mg/mL) diluted 1:10 in low-glucose, serum-free medium was added to each well. The plates were then incubated for 4 hours to allow for formazan formation. To dissolve the resulting crystals, 100 µL of 10% sodium dodecyl sulfate (SDS) was added to each well. Absorbance was subsequently measured at 570 nm using a microplate reader (Sunrise, Tecan GmbH, Austria) to determine cell viability.

2.3. Wound Healing Assay

LNCaP cells were seeded at a density of 1×10^5 cells per well in 6-well plates and cultured under standard conditions (37 °C, 5% CO_2) until they reached approximately 70–80% confluency within 24 hours. To perform the wound healing assay, a linear scratch was made through the cell monolayer at the center of each well using a sterile 1 mL pipette tip. Detached cells and debris were removed by rinsing the wells twice with phosphate-buffered saline (PBS).

After cleaning the wound area, fresh culture medium supplemented with bee venom at five different concentrations (0.625, 2.5, 7.5, 10, and 15 µg/mL) was added to each well. The plates were then incubated for an additional 24 hours. Following treatment, the cells were gently washed three times with PBS, and wound closure was monitored by capturing images at two-hour intervals over 30 hours. The remaining scratch area was analyzed using Leica Application Suite software, and the percentage of wound closure was quantified and compared across treatment and control groups.

2.4. Statistical analysis

Statistical analysis was performed to determine the effects of different bee venom concentrations on LNCaP cell viability as measured by the MTT assay. A two-way analysis of variance (ANOVA) was used to evaluate the interaction between concentration and response. Where significant differences were detected, Tukey's post hoc test was applied to identify specific group differences. All data were analyzed using GraphPad Prism (GraphPad Software, USA), and results were expressed as mean ± standard deviation (SD). Statistical significance thresholds were set as follows: *P <0.05, **P < 0.01, ***P < 0.001, and ****P < 0.0001.

3. Result

3.1. Bee Venom Determination

The quantification of major bioactive components in bee venom was carried out using high-performance liquid chromatography (HPLC) equipped with a variable wavelength detector (VWD). The analysis identified apamin, phospholipase A2, and melittin as the primary constituents, with relative abundances of 4.05%, 14.36%, and 70.98%, respectively.

3.2. Cell Viability Assay

The cell viability assay was performed on LNCaP cells treated with bee venom at concentrations of 0.312, 0.625, 1.25, 2.5, 5, 7.5, 9, 10, 12, 15, 18, and 20 µg/mL. To quantify viable cell numbers, a calibration curve was constructed using absorbance values corresponding to known cell counts of 500, 1000, 2000, 3000, 4000, 6000, 8000, and 12,000 cells. The absorbance values obtained from each experimental group were then interpolated onto this standard curve to estimate the number of viable cells per well following treatment.

Cell viability analysis revealed no significant difference between the 0.312 µg/mL bee venom group and the control. A gradual decline in viability was observed from 0.312 µg/mL to 5 µg/mL, with the 5 µg/mL concentration resulting in a significantly lower viability compared to the control ($P < 0.05$). From 5 µg/mL to 10 µg/mL, viability increased, and although the 10 µg/mL group was not significantly different from the control, it was significantly higher than the 5 µg/mL group ($P < 0.05$). Beyond 10 µg/mL, viability declined again, showing a significant decrease compared to the control ($P < 0.05$). These findings indicate a biphasic effect of bee venom on LNCaP cell viability.

3.3. Wound Healing Assay

Wound healing analysis was conducted on cells treated with bee venom at concentrations of 0.625, 2.5, 7.5, 10, and 15 µg/mL, along with a control group. Complete wound closure was observed at 24 hours in both the 10 µg/mL group and the control. In contrast, the other treatment groups (0.625, 2.5, 7.5, and 15 µg/mL) required up to 30 hours to achieve full closure. These findings suggest that 10 µg/mL bee venom preserves migratory and proliferative capacity comparable to the control, whereas deviations from this concentration result in delayed wound healing.

4. Discussion and Conclusion

This study's exploration of the cytotoxic and proliferative effects of bee venom (BV) on LNCaP prostate cancer cells provides significant insights into the dose-dependent responses elicited by BV, supporting existing literature on its complex biological activity. The findings demonstrate a biphasic response, where low to moderate doses of BV promote cell viability and migration, while high concentrations are cytotoxic. The MTT assay results illustrate that a minimal BV concentration of 0.312 µg/mL did not significantly alter viability compared to controls, highlighting a crucial threshold below which BV remains inactive. As concentrations increased, cell viability decreased until reaching 5 µg/mL, which showed notably reduced viability ($P < 0.05$). This cytotoxic onset aligns with previous studies, suggesting that various cancer cells, including prostate cancer, exhibit diminished proliferation under high BV concentrations, as observed in other types of tumors such as HEp-2 and HeLa (Gajski & Garaj-Vrhovac, 2010; Rady et al., 2017).

Interestingly, the viability began to increase again at the 10 µg/mL concentration, which did not differ significantly from the control, yet demonstrated a statistically significant improvement relative to the 5 µg/mL condition ($P < 0.05$). This indicates a potential stimulatory effect on proliferation at moderate doses, corroborating findings that melittin,

the primary component of BV, may activate proliferative signaling pathways through various mechanisms, including transient calcium influx and modulation of growth factor pathways (Rady et al., 2017; Badawi, 2021; Lee & Bae, 2016). The notion of sub-cytotoxic doses accentuating cellular growth and migration, as observed in this study, has been supported by similar observations across multiple cancer types, reinforcing the dual potential of melittin as both a proliferative and cytotoxic agent (Rady et al., 2017; Kim et al., 2015).

The wound healing assays reaffirm the complexity of BV's effects, showing that complete closure occurred within 24 hours for LNCaP cells treated with 10 µg/mL BV, suggesting enhanced migratory and proliferative responses at this dosage. In contrast, both lower (0.625-7.5 µg/mL) and higher (15 µg/mL) concentrations delayed wound healing, taking as long as 30 hours for complete recovery, which posits 10 µg/mL as an optimal balance where beneficial effects on cellular dynamics occur without eliciting significant cytotoxicity (ELFIKY et al., 2019). This optimal dose may have practical implications for regenerative medicine applications, particularly in scenarios necessitating enhanced tissue repair processes post-surgery (Badawi, 2021; Tetikoğlu et al., 2024; Karabulut and Uzuner, 2020).

Together, the data illustrate that BV’s impact on LNCaP cells is context and dose-dependent, with prospects for both therapeutic use in proliferative contexts and as an anticancer agent at higher concentrations. The study underscores the necessity for precision in dosing, particularly when translating such findings into clinical environments, where the therapeutic window remains a paramount consideration (Kim et al., 2015). The compelling biphasic effect noted from the current study adds to the expanding body of literature on BV's pharmacological potential, necessitating further investigation into the underlying molecular mechanisms driving these responses, as well as examination in vivo to fully elucidate their practical applications in cancer treatment.

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ACUTE KIDNEY INJURY DUE TO COVID-19 AND NURSING CARE

ABSTRACT

The coronavirus disease, which has been affecting worldwide and is considered one of the biggest epidemic diseases of recent times, has been affecting many systems, especially the renal system, due to the development of severe respiratory failure in patients. The fact that the kidneys are affected has worsened the clinical picture of patients, leading to an increase in mortality and disability rates worldwide. For this reason, nurses have taken heavy responsibility and played an active role in the treatment processes of the patients. The aim of this review is to examine the nursing care of patients who develop acute kidney injury due to coronavirus.

Keywords: Acute kidney injury, COVİD-19, Nursing care.

COVİD-19 NEDENİYLE GELİŞEN AKUT BÖBREK HASARI VE HEMŞİRELİK BAKIMI

ÖZET

Dünya çapında etki gösteren ve son zamanların en büyük salgın hastalıklarından biri olarak kabul edilen, Aralık 2019'dan itibaren etkisi devam eden koronavirüs hastalığı, hastalarda ağır solunum yetmezliği tablosunun gelişmesi nedeniyle renal sistem başta olmak üzere birçok sistem etkilenmiştir. Böbreklerin etkilenmesi hastaların klinik tablosunun daha da kötüleştirmesi dünya çapında ölüm ve sakatlık oranlarının artmasına neden olmuştur. Bu nedenle hastaların tedavi süreçlerinde hemşireler ağır sorumluluk almış ve aktif rol oynamışlardır. Bu derlemenin amacı koronavirüs nedeniyle akut böbrek hasarı gelişen hastaların hemşirelik bakımının incelenmesidir.

Anahtar sözcükler: Akut böbrek hasarı, COVİD-19, Hemşirelik bakım.

GİRİŞ

Tarihte insanları derinden korkutan ve aynı zaman dilinde etkileyen savaş, kıtlık, göç ve en önemlisi salgın hastalıklar gibi olağandışı durumlar olmuştur. Her bir salgının şiddeti ve topluma yarattığı zararların etkisi farklı olabilmektedir (Yurtlu & Erkan, 2023). Koronavirüs hastalığı-2019 (COVID-19), önemli morbidite ve mortalite ile dünya çapında milyonlarca kişiyi etkilemiştir (Renberg, ve diğerleri, 2021). Bu süreç bu nedenle 11 Mart 2020'de Dünya Sağlık Örgütü (DSÖ) tarafından COVID-19 hastalığı küresel salgın hastalık (pandemi) olarak ilan edilmiştir (Ronco, Reis, & Husain-Syed, 2020). Çin'in Hastalık Kontrol ve Koruma merkezinin ilk verilerine göre hastaların %81'inin klinik bulguları hafif, %14'ünün akciğerlerinde %50'den fazla tutulumun olduğu ve %5'inin klinik bulgularının ağır (şok, multiorgan yetmezliği vb.) seyrettiği saptanmıştır (Demirdağ & Hindistan, 2020). COVİD-19 hastalarının %80'inde hafif/orta şiddette semptom gözlenirken %20'sinde ağır semptomlar gözlenmiş ve hastaların yoğun bakım desteği almaları gerekmiştir (Hiçerimez & Enç, 2021). Ülkelerin birçoğunda yoğun bakımlarda ve servislerde sınırlı yatağın olması nedeniyle COVİD-19 hastalığından hayatını kaybeden birey sayısı çok olmuştur. COVİD-19 salgını bu nedenle tüm dünyada ekonomik, sosyolojik ve psikolojik krize yol açmıştır (Rollas & Şenoğlu, 2020).

Dünya'da 16 Ağustos 2022 tarihinde yaklaşık 595 milyon olgu kayıtlara geçmiş ve hayatını kaybeden birey sayısı 6.4 milyon üzerinde olmuştur. Aynı zaman diliminde ülkemizde ise 16 milyonun üzerinde olgu saptanmış iken hayatını kaybeden kişi sayısı ise 100.000 üzerinde olmuştur (Tercan, 2020).

Korona virüsün genellikle solunum sistemi ile yakınmaları ön planda yer alırken COVİD-19 geçiren hastalarda solunum sistemi belirti ve bulguları dışında kardiyolojik, gastrointestinal ve renal sistem belirti ve bulgularının gözlendiği ortaya çıkmıştır. Renal sistem tutulumu pandeminin ilk zamanlarında önemsenmemiş fakat pandemi sürecinin ilerleyen zamanlarında özellikle yoğun bakımda tedavi gören hastaların mortalite sebebi olmuştur (Bayrakçı & Özkan, COVID-19 Pandemisinde Nefroloji Klinikleirinin Yönetimi, 2020). SARS-CoV 2 hastalarında akut böbrek hasarı sık gelişebilen bir komplikasyondur. Bu nedenle serviste yatan hastaların %46'sında yoğun bakımda tedavi gören hastaların ise %76'sında akut böbrek yetmezliği tanısının konduğu tespit edilmiştir. Bu nedenle ABH, COVİD-19'un hasta mortalitesinin en önemli nedeni olarak tanımlanmaktadır (Dheir & Sipahi, 2023).

Bu süreçte Uluslararası Hemşireler Konseyi Başkanı Annette Kennedy *"Hemşireler yeni doğanların ilk çığlıklarını duyar ve ölenlerin son nefeslerine ve hayatın en değerli ve en trajik anlarından bazılarına tanıklık ederler."* Sözleriyle hemşirelerin özveriyle çalıştıklarını vurgulamıştır (Baykara & Eyüpoğlu, 2020). Bu derlemenin amacı; COVİD-19 ile ilişkili akut böbrek yetmezliği olan hastaların hemşirelik bakımının incelenmesidir.

TARİHÇESİ

Dünyada en şiddetli küresel salgın 1918-1919 yılında H1N1 virüsü nedeniyle gelişen influenza pandemisi olmuştur. Bu salgın sürecinde H1N1 kendini farklı şekillerde göstermiştir. Birinci şekli, ülkemizde de gözlenmiş hızla yayılmış ve komplikasyonlarının az olduğu dönem olmuştur. İkinci şekli ise ekim ayında başlamış, Amerika, Afrika, Asya ve Avrupa'ya yayılmış ve bu ülkelerde yaşayan hastaların kliniği ağır seyretmiş hatta birçok insan hayatını kaybetmiştir. Dünya koronavirüs ile 1960'lı yıllarda tanışmış ve bu salgın ile 1960'dan beri mücadele etmektedir (Özlü & Öztaş, 2020).

İlk yeni koronavirüs türleri 2002 yılından sonra gözlenmeye başlamıştır. İlk pandemi süreci Şubat 2003 yılında Çin'in Guangdong bölgesinde yarasalardan kedilere ve misk kedilerinden insanlara bulaşmıştır. Bu hastalığa SARS-CoV adı verilmiştir. Bu enfeksiyon nedeniyle 8000 kişi hastalanmış ve 800 kişi hayatını kaybetmiştir. İkinci pandemi süreci 2012'de Suudi Arabistan'da gözlenmiş ve develerden insanlara bulaşmıştır. Bu hastalığa MERS-CoV adı verilmiştir. Bu pandemi süreci 2012'den 2018'e kadar devam etmiştir. Bu pandemi sürecinde pozitif olgu sayısı 2229 iken hayatını kaybeden hasta sayısı 791 olmuştur (Uludağ, 2020).

Aralık 2019'da Çin'in Wuhan şehrinde nedeni belli olmayan zatürre (pnömoni) olguları kayıtlara geçmiştir. 12 Ocak 2020 yılında geçici olarak bu olgulara *"2019-nCoV"* adı verilmiştir. Dünya Sağlık Örgütü 30 Ocak'ta artan 2019-nCoV vakalarına *"Uluslararası sağlık acil durum"* olan ilan etmiş ve 11 Şubat'ta ise bu pnömoni olgularına Dünya Sağlık Örgütü tarafından *"COVİD-19"* adı verilmiştir. Hastalığın üç ay içinde çok hızlı dünyada yayılması nedeniyle DSÖ COVİD-19'u pandemi olarak kabul etmiştir (Yurtlu & Erkan, 2023; Hiçerimez & Enç, 2021; Kiyat, Karaman, Ataşen, & Kiyat, 2020).

EPİDEMİYOLOJİSİ

Aralık 2019'da Çin'de nedeni belli olmayan zatürre (pnömoni) olguları saptanmış ve kısa zamanda pozitif olgu sayısı 44'e ulaşmıştır. Bu pnömoni olgularının kaynağının deniz ürünleri pazarı olduğu tahmin edilmektedir (Yılmaz & Enç, 2023). Salgının yayılmaya devam ederken Çin'de ocak sonu şubat başında pozitif olgu sayısı pik yapmış ve mart ayında ise olgu sayısı azalmıştır (Dikmen, Kına, Özkan, & İlhan, 2020). Mart 2020'de Çin'de hastalığa yakalanan insan sayısı 81.589 iken hayatını kaybeden insan sayısı ise 3318 olmuş (Özlü & Öztaş, 2020) olup nisan ayında CDC, DSÖ gibi kuruluşların raporlarına göre dünya çapında 176 ülkeye yayılmış, hastalığa yakalanan kişi sayısı 2.250.000'i aşmış ve 160.000'den fazla kişi hayatını kaybetmiştir. Aralık ayından mart ayına kadar süren üç aylık süreç içinde COVİD-19 olguları hızla artması ve dünyaya yayılması sonucu bu hastalığı pandemiye dönüşmüştür (Yurtlu & Erkan, 2023; Özlü & Öztaş, 2020; Karcıoğlu, 2020; Ören & Zengin, 2019).

Ülkemizde ise aynı tarihler arasında bu hastalığa yakalanan hasta sayısı 2.043.704 olup hayatını kaybeden insan sayısı ise toplam 18.351 olarak bildirilmiştir (Kızıltan & Usta, 2020). Mart 2020 ile Ağustos 2022 sürecinde COVİD-19 insanlar arasında hışla yayılmış ve pozitif olgu sayısı yaklaşık 16 milyon iken hayatını kaybeden olgu sayısı ise 100 bin üzerinde olduğu saptanmıştır (Özlü & Öztaş, 2020; Karcıoğlu, 2020).

Dünyanın 1/3 'nün asemptomatik olduğu gözlenmiş 2/3'nün %80'ninde hafif, %20'sinde ise ağır semptomlar gelişmiştir. COVİD-19 nedeniyle hayatını kaybeden kişi oranı %3 iken ağır semptom yaşayan kritik olgularda ise bu oran %50'ye ulaştığı gözlenmiştir (Głowacka, Lipka, Młynarska, Franczyk, & Rysz, Acute Kidney Injury in COVID-19, 2021). Kritik olgularda ARDS (akut solunum sıkıntısı sendromu) gelişmesiyle akut böbrek hastalığı gelişebilmektedir. Ancak raporlarda COVİD-19 ile akut böbrek yetmezliği arasındaki ilişkinin sıklığı ve klinik seyri arasındaki ilişki hakkında yeterli veri bulunamamıştır (İskit, Tanrıöver, & Uzun, 2020).

ABD'nin Washington eyaletinde yayınlanan ilk rapora göre ağır semptom yaşayan 21 COVİD-19 hastada ABY (akut böbrek yetmezliği) gözlenme oranı %19 olarak saptanmış ve Nev York City'deki bir hastanede yayınlanan geniş kapsamlı veriye göre de bu oran %22 olarak bildirilmiş olup %3'ünde diyalize tedavisine gereksinim duyulmuştur. Mohamed ve

ark.'nın (2020) yaptığı bir araştırmada COVİD-19 nedeniyle hastaneye yatan hastalarda ABY gözlenme oranı %28 olarak bulunmuş ve bu ABY (akut böbrek yetmezliği) olgularının %65'i yoğun bakım ünitesinde tedavi edilirken geriye kalan %35'lik kısım ise servislerde bakım verilerek iyileşme olanağı bulmuştur.

Yoğun bakımda COVİD-19 nedeniyle yatıp ABY gelişen hastaların %73'üne RRT uygulanmıştır (Mohamed, ve diğerleri, 2020). Prasad ve Agrawal'ın (2020) araştırmasına göre Hindistan'da 300 milyon insanın %10'u COVİD-19 enfeksiyonu gözlendiği bu 30 milyon insanda ABY gözlenme oranının %5,1 olduğu ve birçok hastaya RRT uygulandığı belirtilmiştir (Prasad & Agrawal, 2020).

COVİD-19 ile ilişkili akut böbrek yetmezliğinin (ABY) gözlenme oranı farklılık göstermektedir. Çin'deki COVİD-19 nedeniyle ABY gelişen hastaların oranı %5-29, Amerika Birleşik Devletleri'nde (ABD) %37-57 oranları arasında seyretmiştir. Çin'deki bu hastaların ABY şikayetleri 7-14 gün içinde gelişirken Amerika'da ise daha kısa sürede geliştiği saptanmıştır. Brezilya'da ise bu hastaların %56'dan fazlasında ABY gözlenmiş ve bu oranın %67'sinde 3'üncü evre akut böbrek yetmezliği tespit edilmiştir. COVİD-19 ile ilişkili olan ABY vakalarının %4.9'una renal replasman tedavisi uygulanmıştır. Amerika Birleşik Devletleri'nde bu oran %19'a kadar ulaşmış ve Brezilya'da ise bu oran %47'yi aşmıştır. ABY nedeniyle yatan hastalara genellikle uzun süreli veya aralıklı renal replasman tedavisi uygulanmıştır (Głowacka, Lipka, Młynarska, Franczyk, & Rysz, Acute Kidney Injury in COVID-19, 2021).

COVİD-19 İLE AKUT BÖBREK HASARI ARASINDAKİ İLİŞKİ

Koronavirüs, RNA virüsleri içinde en büyük genom yapısına sahip olan insanda ve hayvanda hastalık yapabilen bir RNA virüsüdür (Dheir & Sipahi, 2023). COVİD-19, beş başlıklı, tek sarmallı, 32kb arasında değişen bir büyüklükte, 80 ile 120 nm arasında uzunluğu değişen ve zarlı bir RNA virüsüdür (Uludağ, 2020; Oğuz, 2022). COVİD-19'un alfa, beta, gama ve delta olmak üzere dört çeşidinin saptandığı ve zarlı yapısının içinde çubuksu yapıların bulunduğu gözlenmiştir. COVİD-19'da *"taç"* ya da *"ışık halkası"* denilen çubuksu yapılar bulunmaktadır. Bu virüsün pozitif polaritesi vardır ve COVİD-19 RNA polimeraz enzimi içermez. Ancak RNA'ya bağımlı olarak genomlardan bu yapıyı kodlar. Büyük genoma sahip olması bu virüsün konak hücreye olan bağımlılığını azaltır (Dheir & Sipahi, 2023; Özlü & Öztaş, 2020; Uludağ, 2020).

Alfa ve beta tip koronalar memelileri enfekte etmekte iken insanların solunum yollarını ve hayvanların ise gastrointestinal sistemini etkilerler. Gama ve delta koronalar kuşları enfekte etmektedirler. Ayrıca COVİD-19, SARS-CoV'a %79, MERS-CoV'a %59 oranında benzediği için SARS-CoV, MERS-CoV ve COVİD-19 beta tip koronavirüs ailesinin mensubudur (Özlü & Öztaş, 2020; Dikmen, Kına, Özkan, & İlhan, 2020; İskit, Tanrıöver, & Uzun, 2020).

Koronavirüsler İnterlökin (İL)-6 ve (İL)-7 gibi diğer sitokinlerin düzensiz salınımına neden olmakta, T hücrelerinin aktivasyonunu bozduğu için miyokart hasarı oluşmakta ve anjiyotensin dönüştürücü enzim-2 (ACE-2) ile sitokin fırtınası oluşturarak kalp, karaciğer, bağırsak ve böbrekler hasar görmektedir (Uludağ, 2020; Yılmaz & Enç, 2023).

COVİD-19 ortaya çıktığında sadece akciğerlerde tutulum vurgulanmış fakat vakaların çoğalması ile farklı klinik tablolar ve organ tutulumları ortaya çıkmıştır. Bunlardan biride böbreklerin tutulumudur. Genellikle kronik böbrek yetmezliği olan hastalarda yaş, diyabet,

yüksek tansiyon gibi komorbid nedenlerin bulunması COVİD-19 hastalığında riskli grubu oluşturmaktadırlar. COVİD-19 geçirmeden önce böbrek fonksiyonları normal olan bireylerde de böbrek hasarının oluştuğu gözlenmiştir. Korona virüsün akut böbrek hasarı ile ilişkisi çok yönlüdür ve henüz nedeni tam olarak bulunamamıştır. COVİD-19 hastalarında gelişen akut böbrek hasarının hem doğrudan hem de dolaylı olarak mekanizmaları bulunmaktadır (Dheir & Sipahi, 2023; Yılmaz & Enç, 2023; Kubat & Şahin, 2020; Kazak, 2020)

COVİD-19'un belirtilerinden olan ateş, bulantı kusma nedeniyle gelişen dehidratasyon sonucu vücuttaki sıvı plevral boşluğa kaçarak rabdomiyolize neden olmakta ve kaslarda aşırı derecede sıvı birikmektedir. Dehidratasyon rabdomiyolizin dışında sepsise ve kalp yetmezliği nedeniyle hipotansiyona neden olarak akut böbrek hasarının gelişmesinde rol oynamaktadır. Hastada gelişen uzun süreli dehidratasyon ve hipotansiyon, böbrek tübülerinin genişlemesine ve tübülerde kan hücre kalıntılarının çoğalmasına neden olarak akut tübüler nekroza neden olabilmektedir. Ayrıca COVİD-19'un İL-6 sitokininin salınımını arttırmasıyla kalp yetmezliğinin gelişmesine bağlı pasif olarak böbrek tıkanıklığı, akut tübüler nekrozun gelişmesine neden olmaktadır. COVİD-19 hastalığında gelişen diğer önemli komplikasyon pıhtılaşma sorunudur. Bu pıhtılaşma mekanizması tüm vücutta gözlenebileceği gibi böbreklerde de gözlenebilmektedir. Bu pıhtılaşma mekanizmasında glomerüler damarlarda mikro pıhtılar oluşmasıyla akut böbrek hasarı gelişebilmektedir (Adamczak, Surma, & Więcek, 2022). Çin'de yapılan araştırmada 59 hastanın %63'ü proteinüri, %19'u serum kreatinin yüksekliği ve %27'sinin de kan üre azotu (BUN) seviyesinde yükselme olduğu bildirilmiştir (Yılmaz & Enç, 2023). Koronavirüsün böbrek tübülerini direkt etkilemesinin yanı sıra oksijenasyonun bozulması, sitokin fırtınası, hipoksiye bağlı kardiyopulmoner sendrom ve pıhtılaşma problemleri böbrek hücrelerine de zarar vermektedir (Ersoy, 2020).

Korona virüs ACE-2 inhibitörlerini kullanarak böbreklere hasar vermektedir. ACE-2 inhibitörleri çoğunlukla böbreklerin podositlerinde, proksimal tübülerinde bowman kapsülünün paryetal epiteli ve toplama kanallarında çoğunlukla yer almaktadır. Koronavirüs ACE-2 inhibitörlerini kullanarak böbreklerin bu bölümlerine zarar vermektedir. Koronavirüs sadece böbrekleri değil renin- anjiyotensin-aldesteron sisteminin (RAAS) de bozulmasına neden olmaktadır. RAAS'ın hasar görmesi hiper pıhtılaşma, fibrozis ve doku hasarı oluşturmaktadır (Smarz-Widelska, ve diğerleri, 2021).

Koronavirüs kalp yetmezliğine neden olarak böbreklerde kan durgunluğuna ve hipoperfüzyonun oluşmasına yol açmaktadır. Böbreklerde oluşan dolaşım bozukluğu ve hipoperfüzyon akut böbrek hasarına sebebiyet vermektedir. COVİD-19 ayrıca akut solunum sıkıntısına (ARDS) yol açmaktadır. ARDS sonucu ABH gelişebilmektedir. ARDS nedeniyle hemodinamik dengesizlik, hipoksemi/hiperkapni, asit-baz düzensizliği, inflamasyon ve nörohormonal etkiler olmak üzere beş farklı nedenle ABH gelişmesine yol açmaktadır. Bu beş nedenle oluşan böbrek hasarı akciğer -böbrek karışımı teorisi ile açıklanmaktadır. Bu teoriye göre ABH İl-6 sitokininin aşırı derecede salınımı sonucu alveol kılcal damarlarda genişlemeye, pulmoner kanamaya ve hatta bu aşırı salınan sitokinler böbreklerde damar endotelinde hasara yol açmaktadır (Głowacka, Lipka, Młynarska, Franczyk, & Rysz, Acute Kidney Injury in COVID-19, 2021).

KLİNİK BELİRTİ VE BULGULAR

COVİD-19'un kuluçka süresi 2-14 gün arasında değişmektedir. Hasta virüsle temas ettikten dört-beş gün sonra klinik belirti ve bulgular ortaya çıkar ve bu süreç ortalama 11,5 gün

sürmektedir (Karcıoğlu, 2020). Koronavirüs ilk olarak hapşırma, konuşma, öksürme gibi sekresyonların dışarı çıkmasıyla solunum yoluyla, direkt temas ile bulaştığı gözlenmiştir. Nazofarengeal sürüntüde, idrarda, kanda, dışkıda ve tükrükte saptanmıştır. Bu virüs hastanın temas ettiği yüzeylere direkt temas ile de bulaşmaktadır. Hastadan alınan testüküler ve semen örneklerinde virüse rastlanmamış olup bu hastalık cinsel yolla bulaşmadığı saptanmıştır (Türken & Köse, 2020).

SARR-CoV ve MERS-CoV insanlarda üst solunum yollarını etkilerken COVİD-19'un hedefi alt solunum yollarıdır. COVİD-19 ciddi olgularında hipoksi, takipne, solunum sıkıntısı, dispne gözlenmektedir. Hastalığın şiddeti %85-93 arasında hafif seyrederken %15'inde tıbbi yardımın, %7'sinde ise kritik bakımın olmasının gerektiği bildirilmiştir. Kritik bakım gerektiren olguların %50'si hayatını kaybetmektedir (Karcıoğlu, 2020).Koronavirüsün hastalığa özel belirti ve bulguları bulunmamaktadır. İlk tespit edilen olgularda en çok ateş, öksürük, miyalji, yorgunluk, balgam, baş ağrısı, hemoptizi, ishal ve nefes darlığıdır (Kubat & Şahin, 2020). DSÖ ise bu hastalığı ateş, yorgunluk, kuru öksürük, nefes darlığı, miyalji ve boğaz ağrısı olarak tanımlamıştır (Dikmen, Kına, Özkan, & İlhan, 2020; Kubat & Şahin, 2020; Yılmaz & Yılmaz, 2021).

Hastaların en çok akciğerleri etkilenirken kalp, karaciğer, GİS ve en önemlisi böbrekler de etkilenmektedir. Böbrekleri hasar görüp akut böbrek yetmezliği gelişen hastaların kliniği ağır seyretmekte ve hastaların %92'si hayatlarını kaybetmektedir (Prasad & Agrawal, 2020; Şit & Kayabaşı, 2020) Akut böbrek hasarı sonucunda hastaların serum kreatinin seviyesinde artış, idrarda hematüri ve proteinüri gözlenmektedir (Demirdağ & Hindistan, 2020; Dheir & Sipahi, 2023; Głowacka, Lipka, Młynarska, Franczyk, & Rysz, Acute Kidney Injury in COVID-19, 2021). COVİD-19 nedeniyle gelişen akut böbrek yetmezliği olan vakalarda 48 saatte serum kreatinin değerinin 0,3 mg/dl oranında arttığı, 7 gün içinde ise bu artış %50 oranında olduğu saptanmış ve olguların idrarında protein, eritrosit ve lökosit saptanmıştır. COVİD-19 hastalarının hastaneye yattıktan beş-dokuz gün sonra akut böbrek hasarının geliştiği gözlenmektedir (Yılmaz & Enç, 2023).

TEDAVİ VE ÖNLEM

Koronavirüs hastalarında ABH gelişme riskleri, ileri yaş, diyabet, hipertansiyon, kardiyovasküler hastalık ve solunum yetmezliğidir. Akut böbrek hasarını en çok tetikleyen nedenler ise çoklu organ yetmezliği, sepsisin neden olduğu hipotansiyon ve böbreklerdeki yetersiz kanlanma sonucu böbrek fonksiyon bozukluğudur. Koronavirüs nedeniyle ABY gelişen hastaların tedavisi, Küresel Sonuçları İyileştirme Kılavuzları (KDIGO) tedavi stratejisine göre olmalıdır (Dheir & Sipahi, 2023).

Akut böbrek yetmezliğinin primer tedavisi sırasında temel hedef; sıvı elektrolit dengesizliğinin önlenmesi ve üremik semptomların tedavisidir (Ören & Zengin, 2019). Akut böbrek hasarında sıvı replasmanı diyaliz tedavisinden önce tercih edilen yöntemdir. Sıvı replasmanı yapılırken volüm fazlalığı ve ödem gelişmemesi için sıkı takip yapılmalıdır (Prasad & Agrawal, 2020). Covid-19 nedeniyle akut böbrek hasarı tanısı konan ve KDIGO Tedavi stratejilerinin 3. evresinde olan hastalara renal replasman tedavileri (periton diyalizi, hemodiyaliz ve sürekli renal replasman tedavisi) uygulanmaktadır. Renal replasman tedavileri üremik tabloyu düzenlediği ve septik toksinleri temizlediği gözlenmiştir (Hamzagic, ve diğerleri, 2017). Koronavirüs nedeniyle akut böbrek hasarı olan hastaların %19'una RRT uygulanmaktadır (Dheir & Sipahi, 2023; Özlü & Öztaş, 2020; Ören & Zengin, 2019).

Koronavirüs nedeniyle hastaneye yatan akut böbrek yetmezliği olan hastalarda uygun tedaviyi sağlamak oldukça önemlidir. Bu tedavi hastanın klinik durumuna göre değişkenlik göstermektedir. Hemodinamisi iyi olan hastalara hemodiyaliz veya periton diyalizi yapılmakta iken hemodinamisi bozuk olan hastalara ise sürekli renal replasman tedavisi (CRRT) uygulanmaktadır (Dheir & Sipahi, 2023). ABY'de birçok organ etkilenebilmekte ve etkilenen organların değerlendirilmesi gerekmektedir. Bu nedenle hastanın hastalık hikayesi ayrıntılı olarak alınmalı ve hastada hematüri, dizüri, proteinüri ve ani sıkışma hissi (urgency), özellikle yaşlı hastalarda akıntı, idrar tutamama, prostat hastalığının varlığı sorgulanmalıdır (Baykara & Eyüpoğlu, 2020; Ören & Zengin, 2019; Çınar & Birengel, 2021)

Hastanın hastalık hikayesi sorgulandıktan sonra hatanın klinik bulgularına (biyokimyasal değerleri, vital bulguları, AÇT değerleri vb.) bakılmaktadır. Hasta yoğun bakıma kabul edildiğinde ilk yaşamsal bulguları takip edilmekte ve solunum sayısını, nabzını, kalp ritmini, kan basıncını takip etmek için hasta monitörize edilmektedir. Hastanın fiziksel değerlendirmesi yapılırken, hastanın koopere olup olmadığı, COVİD-19 hastalığına dair belirtileri (öksürük, nefes darlığı, ateş vb.) takip edilmelidir (Baykara & Eyüpoğlu, 2020; Ören & Zengin, 2019). COVİD-19'a bağlı gelişen bulantı-kusma, diyare ve ateş hastalarda sıvı elektrolit dengesinin sağlanması oldukça önem arz etmekte olup hastalarda ilk olarak bulantı-kusma, diyare ve ateş kontrol edilmeli ve biyokimyasal değerler takip edilmelidir (Dikmen, Kına, Özkan, & İlhan, 2020; Sofulu, Uran, Avdal, & Tokem, 2020). Akut böbrek hasarının önemli belirteçlerinden biride metabolik ve respiratuvar asidozun gelişmesi, kan üre azotunun (BUN) ve serum kreatinin değerinin yükselmesi nedeniyle GFR'nin azalmaktadır. Glomerüler filtrasyon hızı düşük olan ABY hastalarında potasyum seviyeleri yükselmektedir. Kanda yükselen potasyum değeri hastada EKG ve ritim bozukluklarına neden olmaktadır (Sofulu, Uran, Avdal, & Tokem, 2020; Uysal & Karataş, 2017).

Hastalarda ABY, hematüri, proteinüri ve kanama bulgularıyla ortaya çıkarabilmektedir. Bu nedenle hastadan hemogram, koagülasyon alınarak, hastanın trombosit, hemoglobin, hemotokrit değerleri ve pıhtılaşma faktörlerine bakılmalı ayrıca hastalar hematemez, melena ve anemi yönünden takip edilmelidir (Ören & Zengin, 2019).

Koronavirüs hastalığının belirtilerinin (bulantı-kusma, ateş, öksürük, diyare vb.) olması sağlık personellerine kolay bulaşmasına neden olmaktadır. Bulaş yollarının hava, damlacık ve temas yolu olması nedeniyle sağlık personelleri kişisel koruyucu ekipmanı doğru kullanması gerekmektedir. Bu ekipmanı (maske, eldiven gözlük ve önlük) nasıl kullanacağı konusunda sağlık personeli önemli görevler üstlenmektedir. Ayrıca bu ekipmanlar her hastadan sonra değiştirilmelidir (Başaran & Şahan, 2021). Akut böbrek hasarı gelişen hastalarda sağlık personeli yoğun bakım ve diyaliz ünitelerinin izole alanlarında birebir ilgilenecek şekilde hemodiyaliz tedavisini uygulamalıdırlar (Heper, 2020; Bayraktaroğlu & Fidan, 2020). Akut böbrek hasarı olan hastaların birçoğunda kanama olgusu gözlenmekte ve bu kanama şikayeti hastanın enfeksiyona yatkınlığını arttırmakta olduğu için bu dönemde ziyaretçi kısıtlaması yapılmalıdır (Ören & Zengin, 2019; Bayraktaroğlu & Fidan, 2020).

HEMŞİRELİK BAKIMI

Akut böbrek hasarı gelişen hastanın öyküsü detaylı bir şekilde alınmalıdır. Hastanın vital bulguları takip edilmeli gerekiyorsa monitörize edilmelidir. Oksijen desteğinin daha iyi olması için hastaya semi fowler, ortopne ya da prone pozisyonları verilmelidir. Hastada sıvı volüm dengesinin bozulması sonucunda hipotansiyon veya hipertansiyon gelişebilmekte olup hastanın kan basıncı takibi yapılmalıdır. Hastada ödem takibi, aldığı çıkardığı ve kilo takibi yapılmalı ve değişiklikler kaydedilmelidir (Ören & Zengin, 2019; Bayraktaroğlu &

Fidan, 2020). COVİD-19 hastasının ilk bakım gereksinimi öksürük ve nefes darlığı şikayetlerinin giderilmesi olduğundan oksijen desteğinin sağlanması gerekmektedir. Hastanın spontan solunumu varsa oksijen satürasyonu %95-100'ün altına düşürülmemelidir. Hastaya oksijen maskesi desteğiyle saatte 5 L/ dk oksijen sağlanmalıdır (Yılmaz, Ceylan, Yıldırım, Erkut, & Palandöken, 2020).

Yükselen ateş ve solunum güçlüğü metabolizma hızını arttırmaktadır. Ateşin düşürülmesine yönelik önlemler alınmalı, hastanın yeterli beslenmesi sağlanıp hasta sıvı tüketmesi konusunda desteklenmelidir. Hastada gelişecek ABY riskine karşı da hastanın aldığı çıkardığı takibi yapılmalı ve sıvı replasman tedavisi planlanmalı, takibi yapılmalı ve uygulanmalıdır (Dheir & Sipahi, 2023; Prasad & Agrawal, 2020).

Akut böbrek hasarında metabolik asidoz gelişebilmekte ve hastada bulantı-kusma, kusmual solunum, hiperkalemi, taşikardi, mental durum değişiklikleri gözlenebilmektedir. Bu nedenle düzenli aralıklarda hastadan arteriyel kan gazı alınarak metabolik asidoz varlığı kontrol edilmelidir. Hastalardan alınan kanda biyokimya değerlerinde özellikle sodyum ve potasyum değerleri dikkatle izlenmeli ve hiperkalemi gelişmemesi için önlem alınmalıdır. Hiperkalemi kardiyak sistemi etkiler ve EKG'de T dalgasında değişmeler, ST segment depresyonu, uzamış PR aralığı, geniş QRS kompleksi, kardiyak fibrilasyon ve arrest oluşabilmektedir. Bu nedenle hasta monitörize edilip 12 derivasyonlu EKG çekilmelidir. Hiperkaleminin gelişmesi durumunda dekstroz içine insülin konularak infüzyona başlanmalıdır. Hastanın glikoz seviyesi ve aldığı çıkardığı takibi (AÇT) yapılmalıdır. AÇT ile dehidratasyon için de gerekli izlem yapılmış olacaktır (Ören & Zengin, 2019; Çınar & Birengel, 2021).

Oral alımı olmayan hastalarda parenteral yolla beslenme tercih edilmeli, belli aralıklarla tartılmalı, aldığı çıkardığı takibi yapılmalıdır. Oral alımı kısıtlı olan hastanın belli aralıklarla oral mukoz membranların bakımı sağlanmalıdır. Sürekli yatan hastalarda iki saatte bir pozisyon değişikliği ve dekübit oluşma riski yönünden basınç ülserlerinin değerlendirilmesi yapılmalıdır. Basınç yarasının varlığında ise yaranın lokalizasyonu, genişliği, derinliği, rengi, kokusu ve akıntının varlığı değerlendirilmelidir. Hastada gelişen kas iskelet sisteminde dengesizlik ve kuvvetsizlik sorununu gidermek için hastaya aktif-pasif ROM egzersizleri yaptırılmalıdır (Yılmaz, Ceylan, Yıldırım, Erkut, & Palandöken, 2020).

Akut böbrek yetmezliğinde bir diğer sorun ise oligüri veya oligüri olmaksızın kanda üre, BUN, kreatinin ve potasyum seviyelerinde hızla yükselmektedir. ABY'nin düzeltilmesi için sıvı elektrolit denge bozukluğunun önlenmesi, enfeksiyon kontrolü, optimal beslenme desteğinin sağlanması, hastaya ve yakınlarına ABY hakkında bilgi verilmesi ve bakımının sağlanması önem taşımaktadır (Uysal & Karataş, 2017).

Akut böbrek hasarında hastada kanama (hematüri, hematemez, melena vb.) şikayetleri gözlemlenebilir. Kanama şikayetleri nedeniyle hastanın immün sistemi etkilenebilmekte ve enfeksiyona yatkınlık artmaktadır. Hastadan bu nedenle koagülasyon, hemogram, kan ve idrar kültürleri alınmalıdır. Sağlık ekibi tarafından hastalara akut böbrek hasarı konusunda ne yapması ve nelere dikkat etmesi gerektiğine ilişkin eğitim desteği sağlanmalıdır.

Akut böbrek hasarı gelişen hastada sıvı kısıtlaması, tansiyon, kilo ve ödem takibi ve bu konularda hasta eğitimi yapılmalıdır (Ören & Zengin, 2019). Hastada volüm kayıplarının (kanama, poliüri, kusma ve ishal gibi.) varlığı sorgulanmalıdır. Hastada olan ek kronik hastalıklar ve ek ilaçları kayıt altına alınmalıdır. Hastanın hastanede kaldığı sürece diyaliz

ihtiyacının olup olmadığı hakkında bilgi edinmek için biyokimyasal değerleri kontrol edilmelidir (Bayraktaroğlu & Fidan, 2020; Gerkuş & Sivrikaya, 2020)

Akut böbrek hasarı gelişen hastada sıvı replasman tedavisi önem taşımaktadır. Renal perfüzyonun düzeltilmesi amacıyla KDİGO sıvı replasman yönetiminde hemorajik şok yoksa izotonik, kristoloidler veya kolloidlerin tedavide tercih edilmesini önermektedir. (Yılmaz, Ceylan, Yıldırım, Erkut, & Palandöken, 2020; Bayrakçı, ve diğerleri, 2022).

SONUÇ VE ÖNERİLER

Koronavirüs Aralık 2019'dan beri tüm dünyaya hızlı yayılması nedeniyle insanlarda korku yaratan, hayati tehlike oluşturan bir hastalık olmuştur. COVİD-19 hastalığı doğrudan ya da dolaylı olarak akut böbrek hasarına neden olmaktadır. Akut böbrek yetmezliği COVİD-19 hastalığının klinik tablosunu kötüleştirmekte ve mortalite oranını arttırmaktadır. Hemşireler bu süreçte hastaların tedavisi sırasında bireysel/sosyal izolasyonlarını sağlayarak hem kendilerini korumuş hem de yeni pozitif olguların çoğalmasına engel olmalıdırlar.

Koronavirüsün klinik yönetiminde ve enfeksiyonun önlenmesinde hemşirelere büyük sorumluluk düşmektedir. Sağlık personeli için bu sorumluluk; yeterli bilgi düzeyine sahip olmak, doğru uygulamaları yapmak ve enfeksiyon bulaş zincirini kırmaktır. Pandemi sürecinde hemşireler, COVİD-19 hastalığının nasıl bulaştığı, klinik belirtileri ve bulguları, nasıl tanı konduğu, tedavi ve bakımının nasıl yürütülmesi gerektiği hakkında bilgi sahibi olmalıdır. Hemşireler pandemi sürecinde hastaların klinik yönetimini diğer sağlık personelleriyle iletişime geçerek, literatür bilgilerinden faydalanarak, güncel bilgileri takip ederek, uluslararası rehberlerin takipleri yapılarak planlanmalıdır. Bu süreçte hemşireler klinik bilgileri, hizmet içi eğitimlerle desteklenmelidir.

Sonuç olarak, COVİD-19 nedeniyle gelişen akut böbrek hasarı dünyada ve ülkemizde önemli bir sağlık problemidir. Koronavirüs vakalarında akut böbrek hasarının erken tanısı, tedavisi ve bakımı önem arz etmektedir. COVİD-19 hastalığının her döneminde hastanın akut böbrek yetmezliğinin belirti ve bulguları takip edilmelidir. Sağlık personeli hasta ve ailesine uygun içerikte eğitim verilmeli, hastaların klinik yönetim ve bakımını bütüncül bir yaklaşımla oluşturmalıdır.

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CAUSES AND CONSEQUENCES OF NURSE WORKFORCE MIGRATION

ABSTRACT

Purpose: This study was conducted as a compilation in order to comprehensively address the results of studies in the literature that reveal the reasons and consequences of nurse workforce migration.

Findings: Many factors such as the difficulty of working life in countries of migration, increase in workload, failure to meet wage expectations, inadequate working conditions, institutional services and institutional management style not meeting nurses' expectations, material and human resource deficiencies, lack of job security, mobbing, violence, and being under pressure cause nurse workforce migration.

Conclusion: It is seen that employment is negatively affected by the free and independent movement of health workers in the international market, and the effects of nurse workforce migration and nurse shortage are felt even more. In this regard, there is a need for further research on the reasons and consequences of nurses' migration tendency in our country, and initiatives that can solve this problem.

Keywords: Migration, nurse workforce, nurse migration.

HEMŞİRE İŞ GÜCÜ GÖÇÜNÜN NEDENLERİ VE SONUÇLARI

ÖZET

Amaç: Bu çalışma, literatürde hemşire iş gücünün göç nedenlerini ve sonuçlarını ortaya koyan çalışmaların sonuçlarını kapsamlı bir şekilde ele almak amacıyla derleme olarak gerçekleştirilmiştir.

Bulgular: Göç veren ülkelerde iş yaşamının zorlaşması, iş yükünün artması, ücret beklentilerinin karşılanmaması, çalışma koşullarının yetersizliği, kurumsal hizmetlerin ve kurum yönetim şeklinin hemşirelerin beklentilerini karşılamaması, malzeme ve insan kaynağı eksiklikleri, iş güvencesinin olmayışı, mobbing, şiddet, baskı altında kalma gibi pek çok etmen hemşire işgücü göçüne sebep olmaktadır.

Sonuç: Sağlık çalışanlarının uluslararası piyasada serbest ve bağımsız dolaşımıyla, istihdamın olumsuz etkilendiği görülmekte ve hemşire işgücü göçü ile hemşire eksikliğinin etkileri daha da fazla hissedilmektedir. Bu konuda ülkemizde özellikle hemşirelerin göç eğiliminin nedenlerinin ve sonuçlarının daha fazla araştırılmasına ve bu soruna çözüm olabilecek girişimlere ihtiyaç vardır.

Anahtar Kelimeler: Göç, hemşire işgücü, hemşire göçü

GİRİŞ

Göç, bireylerin veya toplulukların uzun süreli ya da kısa süreli, kalıcı ya da geçici olarak yaşadıkları yerleri değiştirmeleridir (Nakhoul, 2014). Bu durum, özellikle vasıflı bireyler için söz konusu olduğunda "beyin göçü" olarak adlandırılmaktadır. Sağlık iş gücü göçü de, beyin göçünün en önemli örneklerinden biridir. Göçün sebepleri yüzyıllardır benzer kalmakla birlikte, özellikle ekonomik nedenler başta olmak üzere birçok farklı faktör bu olayı tetiklemektedir (Guano, 2008). Dünya çapındaki sağlık iş gücü krizi, gelişmiş ve gelişmekte olan ülkeleri giderek artan şekilde etkilemektedir. Gelişmiş ülkeler, sağlık iş gücü kaynağını büyük ölçüde yaşlanan nüfuslarından temin etmekte zorlanırken, gelişmekte olan ülkeler ise sağlık çalışanlarının daha iyi fırsatlar için başka ülkelere göç ettiğini bildirmektedir. Bu durumun sebepleri, gelişmiş ülkelerin sağlık çalışanlarına olan yüksek talep ("çekme" faktörü), gelişmekte olan ülkelerin ise sağlık çalışanlarına olumsuz çalışma koşulları sunması (altyapı eksiklikleri, düşük maaşlar, yetersiz teşvikler, yetersiz tıbbi malzemeler ve kariyer fırsatları gibi) ("itici" faktör) olarak sıralanmaktadır (Omaswa, 2008). Bu bağlamda, ABD ve İngiltere gibi gelişmiş ülkeler, hemşire iş gücü eksikliklerini gidermek amacıyla çeşitli yöntemler benimsemiş ve yurtdışından işe alım kampanyaları başlatarak bu boşlukları doldurmayı hedeflemişlerdir (Buchan ve ark., 2003). Son yıllarda, çeşitli nedenlerle yurt dışına çalışmaya giden hemşire sayısında artış gözlemlenmekte, özellikle genç hemşireler arasında bu eğilimin giderek arttığı görülmektedir. "Mesleki göç" olarak adlandırılan bu durum, tüm ülkelerde olduğu gibi gelecekte Türkiye'de de hemşire insan gücü açısından önemli sorunlara yol açabilecek bir durum olarak öngörülmektedir. Bu süreç, sağlık hizmetlerinin sunumu ve planlanmasında, göçün mevcut sağlık altyapısını aksatacağı ve ilerleyen dönemlerde yapılacak planlamaları olumsuz yönde etkileyeceği, ayrıca mesleki dengeyi bozacağı şeklinde değerlendirilmektedir (Yıldırım, 2010). Hemşire iş gücü göçü konusunda, küresel bilgilere daha kolay erişim, internetin yaygınlaşması ve ulaşım araçlarının hızlanması, hemşirelerin ülkeler arasındaki hareketliliğini daha kolay hale getirmiştir (Thupayagale-Tshweneagae, 2007). Gelişmekte olan ülkeler, daha ucuz, hızlı ve kolay bir hemşire iş gücü kaynağı olmak amacıyla, bu iş gücünü başka ülkelere göndermekte ve bu süreç, genellikle ortak dil, benzer eğitim müfredatları ve eski kolonilerle devam eden bağlar sayesinde kolaylaştırılmaktadır (Buchan, 2001;Kingma, 2006). Bu faktörler, hemşire iş gücü göçünü daha cazip hale getiren unsurlar arasında yer almaktadır.

1. HEMŞİRELERİN GÖÇ ETME NEDENLERİ

Yapılan araştırmalar, küresel ölçekte hemşire iş gücü göçüne neden olan çeşitli faktörleri ortaya koymaktadır. Bu faktörler ve etkileri aşağıda detaylı bir şekilde açıklanmıştır.

- **Küresel Pazar Taleplerinin Etkisi**

Gelişmiş ülkelerdeki hemşire iş gücü, yaşlanan nüfus nedeniyle zorlanırken, aynı zamanda hemşirelik okullarına olan ilgi de azalmaktadır. Ayrıca, okulu terk edenler için alternatif kariyer fırsatlarının artması, hemşirelik mesleğinin olumsuz imajı ve iş tatminsizliği gibi nedenler de hemşire sayısındaki azalmaya yol açmaktadır (Kline, 2003). Bu faktörler, küresel düzeyde hemşire talebinin artmasına neden olmaktadır. Bugün, serbest piyasa düşüncesinin yaygınlaşması, yaşlanan nüfusa sahip ülkelerin sağlık hizmetleri konusunda dışa bağımlılıklarının artması, hemşire açığının kapanamaması gibi nedenler, hemşire göçünü teşvik eden faktörler arasında yer almaktadır. Ülkeler arası hemşire göçünü etkileyen bir diğer faktör ise, ulusal düzeyde hemşirelerin çalışma koşullarına dair hoşnutsuzluk yaratacak istihdam politikalarıdır (Aiken ve ark, 2014). Küresel talep arttıkça bazı ülkeler,

deneyimli hemşirelerini elde tutmak ve onları işe geri kazandırmak için çeşitli stratejiler geliştirmiştir, ancak bu çabalar genellikle istenilen etkiyi yaratmamıştır (Buchan, 2001). Son yıllarda hemşire göçü, sağlık sektörü ve politika yapıcılar için büyük bir sorun haline gelmiştir (Bach, 2004). Hemşirelere olan küresel talep arttıkça, uluslararası hemşire istihdamı da büyümüş ve yeni pazarlarda rekabet artmıştır (Brush, 2008). Özellikle Afrika, Karayipler ve Asya gibi gelişmekte olan bölgelerden gelişmiş ülkelere doğru yoğunlaşan hemşire göçü, "Güney-Kuzey Göçü" olarak tanımlanmıştır. Bu göç, gelişmiş ülkelerin daha iyi ekonomik fırsatlar sunarak diğer ülkelerden hemşireleri çekmeye yönelik politikalarının bir sonucudur (Muula ve ark., 2003). Küresel pazar taleplerine uygun olan Kaliforniya ve Teksas, hemşire açığının yüksek olduğu bölgelerden biridir. Bu durum, yabancı eğitimli hemşirelerin istihdamının artmasına yol açmıştır (Reineck ve ark., 2005). Polonya ve Hollanda arasında gerçekleştirilen küçük ölçekli bir projede, Polonyalı hemşireler Hollanda'da belirli bir süre çalıştıktan sonra ülkelerine dönerek hizmet vermektedirler (Buchan ve Perfilieva, 2006). Filipinler de, sağlık çalışanlarını, özellikle hemşireleri ihraç etmek amacıyla eğitim vermektedir. Bu bağlamda, Filipinler sağlık çalışanlarının uluslararası göçünü teşvik eden bir kaynak ülke haline gelmiştir. Ülkedeki hemşirelik ve tıp okullarının müfredatlarını yurt dışındaki programlarla uyumlu hale getirerek, öğrencilere yurt dışındaki istihdam seçenekleri konusunda bilgiler sunmakta ve onları desteklemektedir. Ayrıca, özel hemşirelik okullarını akredite ederek ve yabancı işgücü alımını gerçekleştiren hedef ülkelerle ikili anlaşmalar yaparak bu süreci desteklemektedir (Ray ve ark., 2006). Küba, Çin, Hindistan, Endonezya ve Vietnam da sağlık çalışanlarının ihracatına katkı sağlayan ülkeler arasında yer almaktadır (WHO, 2006).

- **Göç Veren ve Göç Alan Ülke Koşullarının Etkisi**

Göç veren ülkelerde, iş yaşamının zorlaşması, ağır iş yükü, düşük maaşlar, yetersiz çalışma koşulları, kurumsal hizmetlerin ve yönetim şeklinin çalışan beklentilerine uymaması, malzeme ve insan kaynağı eksiklikleri, iş güvencesinin olmaması, mobbing, şiddet ve baskı gibi faktörler hemşire göçünü tetiklemektedir (Denton, 2006; Dodani ve LaPorte, 2005). Bu koşullar, göç veren ve göç alan ülkelere bağlı olarak değişiklik göstermektedir (Global Health Watch, 2005). Göç alan ülkelerde ise, hemşire göçü genellikle zorlu bir süreç olmuştur. Bu ülkeler, nispeten düşük maliyetlerle eğitimli ve deneyimli hemşireler kazanarak personel eksikliklerini hızla giderebilmektedirler (Kline, 2003). Ancak, işe alım süreçlerinde bazı zorluklar da yaşanabilmektedir. Bazı ülkeler, hemşire eksikliklerini giderme amacıyla, hemşirelerin göç etme nedenlerine dair gerçek sorunları ele almamaktadırlar. Ayrıca, mesleği terk etme nedenleri ya da hemşireliğe olan ilginin az olması gibi faktörler göz ardı edilmekte ve bu durum, ihtiyaç duyulan hemşire planlaması ve etkili önlemlerin uygulanmasında gecikmelere yol açmaktadır (Kingma, 2001). Yabancı hemşire istihdam eden bazı ülkelerde, bu durum farklı problemlere yol açabilmektedir. Bazı kaynak ülkelerde, hemşirelerin yurt dışına göçü, ülke içindeki bakanlıklar arasında çatışmalara neden olmuştur. Örneğin, sağlık bakanlığı ve uluslararası kalkınma topluluğu, hemşire eksikliği nedeniyle programlarının çökme riskiyle karşı karşıya kalırken, maliye bakanlığı bu durumu görmezden gelmeyi tercih etmiş ve artan yurtdışı ödemeler nedeniyle ekonomik bir sorun olarak değerlendirmiştir (Vasant ve ark., 2004). Hemşire iş gücü göçü nedeniyle, geride kalan meslektaşların etkilendiği ve göç veren ülke koşullarının olumsuz yönde etkilendiği bildirilmektedir. Kaynak ülkede kalan hemşirelerin iş yüklerinin arttığı, stres seviyelerinin yükseldiği ve motivasyonlarının düştüğü ifade edilmiştir (Chikanda, 2005; Stilwell ve ark., 2004). Hemşirelerin göç etmesi, hemşire eksikliğiyle sonuçlanmakta ve vasıflı hemşirelerin ülkeden ayrılması, kaynak ülkelerde ekonomik yatırım kaybına (zaman ve eğitim için yapılan harcamalar) yol açmaktadır. Bu durum, gelişen ülkelerin

Kopenhag Kongresi'nde bu konuda kısıtlamalar talep etmelerine neden olmuştur (Kline, 2003). Bazı göç veren ülkelerde ise bu durumdan faydalanılmıştır. Filipinler ve Hindistan gibi büyük kaynak ülkeler, hemşire eğitiminin ticarileştirilmesiyle alıcı ülkelerdeki eksiklikleri ulusal bir kalkınma stratejisi olarak kullanmışlardır. Filipinler, yarım yüzyıldan fazla bir süredir ABD ve dünya genelinde en büyük hemşire tedarikçisi olmuştur (Choy, 2004). Ancak, dünyanın önde gelen hemşire ihracatçısı olarak bu konudaki liderliği, uluslararası pazara daha fazla hazırlanan diğer ülkeler tarafından ele alınmıştır (Brush ve Sochalski, 2007). Ülkelerindeki ekonomik nedenler (düşük maaşlar, kötü yaşam koşulları, karşılanamayan gereksinimler), çalışma ortamıyla ilgili faktörler (personel eksikliği, aşırı iş yükü, güvensiz çalışma koşulları, malzeme eksiklikleri, motivasyon kaybı, yetersiz eğitim ve kariyer fırsatları) hekimleri ve hemşireleri göçe zorlayan sebepler arasında yer almaktadır (Dohlman ve ark., 2019; Emmanuel ve ark., 2019; Hashish ve Ashour, 2020; Okafor ve Chimereze, 2020).

- **Finansal ve Diğer Teşvikler**

Yapılan araştırmalar, finansal olmayan teşviklerin sağlık çalışanlarının motivasyonunda önemli bir rol oynadığını göstermektedir. Bu teşvikler arasında eğitim imkanları, çalışma izinleri, kaliteli ekiplerde çalışma desteği ve geri bildirim fırsatları bulunmaktadır. Kırsal alanlardaki personeli korumak için bazı teşviklerin etkili olduğu görülmektedir. Bu teşvikler arasında barınma sağlanması, eğitim fırsatlarının arttırılması ve ekonomik teşviklerin sunulması yer almaktadır. 2011 yılında Bulgaristan'da yapılan bir araştırmaya göre, finansal teşviklerin önemi vurgulanmış ve hemşirelerin göç etme nedenlerinin başında %54,5 ile "gideceğim ülkenin ücretlerinin daha yüksek olması" yer almıştır. Ayrıca, göç etmenin en önemli nedeni, hemşirelerin kendi ülkelerindeki düşük ücretler olarak belirlenmiştir (Nedkova, 2011). Düşük ücretler nedeniyle bazı hemşirelerin mesleklerini bırakıp başka sektörlere yöneldikleri de tespit edilmiştir (Dimitrova, 2014). Hemşirelerin diğer ülkelere mesleki göç süreçleri, kurumsal firmalar tarafından organize edilmektedir. Firmaların, kolaylaştırılmış süreçleri hemşirelerin uluslararası göçünü kolaylaştırmaktadır (Dussault ve ark., 2009). Kurumsal firmalar hemşirelerle sözleşmeler yaparak, çalışan hakları ve çalışma şartlarını karşılıklı olarak belirlemekte ve kabul etmektedir. İş göçü, genellikle sosyal ağlardan etkilenmekte ve yeni göçmenlere, çoğu zaman onların bağlantılarına da destek sunan istihdam olanakları yaratmaktadır (Thomas, 2002; Martineau ve ark., 2002; Connel, 2002; Bach, 2004). Finansal olmayan motivasyonların yanı sıra, liderlik ve kariyer teşvikleri ile birlikte, işe alım ajansları hemşirelere ücretsiz seyahat biletleri, sübvansiyonlu konaklama ve vergiden muaf maaş fırsatları da sunmaktadır (Beaton ve Walsh, 2010 ;Kingma, 2006).

- **Göç Hızının Artmasına Etki Eden Diğer Faktörlerin Oluşması**

Göç hızını etkileyen birçok farklı koşul, hemşirelerin göç kararı almalarında önemli bir rol oynamaktadır. Küreselleşme, ekonomik ve politik değişimler, teknolojik gelişmelerin artışı, toplumdaki beklentilerin değişmesi, yaşlanan nüfus, hastalık yükü ve yapısındaki değişiklikler, AB gündemi ve uluslararası kuruluşların etkileri gibi faktörler, hemşirelerin daha yüksek gelir elde etme, kendi ülkelerinde yaşayan ailelerine döviz gönderme ve kariyer gelişimi için daha iyi çalışma koşulları arayışlarını güçlendirmektedir. Ayrıca, daha gelişmiş sağlık teknolojileriyle çalışmak, ileri düzey eğitim fırsatlarına katılmak, yaşam kalitesini artırmak ve aile hayatını daha iyi bir düzeye taşımak gibi unsurlar da önemli etkenler arasında yer almaktadır (Yıldırım, 2009). Vujicic ve ark. (2004) tarafından yapılan bir araştırmaya göre, kaynak ve hedef ülkeler arasındaki ücret farklılıklarının büyüklüğü, göç akışını doğrudan etkilemektedir. Ayrıca, çalışma koşulları ve mesleki gelişim olanakları da göç kararını etkileyen önemli faktörlerdir. Göç etme kararının, göç eden kişilerin ailelerinden de etkilendiği ve özellikle fakir ülkelerden göç eden profesyonellerin

maaşlarının bir kısmını ailelerine gönderdikleri ifade edilmiştir (Connell, 2002). Stresli çalışma koşulları, siyasi istikrarsızlık, ailelerinden ve arkadaşlarından ayrılma (Chikanda, 2005) ve bazı ailelerin çöküşü (Larsen ve ark., 2005) gibi faktörler de, hemşirelerin göç etme kararı almalarında etkili olmaktadır. Bu hemşirelerin ortak özelliği ise, hem kendileri hem de aileleri için yaşam tarzı ve güvenlik açısından değişiklik arayışında olmalarıdır.

- **Ülkeler Arası Anlaşmalar**

Uluslararası Hemşireler Konseyi (ICN), hemşirelerin mesleklerini icra edebilmesi için çalışma izinlerinin verilmesi konusunda çalışmalar yapmaktadır. Ancak, hemşirelerin göç sürecinde bazı etik sorunlarla karşılaştığı da belirtilmektedir (ICN, 2019). Göçün kaçınılmaz bir olgu olarak kabul edilmesi ve sağlık çalışanlarına sınırlı süreli yurtdışı çalışma fırsatları sağlanması amacıyla geçici vizeler verilmektedir. Bu vizeler veya işçi alımına yönelik kurumsal anlaşmalar, çift taraflı müzakerelerle gerçekleştirilmektedir. Gelişmiş ülkeler, bu anlaşmalarda işçi aldıkları ülkelere yatırım yapmayı kabul etmekte veya kaynak ülkeler, kendi sağlık çalışanlarını eğiterek alıcı ülkelere sağlık personeli sağlamaktadır. Bu tür bir sistem, Filipinler'de geleneksel olarak özel hemşirelik okulları aracılığıyla uygulanmaktadır (Lorenzo, 2002).

- **Hemşirelerin Serbest Dolaşımını Etkileyen Unsurların Oluşması**

Sağlık çalışanlarının serbest dolaşımını etkileyen başlıca unsurlar arasında ekonomik ve politik faktörler, küreselleşme, teknolojik gelişmeler, toplumun artan beklentileri, nüfusun yaşlanması ve hastalık yapılarındaki değişiklikler, AB dinamikleri ve uluslararası kuruluşlar yer almaktadır. Bu unsurlar, bireylerin ve ailelerin dışında kalan, daha geniş çapta etkiler yaratan faktörlerdir (WHO, 2001). Bu unsurların etkisiyle birlikte, nitelikli iş gücüne olan talep de artmaktadır (WHO, 2006). Sağlık çalışanlarının uluslararası göçü ile ilgili yapılan araştırmalarda, göçün artmasının, birçok etkileşimde bulunan farklı sebeplere dayandığı ifade edilmektedir (Eastwood, 2005).

Konuyla ilgili yapılan çalışmalarda, sağlık çalışanlarının hareketliliğini etkileyen faktörler genellikle "iten" ve "çeken" faktörler olarak iki kategoriye ayrılmaktadır. Bu faktörler çoğu zaman birbirine zıt etkilere sahip olup, birbiriyle etkileşim içindedir. Çeken faktörler, göç alan ülkenin göçü teşvik eden özellikleridir; iten faktörler ise göç veren ülkenin dış göçü tetikleyen özellikleridir (Arango, 2000; Skar, 2001; Paton ve ark., 2002). İten faktörler arasında, düşük ücretler, sınırlı kariyer fırsatları, iş tatminsizliği, kötü çalışma koşulları, kısıtlı eğitim imkanları, politik zorluklar, ülke beklentilerinin düşük olması, savaşlar ve bulaşıcı hastalıkların etkisi sayılabilir. Çeken faktörler ise, yüksek ücret tatmini, daha iyi çalışma koşulları, eğitim imkanlarının daha gelişmiş olması, aile için güvence sağlayan bir gelecek, yaşam kalitesinin artması, donanımlı sağlık sistemleri, döviz alım ve gönderme imkanı, daha iyi kariyer olanakları gibi unsurları içermektedir. (Arango, 2000; Buchan, 2006; Bundred ve ark., 2004; Gerlinger ve Schmucker, 2007; ILO, 2004; Paton ve ark., 2002; Ray ve ark., 2006; Skar, 2001; Tansel ve ark., 2003; Yıldırım, 2010; WHO, 2006).

2. HEMŞİRE İŞ GÜCÜ GÖÇÜNÜN OLUMLU VE OLUMSUZ ETKİLERİ

Göç veren ülkeler açısından iş gücü göçünün bazı olumsuz etkileri, ersonel eğitimi için ayrılan bütçenin boşa gitmesi, kaybedilen iş gücü nedeniyle artan vergi kayıpları, göç nedeniyle azalan personele düşen hasta ve iş yükü, personel eksikliği sebebiyle sağlık hizmet sunumunun kalitesinin düşmesi ve göç yönetiminin yaratacağı zorluklardır. Göç alan ülkelerde ise olumsuz etkiler yerli çalışanlar arasında motivasyon eksiklikleri, istihdamla

ilgili etik sorunlar, artan istihdam maliyetleri, yerli çalışanların maaşları ve çalışma koşullarına bağlı çatışmalardır.Bununla birlikte, göç veren ülkelerde iş gücü göçünün olumlu etkileri de vardır. Bu etkiler arasında, göç eden sağlık çalışanlarının geri döndüklerinde ülkelerine katkı sağlaması, bireysel refaha ulaşan sağlık çalışanları, döviz girişi ve bazı iş kollarındaki işsizlik oranlarının düşmesi sayılabilir. Göç alan ülkelerde ise iş gücü göçünün olumlu etkileri arasında, ulusal rekabetin artması, sağlık sektöründeki insan gücüne erişimin hızlanması ve bu alanda daha fazla fırsatın oluşması yer alır. (Aluwihare, 2005; Bach, 2006; Eastwood ve ark., 2005, Gerlinger ve Schmucker, 2007, Ray ve ark., 2006; Paton ve ark., 2002 , Xaba ve Phillips, 2001; Zajac, 2002).

3. GÖÇÜN OLUMSUZ ETKİLERİNDEN KORUNMAK İÇİN NE YAPILABİLİR?

Ülkeler, iş gücü göçünün olumsuz etkilerinden korunmak ve potansiyel zararları azaltmak için çeşitli stratejiler geliştirebilir. Hedef ülkelerin uygulayabileceği etkili stratejilerden biri, sağlık çalışanlarını elde tutmaktır. Bu amaçla, esnek iş sözleşmeleri, çalışma koşullarının iyileştirilmesi, performansa dayalı ücretlendirme ve fazla mesai ödemeleri gibi çeşitli teşvikler kullanılabilir. Ayrıca, sağlık çalışanı sayısının artırılması da personel kaybını engellemeye yardımcı olabilir. Göçün yönetilmesinde, hükümetler ve diğer ilgili kuruluşların daha stratejik bir yaklaşım benimsemesi de önemlidir. Bazı kaynak ülkelerde sağlık çalışanları ile yönetim arasındaki diyalog eksiklikleri ve toplu pazarlık ya da grev haklarının olmaması, çalışanların motivasyonunu olumsuz etkileyebilir ve bu durum, kişileri göç etmeye teşvik edebilir (Ray ve ark., 2006). Göçü önlemek için aile bireylerine yönelik ulaşım, barınma ve eğitim imkanlarının iyileştirilmesi de önemli stratejiler arasındadır (WHO, 2006). Bunun yanı sıra, uzmanlık eğitimleri için altyapı oluşturmak, uzun vadede beyin göçünü engellemeye yönelik bir adım olabilir. Ancak, bu tür programların başlatılması finansal kaynaklar, eğitimli kadro ve gerekli malzemeler gibi unsurlara bağlı olduğundan, özellikle düşük gelirli ülkelerde bu tür girişimler zorlu olabilir (Muula, 2005). Yerel ihtiyaçlara ve koşullara odaklanmış bir eğitim sistemi de sağlık çalışanlarının göç etmesini sınırlamaya yardımcı olabilir (WHO, 2006a). Göç veren ülkeler, eğitim müfredatlarını ve içeriklerini gözden geçirip, bu programları ülkenin sağlık sorunlarına yönelik daha etkili bir şekilde yeniden yapılandırabilir (Stewart ve ark., 2007). Ayrıca, kaynak ülkeler sağlık çalışanlarının göçünü engellemek amacıyla, hekim ve hemşireler için zorunlu hizmet uygulamaları geliştirebilir (Ray ve ark., 2006). Bazı gelişmekte olan ülkeler, "bonding" adı verilen bir yöntemi benimsemektedir. Bu yöntemde, sağlık çalışanları, eğitim aldıkları dönemde devlet tarafından sağlanan destek karşılığında belirli bir süre zorunlu hizmet yapmak zorundadır. Ancak, bu zorunlu hizmet şartını yerine getirmeyen kişilere, tazminat ödeme yükümlülüğü getirilebilir (Muula, 2005; Ray ve ark., 2006; Stewart ve ark., 2007). Beyin göçü sorununu çözmenin bir diğer yolu ise sendikaların güçlendirilmesidir (Muula, 2005). Yurt dışında geçirilen çalışma süresi, sağlık çalışanlarının maaşları ve terfilerinde dikkate alınabilir. Ayrıca, emeklilik hakları garanti altına alınabilir ve barınma gibi ek yardımlar sunulabilir. Yurt dışında kazanılan paranın yerel ekonomiye yatırılması ise vergi avantajları veya diğer teşvikler ile kolaylaştırılabilir (Ray ve ark., 2006). Özel sektörün geliştirilmesi de göçmenlerin geri dönmesini teşvik etmek için bir araç olarak kullanılabilir (Aluwihare, 2005).

4. HEMŞİRE GÖÇÜ İLE İLGİLİ YAPILAN ARAŞTIRMA SONUÇLARI

Türkiye'den yurt dışına göç eden hemşirelerle ilgili yapılan araştırmalar sınırlıdır. Türkiye'de sağlık çalışanlarının göçüyle ilgili sistematik bir veri tabanının eksikliği olduğu vurgulanmaktadır (Mollahaliloğlu ve ark., 2014). 2022 yılında Türkiye'den farklı ülkelere çalışmak amacıyla göç etmiş 130 hemşireyle yapılan bir araştırmaya göre, göç eden hemşirelerin %72,3'ü kadın, %38,5'i 31-35 yaş arasında, %58,5'i bekar, %72,3'ü lisans mezunu ve %92,3'ü hemşirelik mesleğini isteyerek seçmiştir. Hemşirelerin %97,7'si Türkiye'de hemşirelik yaparken, %63,8'i özel sektörde çalışmış, %55,4'ü ise istediği birimde görev yapmamıştır. Ayrıca, %48,5'i Türkiye'de mesleğinden kısmen doyum aldığını belirtmiştir. Hemşirelerin göç kararlarında etkili olan faktörler arasında, çalışma saatleri, yan haklar, sosyal imkanlar, iş ve yaşam kalitesi gibi unsurlar öne çıkmıştır. Göç edilen ülkeler arasında Almanya, Amerika, Avustralya, İngiltere, İsviçre, Kanada, Kıbrıs, Norveç, Avusturya, Yeni Zelanda ve Azerbaycan yer almaktadır. En fazla göç veren şehirler ise İstanbul (%38,4), İzmir (%13,8), Antalya (%11,5) ve Ankara (%9,2) olarak belirlenmiştir. Hemşirelerin göç nedenleri arasında, bilgi ve beceri arttırma, teknolojiyi takip etme, daha iyi kariyer fırsatları ve mesleki gelişim isteği öne çıkmaktadır. (Duran ve Altuntaş, 2025).

Türkiye'den İngiltere'ye göç etmiş 128 hemşiresi ile yapılmış bir çalışmadaysa; %89,8'inin İngiltere'deki mesleki doyumdan memnun olduğu, %95,3'ünün ise orada yaşamaktan memnun olduğu belirlenmiştir. Göç etme nedenlerinin %64,8'i politik, %55,5'i gelecek kaygısı ve %53,1'i ekonomik sebepler olarak sıralanmıştır. İngiltere'deki yaşam doyumunun yüksek olması, Türk hemşirelerin oraya göç etmelerindeki önemli bir faktördür (Şen ve Yurt, 2023). Literatürde, Türkiye'nin beyin göçünde otuz dört ülke arasında yirmi dördüncü sırada yer aldığı ifade edilmektedir (Babataş, 2007; Doğan, 2020). Türk Hemşireler Derneği'nin 2023 yılı göç eğilim raporuna göre, Türk hemşirelerin en fazla göç etmek istedikleri ülkeler arasında Amerika, Kanada, İngiltere ve Almanya yer almaktadır (THD, 2023). Beyin göçünün, özellikle gelişmekte olan ülkelerde nitelikli sağlık hizmetlerinin sunumunu engellediği ve sağlık hizmetlerine erişimde ciddi sorunlara yol açtığı öngörülmektedir (Öncü ve ark., 2018; Pang ve ark., 2002). 2008 yılında Ankara ve Muş'taki Sağlık Bakanlığı hastanelerinde çalışan 485 hekim ve 569 hemşire ile yapılan bir araştırmada, hekimlerin %66,2'si ve hemşirelerin %65,2'si başka bir AB ülkesinde çalışmayı düşündüklerini belirtmiştir. Bu araştırmada, katılımcıların yurt dışına gitme isteğinde etkili olan başlıca faktörler arasında daha iyi çalışma şartları, gelişmiş tıbbi teknolojiye erişim ve daha iyi eğitim fırsatları yer almıştır. (Yıldırım,2009). Uluslararası bir araştırma, yüksek gelirli ülkeler olan Avustralya, Birleşik Krallık ve Kanada'ya göç eden yabancı hemşirelerin, seyahat etme ve farklı yaşam stillerini deneyimleme isteğiyle göç etmeye eğilimli olduklarını ortaya koymuştur (Higginbottom, 2011; Vafeas ve Hendricks, 2018). Göç eden hemşirelerin motivasyonları arasında, beceri geliştirme, teknolojiyi takip etme, niteliklerini artırma ve kariyerlerinde ilerleme arzusu bulunmaktadır (Adhikari ve Melia, 2015; Alexis ve Shillingford, 2015; Higginbottom, 2011). Düşük gelirli ülkelerden gelen uluslararası hemşireler, göç etmeyi, kendi ülkelerindeki elverişsiz çalışma koşulları ve düşük maaşlar nedeniyle tercih etmektedir (Salami, 2018; Lin, 2014; Kishi ve ark., 2014). Türkiye'den göç eden hemşirelerle yapılan araştırmada ise hemşirelerin çalışma koşulları ve ücret yetersizliği, bu bulguları destekleyen faktörlerdir (Duran ve Altuntaş, 2025).

5. SONUÇ

Sağlık çalışanlarının uluslararası alandaki serbest dolaşımının artmasıyla, hemşire göçü ve bunun yarattığı eksiklikler daha belirgin hale gelmiştir. Türkiye'de, hemşirelerin göç eğilimlerini araştıran ve göç eden hemşirelerin sayı ve niteliklerini ortaya koyan istatistiksel verilere ihtiyaç duyulmaktadır. Bu tür veriler, göçün etkilerini anlamak ve çözüm önerileri geliştirmek açısından önemlidir.

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IN ANIMAL HEALTH AN APPROACH TO THE HEALTH-PREVENTION IS BETTER THAN CURE STRATEGY: THE EXAMPLE OF EU COUNTRIES

ABSTRACT

All people care about the welfare of animals. In addition to the economic expenses that can lead to epidemics, this worry stems from the public health and food safety aspects of animal welfare as well as the impacts of disease control. This method offers guidance for creating animal health policies that strictly adhere to extensive, high requirements for animal care. It will be easier to examine and agree on acceptable and appropriate standards if priorities are set in accordance with the approved strategic objectives. The idea of animal health includes both the absence of sickness in animals and the important connection between animal welfare and health. It is also a cornerstone of the EU Commission's policy on food safety and public health. The strategy covers food, farming, sport, companionship, recreation and the health of all animals kept in zoos in the EU. It also includes wild animals and animals used in research that pose a risk of transmitting disease. This approach also covers the welfare of animals transported to, from and within the EU. It is aimed at the entire EU, including pet owners, the veterinary profession, food chain businesses, animal health industries, animal interest groups, researchers and teachers, governing bodies of sports and leisure organisations, educational facilities, consumers, travellers, competent authorities of Member States and EU Institutions. This approach is based on the existing animal health legal framework in the EU and the standards and guidelines of the World Organization for Animal Health. It also aims to ensure consistency with other EU policies and the EU's international commitments.

It will guide the development of new policies or guidelines and ensure that existing animal welfare regulations in the community are improved, based on scientific risk assessments and taking into account social, economic and ethical considerations. A high level of environmental protection will also be ensured by taking into account the impacts on the environment in the development of the policy framework for animal health and welfare to be implemented. This future strategy will aim to replace the current series of linked and interrelated policy actions with a single policy framework. The Animal Health Strategy will strive for a single clear regulatory framework incorporating OIE/Codex standards and guidelines wherever possible. This regulatory framework will include animal nutrition and animal welfare measures. In this article; After emphasizing the importance of health-protection, summary information will be given about the strategies implemented, especially in EU countries, and their results.

Keywords: Animal health, strategy, disease control, animal welfare

ÖZET

Hayvan sağlığı tüm insanlar için bir endişe kaynağıdır. Bu endişe, hayvan sağlığının halk sağlığı ve gıda güvenliği yönlerinden kaynaklanmakta, ancak aynı zamanda salgın hastalıkları tetikleyebileceği ekonomik maliyetlerden ve hastalık kontrolünün etkileri de dahil olmak üzere hayvan refahı hususlarından da kaynaklanmaktadır. Bu yaklaşım, kapsamlı yüksek hayvan sağlığı standartlarına sıkı sıkıya bağlılığa dayalı olarak hayvan sağlığı politikasının geliştirilmesi için yön verir. Benimsenen stratejik hedeflerle tutarlı önceliklerin oluşturulması, kabul edilebilir ve uygun standartların gözden geçirilmesini ve bunlar üzerinde anlaşmaya varılmasını kolaylaştıracaktır. Hayvan sağlığı kavramı yalnızca hayvanlarda hastalık olmamasını değil, aynı zamanda hayvanların sağlığı ile refahı arasındaki kritik ilişkiyi de kapsar. Ayrıca, AB komisyonun halk sağlığı ve gıda güvenliği politikasının da bir ayağıdır. Strateji, AB'de gıda, çiftçilik, spor, arkadaşlık, eğlence ve hayvanat bahçelerinde tutulan tüm hayvanların sağlığını kapsar. Ayrıca, yaban hayvanları ve hastalık bulaştırma riski olan araştırmalarda kullanılan hayvanları da kapsar. Bu yaklaşım, AB'ye, AB'den ve AB içinde taşınan hayvanların sağlığını da kapsar. Hayvan sahipleri, veterinerlik mesleği, gıda zinciri işletmeleri, hayvan sağlığı endüstrileri, hayvan ilgi grupları, araştırmacılar ve öğretmenler, spor ve eğlence kuruluşlarının yönetim organları, eğitim tesisleri, tüketiciler, gezginler, Üye Devletlerin yetkili makamları ve AB Kurumları dahil olmak üzere tüm AB'yi hedeflemektedir. Bu yaklaşım, AB'deki mevcut hayvan sağlığı yasal çerçevesi ve Dünya Hayvan Sağlığı Örgütü'nün standartları ve yönergelerine dayanmaktadır. Diğer AB politikaları ve AB'nin uluslararası taahhütleriyle tutarlılığı sağlamayı da amaçlamaktadır. Yeni politika ya da yönergelerin geliştirilmesine rehberlik edecek ve bilimsel risk değerlendirmelerine dayalı olarak ve sosyal, ekonomik ve etik hususları dikkate alarak topluluktaki mevcut hayvan sağlığı düzenlemelerinin de geliştirilmesini sağlayacaktır. Uygulanacak hayvan sağlığı ve refahına yönelik politika çerçevesinin geliştirilmesinde çevre üzerindeki etkileri dikkate alarak yüksek düzeyde çevre koruması da sağlanacaktır.

Gelecekteki bu strateji, mevcut bağlantılı ve birbiriyle ilişkili politika eylemleri serisini tek bir politika çerçevesiyle değiştirmeyi amaçlayacaktır. Hayvan Sağlığı Stratejisi, mümkün olduğunca OIE/Kodeks standartları ve yönergeleriyle birleşen tek bir net düzenleyici çerçeve için çabalayacaktır. Bu düzenleyici çerçeve, hayvan beslenmesi ve hayvan refahı önlemlerini içerecektir. Bu makalede; sağlık-korumanın önemine vurgu yapıldıktan sonra başta AB ülkeleri olmak üzere uygulanan stratejiler ve bunların sonuçları konusunda özet bilgiler verilecektir.

Anahtar Kelimeler: Hayvan sağlığı, strateji, hastalık kontrolü, hayvan refahı

Introduction

A new Animal Health Strategy (AHS) for the European Union (2007–2013) was released by the European Commission in 2007 with the goal that "prevention is superior to a cure (Blanco-Penedo et al., 2019). Assuring a high standard of public health and food safety, promoting animal health to support farming and the rural economy, enhancing economic growth, cohesion, and competitiveness, and promoting farming practices and animal welfare that minimize environmental impacts and prevent threats to animal health are the objectives of this strategy. There are four designated areas of activity: science, innovation, and research; a new framework for animal health; prevention, surveillance, and preparedness of threats relating to animals; and prioritizing EU intervention. Regarding the first area, animal health risks will be evaluated to ascertain their applicability to the AHS's objectives, the "acceptable level of risk" for the community and the order of importance of risk reduction measures. Reducing risk to a negligible level is the aim for major hazards to human health and the rural economy.

Systems for raising livestock are currently dealing with a number of complex issues that call for them to become more environmentally and economically sustainable (Augustin et al., 2013). A important component of the European Commission's "Farm to Fork" policy, high standards of animal health and wellbeing are essential for enhancing food quality, lowering the use of antibiotics on farms, increasing production efficiency, and lowering greenhouse gas emissions (Stojanovic, 2021). Farmers have a significant impact on improving the health and welfare of the animals on their farms through management decisions, which is crucial to successfully lowering the incidence and spread of disease. In order to reduce the risks of cattle diseases on the farm, it is crucial to make sure dairy farmers have access to the assistance they need (Emanuelson et al., 2018).

Different European nations have different dairy farming systems and health issues (EFSA, 2009). Spain in southern Europe and the United Kingdom in northern Europe serve as prime examples of these distinctions. Dairy herds in Spain are typically smaller than those in the UK (Blanco-Penedo et al., 2019; MAPAMA, 2020), are more likely to be housed or kept in open yards year-round, as opposed to the UK's greater reliance on grazing (AHDB, 2016), and are likely to be impacted by climate change in different ways. For example, heat stress is becoming a bigger problem in southern Europe (Kipling et al., 2021), and UK farmers are facing challenges related to warmer, wetter winters and their associated disease impacts, such as helminth burdens. In this regard, it is critical that the resources used for animal health decision support are adapted to the various requirements of various geographic and socioeconomic contexts (Perry et al., 2018). Few models have concentrated on the particular requirements of organic dairy systems, despite the fact that conventional and organic systems are likely to have different demands for animal health guidance (Krieger et al., 2020).

In addition to economic imperatives, farmers base their decisions on a broad array of factors, such as reciprocity, social preferences, moral convictions, intrinsic motivations, and the influence of peer groups (de Lauwere et al., 2020). If farmers anticipate that innovation and change will help them accomplish their goals—which may include social, economic, environmental, and animal welfare objectives (Liu et al., 2019) they are more inclined to embrace it. However, even when change is perceived to be in the farmer's best interests, it may be thwarted by practical (resource availability, nature of current system), knowledge (of change options, effective implementation, and likely outcomes), and cognitive (strategies to manage complex information and conflicting aims under pressure) barriers (Kipling et al.,

2021). Accordingly, the resources needed to enable transformation will probably differ among farming systems, geographical areas, and individual farmers (Brodt et al., 2011).

According to Regulation (EU) 2016/429, the current European Union Animal Health Law, farm biosecurity is necessary for the efficient management of animal health. According to Blanco-Penedo et al. (2022), such management needs to be adaptive and flexible to various production systems and local circumstances. Therefore, it's critical to comprehend how much the needs of conventional and organic dairy producers vary with regard to disease prevention and whether these groups have access to the assistance they require to reduce health risks to their animals.

The percentage of organic dairy farms varies greatly throughout European nations, and while organic milk production has nearly doubled in the EU, it still only made up 3.4% of total EU milk output in 2019 (Willer et al., 2024). Because organic milk may be sold for more than non-organic, and because many consumers are choosing organic products, farm conversions have occurred in reaction to the dairy issue. By 2030, the European Commission (EC) has set the lofty target of raising the proportion of organic farming to 25% (EC, 2020).

Risk managers for animal health have access to a variety of models and support resources for risk mitigation. A significant step toward increasing the adoption of efficient disease control strategies would be to enhance the degree to which such tools take into account the requirements and viewpoints of farmers in both their scope and outputs. Additionally, a deeper comprehension of the disparities in the requirements of various farmer groups might guide improvements in the customization of the entire spectrum of information exchange strategies employed in the farming industry to solve particular problems in particular situations (Kipling & Becoña, 2019).

In order to improve decision-making, mathematical models and decision support systems can be crucial in filling in farmers' knowledge gaps and deciphering the many variables influencing animal health (Özkan et al., 2016). To promote change, models need to be viewed by stakeholders as genuine, relevant, and credible (van Bruggen et al., 2019). Along with recognizing the significance of how, when, in what form, and by whom knowledge is provided (Svensson et al., 2020), this calls for a focus on communicating modeling to stakeholders (Kipling & & Becoña, 2019).

The differing dairy cow production industries in Spain and the UK offer a chance to investigate how farmers' needs vary between systems and nations with regard to decision support for disease control. In 2020, the UK and Spain had comparable percentages of organic and conventional dairy cows, at 1.9% and 1.4%, respectively (DEFRA 2021). Due to climate-related variations in grass availability, an estimated 80–95% of dairy cows in the UK were grazed for at least part of the year in 2018, compared to barely 20% in northwestern Spain (van den Pol-van Dasselaar et al., 2020). In the UK, all farms are members of the Agriculture and Horticulture Development Board (AHDB), which offers guidance and assistance on best practices, and they all pay a statutory levy board fee. Small-scale family farms make up the majority of organic dairy farming in Spain; these farms have limited access to knowledge and little involvement in cooperative dairy firms (Blanco-Penedo et al., 2019). All dairy cattle farms have different veterinarian profiles, such as private veterinarians, veterinarians who work in animal health programs (either through an Animal Health Defense Association (HDA) or formal veterinary services of a public enterprise). This could lead to varying opinions and suggestions for farmers (Stojanovic, 2021).

Antibiotic Use

In both human and veterinary medicine, antibiotics are essential for treating serious infectious infections. Additionally, it is still challenging to find similarly effective substitutes for them. Therefore, one of the biggest risks to the health of people and animals worldwide today is antibiotic resistance. Limiting use and making sure that antibiotics are used correctly when necessary is a recognized crucial step in preventing the development of antibiotic resistance, despite the fact that resistance development is complicated and not fully understood (WHO, 2020). Animal husbandry currently accounts for a sizable portion of antibiotic use, and it is expected to account for two-thirds of the global increase in antibiotic use. Therefore, it is generally agreed that policy and research activities are required to reduce the use of antibiotics in animal husbandry (Stojanovic, 2021).

To better match actual use with medical recommendations, a lot of research has recently focused on farmer behavior about antibiotic use (Jones et al., 2013; Lam et al., 2017). Antibiotic use by farmers is a result of the dialectic agency–structure connection that defines society rather than an isolated occurrence. As a result, it is caused by a variety of factors, including peer pressure, veterinarian advice, legislation, interactions with farm animals, and farmers' own beliefs and practices (Burton et al., 2012; Hamilton, 2018). Although empirical research is required to determine the proportional impact of different parameters, studies on antibiotic usage in dairy farming have so far tended to favor the agency side of the agency–structure dynamic. Although some recent studies on antibiotics (Buller et al., 2015; Swinkels et al., 2015) and the adoption of biosecurity measures more generally (Higgins et al., 2018; Shortall et al., 2018) recognize the need to study farm practices in their broader context, the topic is still understudied (Swinkels et al., 2015).

Studies in the reductionist tradition of science have concentrated on individual farmers, failing to link them to the larger context in which they live and act, due to the dearth of social scientists in research on ways to improve farm animal health and welfare generally (Burton et al., 2012) and how to lessen the development of antibiotic resistance in farming. For instance, Jansen et al. (2009) investigated farmers' opinions regarding the treatment of mastitis, but they did not examine how the socioeconomic and political environment influences these opinions. A thorough study on the application of a model influencing farmers to modify their behavior with relation to antibiotic use is presented by Lam et al. (2017), who also report that the model was successful in changing farmer behavior. Nevertheless, similar to Jansen et al. (2009), they gave little consideration to how outside forces influenced farmers' actions. According to Jones et al. (2016), who conducted interviews with organic farmers in France, Germany, Spain, and Sweden, more information about suitable techniques won't alter farmers' behaviors; instead, research on the underlying factors that influence and hinder these practices is required. However, no additional research is done on these fundamental motivators and obstacles. In conclusion, although mentioned in the literature as potentially influencing farmers' practices with regard to animal health, welfare, and illness, the ways in which structural societal factors like market prices, policies, and regulations stimulate or hinder farmers' treatment of their animals are still largely unexplored. Therefore, these kinds of studies are necessary to address antibiotic resistance in agriculture and to gain a better understanding of the rationale behind specific methods.

Numerous studies emphasize that maximizing output is a naturalized objective for farmers as well as for members of society in general (Burton, 2004; Shortall et al., 2018) and that high production levels are essential for identifying successful farmers across contexts in

neoliberal society. It's crucial to remember that farmers maximize productivity since it reflects being a good farmer, which makes them respected and accepted by their peers, in addition to wanting to make a good living which would demonstrate individualized and rational behavior (Burton, 2004).

There is a certain tension in this identity of a good farmer when it comes to animal husbandry. According to research conducted in many contexts, being a successful farmer is primarily about taking good care of one's animals and optimizing productivity (Ellis, 2014; Shortall et al., 2018). This may be especially true for dairy cows in particular and animals in general. According to Ellis (2014), farmers must physically touch and work with cattle because to their large bodies, and this close contact makes it challenging to emotionally distance oneself from the animals. Therefore, caring for animals involves more than just fitting in with one's peers; it also involves having a strong emotional bond with the animals. Farmers' feelings for dairy cows are stronger than those for other farm animals because of their close daily contact with them, according to Bock et al. (2007). Additionally, a number of writers stressed that, in capitalist agriculture, the two elements of high productivity and providing cows with a decent life are increasingly at odds (Wilkie, 2005). In order to continue treating their cattle as commodities, farmers must control their emotional attachments to them.

Although the idea of the "good farmer" has been useful in highlighting how individual behavior is socially constructed, farmers' words and actions are largely guided by the political and economic environment in which they live in addition to being impacted by the opinions of other farmers (Shortall et al., 2018). Important frameworks for how farmers can practice farming include agricultural policies, milk prices, and so forth. These frameworks are reflected in farmers' practices and viewpoints; for example, it may be extremely challenging for a farmer to imagine a production system that does not strive for output maximization.

In conclusion, we may anticipate that farmers' actions and discussions over the use of antibiotics in dairy farming will reflect not only their individual beliefs but also the broader dairy farming culture and the broader political economy. Furthermore, farmers are expected to prioritize the wellbeing of their animals for both emotional and personal reasons, as well as because caring for one's cows is a crucial aspect of being a good farmer.

One Health Applications

A new approach that is centered on improved coordination and cooperation amongst many health players is now required due to the emergence of infectious diseases. In order to combat these health emergencies and lessen their negative social and economic effects, they have also emphasized the significance of improved readiness, prevention, detection, and response. The One Health concept is becoming more and more crucial in a world where environmental changes can affect the health of humans and animals, and emerging diseases and public health issues are becoming more prevalent (Mackenzie & Jeggo, 2019).

Recognizing the connection between environment, animal, and human health is the philosophy behind One Health. Humans, animals, ecosystems, and consequently global health have all been significantly impacted in recent years by antibiotic resistance and newly developing infectious illnesses. Since these are pressing public health concerns, there is now widespread recognition of the necessity of tackling health issues globally. It is obvious that the various facets of human, animal, and environmental health must collaborate and adopt a

One Health strategy in order to combat the threat of antibiotic resistance and new zoonotic illnesses (Velazquez-Meza et al., 2022).

Research unequivocally shows that over half of all diseases that affect animals now could be severely harmed and become more problematic due to climate change. Infectious diseases are emerging, re-emerging, and spreading as a result of unprecedented climate change. The geographic distribution of many illnesses is influenced by the favorable conditions that the increase in global temperatures offers for the growth of particular disease vectors (Verbist, 2022). This has led to the spread of zoonotic viruses that were previously limited to warm climates. Previously unaffected areas are now experiencing an upsurge in diseases as a result of regional temperature changes. Animal species are likewise compelled to search for new environments that will allow them to survive. They are being forced to relocate to locations with better conditions due to events like drought, floods, forest fires, and extreme weather. As a result, species that have never lived together will coexist, raising the possibility of virus transmission between naïve hosts—hosts who have never been exposed to these viruses.

Regulation of International Health (IHR)

The International Health Regulations serve as the WHO's reference document and are the primary tool for fighting pandemics. The 196 states that are parties to it, including the 194 WHO member states, are bound by this instrument of international law. Its responsibilities include coordinating the efforts of the several state parties and issuing directives to individuals engaged in health problem prevention, detection, and response. It is urged for all affected industries to collaborate, expanding (WHO, 2019).

The New Veterinary Regulation

As of January 28, 2022, EU Member States are required to abide by Regulation 2019/6 of the European Parliament and Council of December 11, 2018, which repeals Directive 2001/82/EC and deals with veterinary medical goods. Each nation was permitted by the 2001 directive to create national laws that complemented the goals of the European directive. Therefore, it seemed more suitable to create a regulation to guarantee that each Member State applies the European regulations. Furthermore, by incorporating this regulation into national laws, all Member States will have uniform European requirements (Schmerold et al., 2023). However, it is crucial to remember that this new rule gives Member States the freedom to concentrate on particular issues at the national level while honoring the many traditions and distinctive features of every nation. By assuring a high degree of protection of animal health and welfare, maintaining the effectiveness and quality of veterinary pharmaceutical products, preventing antimicrobial resistance, and promoting food safety, Regulation 2019/6 seeks to protect both human and animal health. Antimicrobial usage in animals is now subject to more stringent regulations, and while weighing the advantages and disadvantages of medications, the dangers of antibiotic resistance are taken into consideration (More et al., 2022).

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BLOWFLY STRIKE AND THE IMPORTANCE OF SHEEP BREEDING

ABSTRACT

Fly bites or strikes are other names for the blowfly and the issues it causes with animal welfare. In nations like Australia, New Zealand, and England, this circumstance also results in yearly economic losses of about $300 million, particularly in those where the breeding of wool or wool-meat sheep is widespread. Medicine and veterinary care, labour, time needed to clean the infection, wool value loss, and occasionally animal losses from death are all included in this financial loss. The green bottle (Lucilia sericata) and other related fly species that deposit their eggs on live sheep are mostly responsible for the blowfly's harm to sheep's wool. L. can appear anywhere on the body where the wool is polluted or affected with germs, in contrast to other fly species found in homes or shelters. The blowfly's negative effects are most noticeable during hot weather and on days with a lot of rain. Put another way, the fly's secretions keep the animal's body moist or wet all the time, which deteriorates the fleece. Different body parts are home to various dung fly species. In addition to causing lesions on the feet, head, and horns, it can also create wounds around the reproductive organs in males. The tail or tail area is typically the most common. Sheep bitten by flies have characteristic green or wet patches on their wool, usually around the hips or tail or if there is an open wound where the wool may create a moist area that flies find more attractive. Additionally, fly strikes frequently occur in the male sheep's penis. Once the flock has calmed down, agitated sheep will stomp their feet or turn to chew on their bodies. Preventing the blowfly problem is less expensive than treating it. Chemical application, mulch control, tail docking, spraying, and showering are a few of the control methods used. Furthermore, either direct or indirect selection factors are used to achieve this.

The purpose of this article is to highlight the impact of the dung fly, which is prevalent in sheep, particularly on the yield of wool and wool meat, and to offer guidance on how to implement sustainable production using the best technique while considering the welfare and health of the animals on the farm.

Keywords: Sheep, blowfly strike biology, control and struggle methods

ÖZET

Gübre sineği ve bunun neden olduğu hayvan refahı sorunu, sinek ısırığı ya da çarpması şeklinde de adlandırılmaktadır. Bu durum, Avustralya, Yeni Zelanda ve İngiltere gibi özellikle yapağı ya da yapağı-et tipi koyun yetiştiriciliğinin yaygın olduğu ülkelerde yıllık yaklaşık 300 milyon dolar gibi ekonomik kayıplara da neden olmaktadır. Oluşan bu ekonomik kayıp içinde ilaç ve veteriner, oluşan enfeksiyonu temizlemek için gereken emek, zaman ve yapağı değerinin azalması ile bazen ölüme bağlı olarak oluşan hayvan kayıpları da buna dahildir. Gübre sineğinin koyunlarda yapağıda neden olduğu zarar, çoğunlukla yeşil şişe (Lucilia sericata) ve yaşayan koyunların üzerine yumurta bırakan ilgili sinek türleri tarafından meydana gelir. L.'nin ev veya barınaklarda karşılaşılan diğer sineği türlerinin aksine, yapağının kirlendiği veya bakteriyle enfekte olduğu vücudun herhangi bir yerinde meydana gelebilir. Gübre sineğinin neden olduğu olumsuzluk, özellikle yağışın yoğun olduğu gün ve sıcak havalarda gerçekleşir. Bir başka deyişle, sineğin salgıları nedeniyle hayvan vücudunun sürekli ıslanması ya da nemlenmesi sonucunda yapağıda bir bozulma meydana gelir. Gübre sineğinin neden olduğu farklı vücut bölgelerindeki şekilleri vardır. Genellikle kuyruk veya kuyruk bölgesi en yaygın olanı olup ayakta, baş ve boynuzlarda ve erkeklerde üreme organı çevresinde de yaralara neden olabilmektedir. Sinek çarpmasına uğramış koyunlar, koyunların yününde karakteristik yeşil veya ıslak görünümlü lekelerle, genellikle kalça veya kuyruk çevresinde veya yünün sinekler için daha çekici olan nemli bir alan oluşturabileceği açık bir yaranın olduğu yerde tespit edilir. Erkek koyunlarda penis bölgesi de sinek çarpmasının meydana geldiği yaygın bir alandır. Sürüye yerleştiğinde, enfekte koyunlar ayaklarını yere vurma veya vücutlarını kemirmek için dönme gibi ajitasyon belirtileri gösterir. Gübre sineği sorununu önlemek, tedavi etmekten daha ekonomiktir. Kimyasal uygulama, kuyruğun kesilmesi, çakıldak kontrolü, sprey yöntemi ya da duşlar kullanılan bazı mücadele yöntemleridir. Bunun dışında doğrudan ya da dolaylı seleksiyon parametreleri de bu amaçla kullanılmaktadır.

Bu makalede; özellikle yapağı ve yapağı-et verim koyunlarda çoksık rastlanılan gübre sineğini etkisini vurgulamak ve işletmede hayvan sağlığı ve refahını da dikkate alarak en uygun yöntemle ile sürüdürülebilir üretimin nasıl yapılması gerektiği konsunda bilgi vermek amaçlanmıştır.

Anahtar Kelimeler: Koyun, gübre sineği, biyolojisi, kontrol ve mücadele yöntemleri

INTRODUCTION

A parasite infection with a live insect causes flystrike in sheep, also known as ovine cutaneous myiasis. The Australian Sheep Blowfly (SBF), Lucilia sericata and Lucilia cuprina, is the main culprit in Australia. When the larvae (maggots) hatch from the eggs laid by adult female SBF in dirty wool or open wounds, they burrow beneath the sheep's skin and consume its live flesh. Infested sheep have a direct impact on meat output, food intake, and the growth and quality of their fleece (Lihou and Wall, 2019). Up to 80% of Australian merino sheep herds that produce wool are impacted by flystrike. The industry may lose up to $173 million a year as a result of infestations due to lost output, stock, and control methods (Adamson and Wheeler, 2020).

The primary strategies for preventing flystrikes are strategic chemical management and/or mulesing. Chemical control (wound treatment, jetting, and dipping) is effective but expensive because it involves handling flocks and chemicals, and its effects on the environment are being debated (Beynon 2012). According to Lihou and Wall (2019), the rationale for the selection and timing of chemical applications is frequently weak. SBF has been shown to exhibit mild resistance to organophosphates, and this resistance is growing (Naqqash et al 2016). Although some importing nations limit the entry of meat that exceeds certain chemical residue levels, there are still chemical solutions accessible. This indicates that the entire sector is looking for methods to use fewer chemicals while still producing meat that is suitable for export.

Because of its ecology, SBF is a good candidate for management using the sterile insect technique (SIT), in which sterile males are released to mate with wild females, producing non-viable eggs and a decrease in pest populations in the offspring. This method is already in use for SBF in Bangladesh and has been developed for several pest insects globally. It should be easily possible to eradicate SBF in geographically remote places like islands. By integrating monitoring, modeling, and seasonal releases, an effective decrease will greatly contribute to an acceptable Integrated Pest Management (IPM) for SBF in other mainland locations (Morris, 2005).

1. Sheep Blowfly Lucilia Biology

Fly members of the Calliphoridae family include the SBF, Lucilia (Wiedmann) (Waterhouse and Paramonovo, 1950). Calliphorid flies frequently exhibit behaviors related to feeding on carrion. In the competition to consume enough food to finish developing on carrion, SBF does poorly in comparison to other blowfly species. SBF is now a parasite of both dead fish (Islam et al., 2014) and living sheep (Anderson et al., 1990). Over 90% of all flystrikes (myiasis) in Australia are caused by SBF, making it the most common pest blowfly species in the nation (NSW Department of Primary Industries, 2016). Seldom does SBF appear on sheep or other species' carcasses (Anderson et al., 1990). Although co-infestation with other fly species (Chrysosoma/Callipora) after an initial SBF infestation is common, infestations of sheep with these species alone are uncommon. According to Ashworth and Wall (1994), gravid female SBF are drawn to sheep primarily by olfactory cues and are encouraged to deposit their eggs into the fleece and/or on open wounds. The many pathological consequences of the flystrike are caused by the feeding activity of the following maggots, which can be both mechanical and chemical and, in the worst cases, can be lethal.

Because SBF is used in forensic sciences, information about its biology and pace of development is easily accessible. Nevertheless, there is a dearth of information on phenology, populations, and field ecology.

2. Ecology

Blowflies' rate of development is influenced by temperature, just like that of all other insects (Gunn, 1942). In most Australian locations, several generations can occur when the entire lifecycle (egg to adult) can be completed in 9–15 days. The ideal temperature for SBF is 24–30 degrees (Kotzé et al., 2016). Adults are subjected to the outside temperature. The body temperature of the living sheep "warmed" the eggs and larvae, and when the temperature is low, massive quantities of larvae can also provide heat to speed up development (Kotzé et al., 2016). Larvae and pupae are exposed to varying soil temperatures while they are in the soil. Pupae in soil have a lower developmental threshold temperature of roughly 11 °C.

In Southern Australia, winter causes a stopped development (diapause/quiescence) as pupae (De Cat et al., 2012) or prepupa (a post-feeding larval stage that occurs after quitting the host sheep). Due to low temperatures, adults of SBF are infrequently captured by field traps in Southern Australia between July and September (Kotzé et al., 2016). During summer and early fall, prepupae in the Canberra area pupated within a few days of leaving their host sheep, whereas pupation decreased to nearly zero for prepupae that entered the ground in late March.

Predation and illnesses (such as entomopathogenic fungi, nematodes, and ants) probably cause more than 90% of prepupae and pupae deaths (De Cat et al., 2012). As a result, it is anticipated that few will survive from winter to spring.

Seasonal variation in SBF population densities is influenced by life cycle, developmental characteristics, and environment. Depending on these seasonal factors, targeted management methods for SBF could be implemented with ease. By using adult flies and releasing adult strains during the spring's peak adult field emergence, the Sterile Insect Technique has the potential to drastically lower SBF population sizes. For instance, predictive models for the adult emergence of SBF in the field may be helpful (Dyck et al., 2006).

3. Stages of Life

Larvae (maggots), pupae, adults, and eggs are the four developmental stages of SBF. Numerous facts regarding the developmental parameters of the larvae and eggs are available because SBF is employed in forensics. Adult data are less specific. On sheep, adult females lay hundreds of eggs in batches, paying particular attention to creases, damp, unclean wool, and open wounds. When egg-laying females aggregate (Hall et al., 2003), a single vulnerable sheep is attacked by a huge number of maggots. Collectively, maggots produce extracorporeal secretions of proteolytic enzymes that cause the host tissue to liquefy, leaving wounds exposed.

Maggots fall to the ground after 4–7 days (Wardaugh, 2001), where they either overwinter before pupating or pupate right away by digging up to 5 cm deep in the soil. Depending on the area, season, and climate, pupae may hatch right away after finishing their metamorphosis or remain in the soil until the soil warms up in the spring. Adult flies have a life expectancy of less than three weeks. Every four to eight days, adult females can produce a batch of eggs (Wardaugh, 2001), and they need to eat a diet high in protein to produce eggs of a high enough caliber. When adults consume enough protein, they mate, and the release of juvenile hormones results in the creation of vitellogenin protein (vitellogenesis, or the female's ability to create eggs). A single season may see more than ten generations. It has been demonstrated that flystrike predictive models can reliably forecast when the blowfly season would begin. According to Horton and Hogan (2010), this gives farmers a tool for

selecting control measures. The accuracy of these forecasts may be hampered by rainfall events and inaccurate weather estimates (Robinson et al., 2009).

4. Current Control Strategies

Mackerras (1936) looked into workable control options from the beginning of their work on SBF. Since then, a lot has changed in terms of control strategies, including the development of new insecticides, biological controls, cultural and genetic control, and abandoned products like DDT. Additionally, there have been new developments that may expand the use of the Sterile Insect Technique to control SBF.

4.1. Insecticides

The Australian livestock business has a long history of using insecticides to combat flystrike. The use of synthetic insecticides has been a major component of flystrike prevention (Sandeman et al., 2014). The majority of the synthetic insecticides currently licensed for flystrike are based on cyromazine or ivermectin; imidacloprid, dicyclanil, or spinosad are some substitutes. Due to resistance in SBF, older chemistries (organochlorines, organophosphates) are either no longer registered or have lost their effectiveness (Sandeman et al. 2014). Currently, the most common methods for applying insecticides to the back of adult sheep are dipping them or applying them mechanically by hand or machine jetting, respectively. Sheep ranchers frequently use jetting, which, if the animals can be gathered for application, can offer sufficient protection to the animals during times of high flystrike risk. During the early season, when flies remain dormant over the winter, or prior to fly activity in the spring, insecticides can be used as a prophylactic therapy (Baker et al., 2014). Furthermore, pesticides can be used as part of the wound dressing or as a treatment after mulesing to stop additional fly strikes on sheep's susceptible healing areas. Sheep with long wool may not always be adequately protected during this phase because to the lengthy withholding periods, which are typically two months prior to shearing.

The cost per head rises when afflicted sheep receive curative therapy. Large amounts of ectoparasiticides entering the environment have also raised concerns (Beynon, 2012). To effectively prevent or heal flystrikes in proportion to regional risk, it is important to optimize the following parameters: chemical choice, application time, application method, and dose. However, there are frequently no clear decision-making guidelines or information on the risk of flystrikes (Lihou and Wall, 2019), thus treatments must be scheduled in conjunction with other farm operations. This frequently leads to either insufficient therapies or excessive therapeutic effort (overuse resulting in expense).

4.2. Resistance to Insecticides

There are only four chemical modes of action among the insecticides now on the market for controlling SBF (see; IRAC Classification: https://www.irac-online.org/modes-of-activity/). Cyromazine (IRAC Class 17) and dicyclanil ('unclassified' but probably Class 17) are the most commonly used insecticides for SBF. These are insect growth regulators (IGR) that have a low toxicity to mammals and especially interfere with dipteran moulting. Since 2012, cyromazine resistance has been documented (Levot, 2012), and blowflies that are resistant to cyromazine also exhibit resistance to dicyclanil (Levot et al., 2014).

Neurotoxins; Ivermectin (IRAC Class 6), Spinosad (IRAC Class 5), and imidacloprid (IRAC Class 4a) all work in somewhat different ways. According to Levot and Sales (2008), some Lucilia field strains have increased tolerance to ivermectin and spinosad, while SBF has not acquired resistance to these substances. Imidacloprid is a neonicotinoid that has only recently been used, and there are no indications of decreased sensitivity or resistance.

Any insecticide application may have unintended consequences. Pesticides can permeate the environment both during and after they are applied to sheep (Beynon 2012). When sheep are dipped, the pesticide will drip from the animals, which could result in significant local pollution. The leftover dipping material must be disposed of according to the directions. Sheep will eliminate a portion of the pollutants through their feces and urine. The quantity expelled and the impact of insecticide-contaminated feces and other excretion products on other species are not well understood. As has been noted in the UK for a number of compounds, including ivermectin, such compounds will expose species such as dung beetles and flies that feed on feces and urine, potentially decreasing their numbers and their crucial ecological functions (Gilbert et al., 2019). Due of several studies conducted abroad that have found serious off-target effects, the APVMA is presently reviewing neonicotinoids.

Insecticides are still widely used to treat ectoparasites in sheep. However, there is growing worry about chemical resistance, residues, and environmental runoff. There aren't many chemical alternatives, and there won't be any novel chemistry available anytime soon. Overuse of these compounds increases the possibility of resistance and off-target effects due to poor risk analysis. These worries would be allayed by more ecologically friendly approaches to SBF. SIT offers a chance to create a comprehensive SBF control plan that lessens the need for pesticides, lowers the chance of resistance, opens up new markets, decreases the impact on the environment, and lowers the withholding periods for meat and wool (Bedini et al., 2019).

The effectiveness of natural products (essential oils) and natural product-insecticide combinations for blowfly population control has been the subject of several recent research, (Chaban et al., 2019). Applying feeding deterrents, like aromatic oils, to change blowfly behavior may prevent flystrike from starting. Along with their antibacterial qualities and alleged ability to heal wounds, essential oils also have ovicidal and larvicidal activities, which may further prevent the spread of flystrike. Nevertheless, it appears that these products are not very effective.

4.3. Mulesing

The excision of strips of wool-bearing skin from the area surrounding the breech is known as "mulesing," after the Australian woolgrower John Mules (Beveridge, 1984). This method restricts SBF's access to flystrike-prone parts of a sheep, mainly the breech (back) area where the perineum (dags) and fleece can stay moist and collect urine and feces, creating the ideal conditions for gravid SBF females to lay eggs. In contrast to crutching, which removes only the wool, mulesing removes the skin to permanently protect against flystrike. It is primarily done on lambs. Sheers or a knife are used to remove creases and skin from wool. The skin expands around the wounds as they heal, losing its folds and wool, which would have not allowed blowflies to lay their eggs. Although the industry is working to expand the use of analgesics and anesthetics, the surgery is frequently performed without any kind of anesthesia or post-operative pain treatment. Queensland is expected to make this a requirement soon (Suwannayod et al., 2019). The public's aversion to mulesing has grown within the past 20 years. (Sneddon and Rollin, 2010). Nevertheless, despite studies on non-surgical options and intensive breeding programs, mulesing remains a control method (James, 2013). Animal welfare organizations and the retail and consumer sectors have been pressing for the development of alternatives to mulesing since the implementation of a comprehensive ban on mulesing by 2010. According to sources, markets for nonmulesed, halted mulesing, and flocks where pain treatment was utilized during mulesing have grown

to almost 50% of Australian fleece production, suggesting that this may acquire traction soon (Woods, 2019).

4.4. Genetic Regulation

A "field female killing" strain of SBF was created and successfully tested on an island in the late 1980s (Vogt et al., 1985). A larger island study that followed, though, proved unsuccessful. It was discovered that the strain was unstable; bulk rearing was challenging, and males did not compete with wild fertile males for matings. Funds for more research were constrained by the start of low wool prices. In the United States, transgenic female-lethal lines have been developed as a result of more recent research (Scott, 2014). Although these lines are based on SBF genetics from North America, it would be possible to import a strain under quarantine and cross it with an Australian field strain if the necessary licenses are obtained. Although these lines are based on SBF genetics from North America, it would be possible to import a strain under quarantine and cross it with an Australian field strain if the necessary licenses are obtained. After being mass-reared as a male-only strain for sterilization, it might be released to use SIT to decrease the local population. In favorable habitat circumstances, such those found in New Zealand, SBF has a low propensity to disperse (Sandeman et al., 2014). Localized control strategies like mass trapping or genetic control methods may be able to regulate SBF numbers in such restricted dispersal areas. However, current legislation and social license would limit the possibility of using a transgenic fly for SBF SIT in an operational setting. SIT based on unaltered organisms can be developed right away, but such approaches are probably going to become more accessible and acceptable in the future and might be employed later.

Since female insects are ineffective as control agents, SIT programs prefer to use only male strains. Research on transgenic strains of SBF that restrict the formation of female strains has been prompted by the need for strains of SBF that are exclusively male. Previous studies examining the viability of creating female-killing (FK) systems focused on offering purported advantages at a lower cost than SIT. But according to a recent study (Wright et al., 2004), novel embryonic SBF transgenic sexing strains have potential for SIT and genetic control initiatives.

4.5. Control by Biology

Thus far, biological management against SBF has not produced encouraging outcomes. Wasps that are parasitic Among the earliest biocontrol agents studied for biological control of SBF were a native pupal parasitoid, Nasonia vitripennis, and a European-introduced larval parasitoid, Alysia manducatory. Larval parasitoids from flystrikes on sheep in New Zealand were gathered and identified. Tachinaephagus zealandicus and Aphaereta aotea had an overall parasitism rate of 1.1%, which is probably insufficient to help reduce fly populations in any meaningful way (Sandeman et al., 2014).

According to reports for Nasonia and imidacloprid, the employment of parasitoids in conjunction with pesticide application may result in a decreased biological control efficacy (Tappert et al., 2017). To far, no commercial biopesticides have been produced to manage SBF, despite the fact that a variety of pathogenic bacteria have been described for SBF and allied species (Wright et al., 2019). Since the bacteria can survive in the sheep's wool, strains of Bacillus thuringiensis (BT) unique to the Diptera have been investigated as a potential preventive treatment. To find out if these can be turned into effective control solutions, more research is required.

Although they have been researched, other possible biopesticides (microsporidia, entomopathogenic fungi) have not yet found commercial use (Leathwick et al., 2019). It is undoubtedly possible to incorporate such items into an integrated pest management program that targets SBF. While SBF typically occurs at low population densities and flystrike is episodic, with fly populations rapidly growing when conditions are favorable, the pace of disease and parasite dissemination is nearly always density dependant. As a result, inundative methods or the creation of biopesticides have been the main focus of recent research towards a biological control agent (Wright et al., 2019, Leathwick et al., 2019).

The management of sheep blowflies is a significant barrier to the production of wool and meat sheep. Current chemical control methods are facing resistance and residue problems, and new chemistries are unlikely to be developed. Current physical methods, such as mulesing, are expensive, inefficient, and have negative effects on animal welfare, which lowers the value of the final product. It will probably take some time for new strategies to be developed and put into use using alternative techniques (such as sheep breeding or vaccines). It would be a significant benefit to have SIT for SBF as a supplemental tool, enabling eradication in some places and assisting in long-term sustainable management in others (Leathwick et al., 2019).

Chemical Fly Prevention Treatments

Chemical treatments are not a stand-alone solution; rather, they are a component of an integrated approach to flystrike management. As they land on the wool, blowflies are exposed to the chemical treatment. Depending on the active ingredient, the chemical may interfere with the blowfly's life cycle during the larval stage, affect the blowfly's nervous system, or reduce motor activity, resulting in paralysis .When flystrike is anticipated or to offer protection during the season when flystrike danger is highest, chemical treatments are frequently used (Horton, 2015). According to James et al., (2009), if chemical fly treatment is required, it works best when administered to the breech six weeks following shearing or crutching as opposed to right away. Unless treatment and/or prevention are required, in which case adherence to the wool and meat withholding periods is necessary, it is advised to refrain from using chemicals for three months after shearing. The timing of shearing and crutching as well as the administration of the treatment should be carefully handled in order to lower the frequency of flystrike incidences and the expense of chemical treatments (Lucas and Horton, 2013). The wool is removed along with any chemicals used before shearing (Horton, 2015).

Treatment of Sheep With Flystrike

The probability of flystrike within the flock will be greatly decreased by preventative measures. They might not, however, completely eradicate the occurrence of flystrike. Dark patches on the wool, separation from the flock, decreased feeding (leading to a noticeable decline in physical condition), and/or behaviors like biting or stroking the injured area are all signs that an animal has been struck. If a single animal is attacked, the damaged area and at least 5 cm of unstruck wool surrounding it near the skin are sheared as part of the treatment.

To make sure that no other regions have been impacted, maggot tracks through the wool are tracked. Shearing will assist the region dry up and get rid of a lot of the maggots. The maggots can be eliminated by removing any leftovers and putting the contaminated cuttings in an airtight bag. After applying a recognized dressing, the sheep are put back into the herd

and closely watched to make sure they are healing properly. Any leftover maggots are killed by the bandage, which also permits the lesion to heal without getting re-stricken. Sheep that are flystruck must be treated right away. Animals that are afflicted may eventually die from blood poisoning in addition to the condition's excruciating discomfort (Lucas and Horton,2013).

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THE HISTOLOGICAL EXAMINATION OF ADIPOSE TISSUE IN PCOS MICE

ABSTRACT

Introduction and Aim: Polycystic ovary syndrome (PCOS) is a common reproductive, endocrine and metabolic disorder that affects 5-18% of women worldwide, and its prevalence is increasing. Obesity is very common among PCOS patients. The etiology of PCOS remains unclear. It is a highly complex condition that is rapidly increasing worldwide and poses a serious threat to women's reproductive health. The latest findings emphasize the importance of adipose tissue dysfunction in the development and pathogenesis of PCOS. The aim of this study was the histological examination of adipose tissue in dehydroepiandrosterone (DHEA) induced PCOS mouse model. Methods: 25-day-old female mice were divided into control and PCOS. To create a PCOS model, mice were injected with DHEA for 21 days. Mice in the control group were injected with sesame oil. Subcutaneous adipose tissue was collected from mice of both groups. Hematoxylin-eosin staining was performed to examine changes in adipose tissue histology. Masson trichrome and picro sirius red staining were performed for collagen evaluation. Results: The histological structure of the tissue sections from the control group showed normal. In the PCOS group, there was hypertrophy and hyperplasia of adipocytes. There was also increased collagen deposition in adipose tissue. Conclusion: Our study showed the presence of adipose tissue fibrosis, adipocyte hypertrophy, and adipocyte hyperplasia on histological examination of adipose tissue in the PCOS mouse model. More studies are needed to understand the role of adipose tissue in the development and pathogenesis of PCOS.

Keywords: Polycystic ovary syndrome, Adipose tissue, Obesity

PKOS FARELERİNDE ADİPOZ DOKUNUN HİSTOLOJİK OLARAK İNCELENMESİ

ÖZET

Giriş ve Amaç: Polikistik over sendromu (PKOS) dünya genelinde kadınların %5-18'ini etkileyen ve görülme sıklığı giderek artan yaygın bir üreme, endokrin ve metabolik bozukluktur. Obezite PKOS hastaları arasında çok yaygındır. Tüm dünyada hızla artan ve kadınların üreme sağlığı için önemli bir tehdit oluşturan oldukça karmaşık bir durum olan PKOS'un etiyolojisi belirsizliğini korumaktadır. Son bulgular adipoz (yağ) doku disfonksiyonunun PKOS gelişimindeki ve patogenezindeki önemini vurgulamaktadır. Bu çalışmada dehydroepiandrosterone (DHEA) ile indükleyerek oluşturulan PKOS fare modelinde adipoz dokunun histolojik olarak incelenmesi amaçlandı. Metot: 25 günlük dişi fareler kontrol ve PKOS olmak üzere iki gruba ayrıldı. PKOS modeli oluşturmak için farelere 21 gün boyunca DHEA uygulandı. Kontrol grubundaki farelere bu süreçte susam yağı enjekte edildi. Her iki gruba ait farelerden derialtı adipoz doku örnekleri toplandı. Adipoz doku histolojisindeki değişiklikleri incelemek için hematoksilen-eozin boyaması yapıldı. Kollajen değerlendirmesi için masson trikrom ve picro sirius red boyamaları yapıldı. Bulgular: Kontrol grubuna ait doku kesitleri normal histolojiye sahipti. PKOS grubunda ise adipositlerde hipertrofi ve hiperplazi vardı. Ayrıca adipoz dokuda kollajen birikiminde artış görüldü. Sonuç: Çalışmamız PKOS fare modelinde adipoz doku üzerinde yapılan histolojik incelemelerde adipoz doku fibrozu, adiposit hipertrofisi ve adiposit hiperplazisinin varlığını gösterdi. PKOS gelişimi ve patogenezinde adipoz dokunun rolünü anlamak için daha ileri çalışmalara ihtiyaç vardır.

Anahtar Kelime: Polikistik over sendromu, Adipoz doku, Obezite

GİRİŞ

Polikistik over sendromu (PKOS) reprodüktif çağındaki kadınlarda en sık görülen endokrin bozukluktur. Sendromun prevalansı etnik kökene, yaşa ve kesin tanı için kullanılan kriterlere bağlı olarak %5-20 arasında değişmektedir. Tanı kriterleri arasında hiperandrojenizm, oligo-anovulasyon ve polikistik over morfolojisi bulunmaktadır. PKOS'lu birçok kadın aynı zamanda aşırı kilolu veya obezdir (1).

Obezite hipotalamus-hipofiz-ovaryum (HPO) eksenindeki bozulmadan, düşük oosit kalitesi ve değişen endometriyal reseptivite ile ilişkili olarak artan infertilite riskinden sorumludur (2-3). PKOS hiperandrojenizm, ovulasyon bozukluğu, azalmış fertilite, yüksek oranda obezite oluşumu, insülin direnci ve dislipidemi dahil olmak üzere üreme, metabolik ve endokrin anormallikler ile karakterizedir. PKOS'lu kadınlarda görülen çeşitli metabolik ve endokrin değişiklikler yağ dokusunun dağılımı ve işlevi üzerinde ciddi etkiler göstermektedir. Yapılan çalışmalar PKOS hastalarında adipoz (yağ) dokusundaki anormal fonksiyonun obezite olmasa bile birincil olarak insülin direnci ile bağlantılı olduğunu ve PKOS'lu kadınların vücut kitle indeksinin yüksek olduğunu bildirmektedir. Bu sendroma sahip kadınların %30-75'inin aşırı kilolu olduğu ve bu durumun PKOS semptomlarını şiddetlendirdiği belirtilmektedir (4-6).

PKOS'lu kadınlarda obezite, hipertansiyon, dislipidemi ve hiperglisemi olarak tanımlanan metabolik sendrom prevalansı çok yüksektir. Metabolik sendromun kilit bir bileşeni olan obezite öncelikle HPO ekseninde fonksiyonel değişikliğe neden olduğundan dolayı kadın fertilitesi üzerinde önemli bir etkiye sahiptir. Obezitenin sıklıkla dolaşımdaki yüksek insülin seviyeleri ve ardından artan ovaryan androjen üretimi ile ilişkili olduğu saptanmıştır (7). Fazla yağ dokusu bu androjenlerin östrojene aromatizasyonundan sorumludur, bu da HPO ekseninde negatif bir geri bildirime yol açar ve gonadotropin üretimini etkiler (8). Bu değişiklikler ovulasyon bozukluğuna ve menstrual anormalliklere neden olmaktadır. Obezitenin üreme fizyolojisi üzerinde olumsuz etkilere sahip olduğu görülmektedir. Oligomenore ve hiperandrojenizm ile karakterize olan PKOS patogenezinde hiperinsülineminin temel bir rol oynadığı bilinmektedir. Obezitenin eşlik etmesi insülin direncini daha da artırmakta ve PKOS semptomlarını şiddetlendirmektedir (9). Öte yandan PKOS'da artan androjen üretimi visseral yağ birikimine neden olmaktadır. Bu durum insülin direncini ve hiperinsülinemiyi şiddetlendirerek bu kısır döngüyü daha da teşvik etmektedir (10). Obezite sıklıkla glikoz intoleransı, insülin direnci, dislipidemi ve hipertansiyon ile ilişkilendirilir (11). PKOS ile metabolik sendrom arasındaki bağlantı çeşitli çalışmalar ile bildirilmiştir (12-14). PKOS'daki metabolik ve endokrin değişiklikler yağ dokusunun kütlesini, dağılımını ve adipositlerin fonksiyonunu etkilemektedir.

Bu çalışma dehidroepiandrosteron (DHEA) ile indükleyerek oluşturulan PKOS fare modelinde adipoz dokuda meydana gelen değişiklikleri histolojik olarak göstermeyi amaçlamıştır.

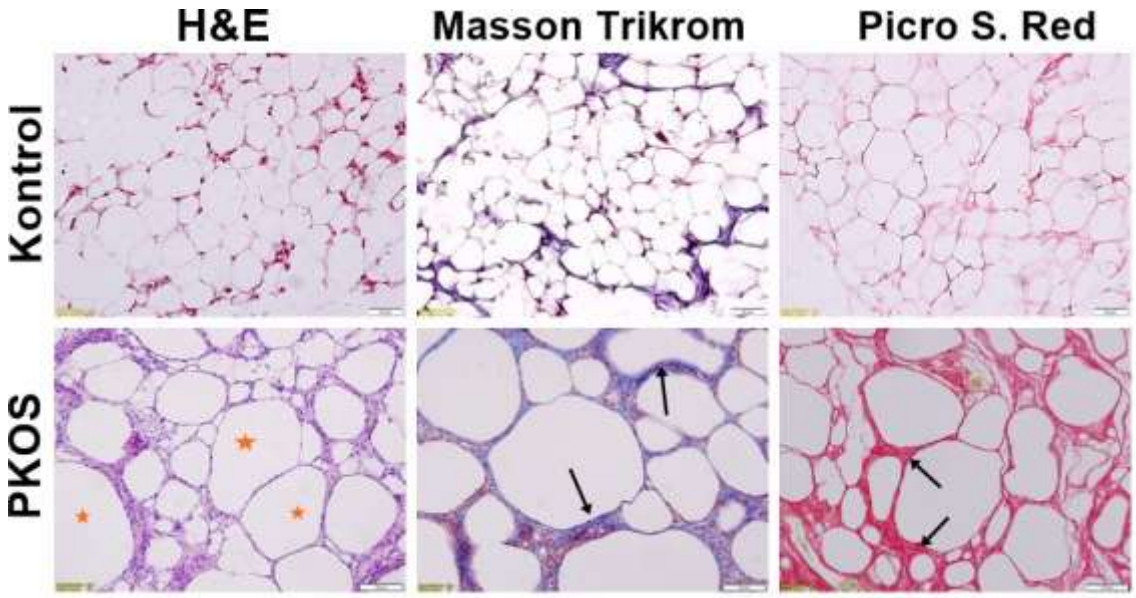
METOT

Bu çalışma için yerel deney hayvanları etik kurulundan onay alındı. Çalışmada 25 günlük dişi fareler kullanıldı. Kontrol ve PKOS olmak üzere iki grup oluşturuldu. PKOS modelini oluşturmak için 21 gün boyunca DHEA (6mg/100g/gün) susam yağında çözülerek 0,2 ml olacak şekilde subkutan olarak enjekte edildi (15). Kontrol grubundaki farelere ise 21 gün boyunca susam yağı enjekte edildi. Deney sonunda sakrifiye edilen farelerden subkutan yağ doku örnekleri toplandı. Dokular %4' lük paraformaldehit ile fikse edildi. Ardından rutin

doku takip aşamalarından geçirildi ve parafine gömüldü. Her iki gruba ait doku bloklarından alınan kesitlere yapı ve morfolojisindeki değişiklikleri incelemek için hematoksilen-eozin boyaması, kollajen değerlendirmesi için masson trikrom ve picro sirius red boyamaları yapıldı.

BULGULAR

Kontrol grubuna ait yağ dokusu kesitlerinde adipositler normal histolojik yapıya sahipti. PKOS grubuna bakıldığında ise adipositlerde hipertrofi ve hiperplazi olduğu görüldü. Ayrıca adipositler arasındaki alanlarda kollajen birikiminde bir artış vardı (Şekil 1).



Şekil 1. Kontrol ve PKOS gruplarına ait yağ dokusunun hematoksilen-eozin boyanması ve kollajen değerlendirmesi için masson trikrom ile picro sirius red boyanma görüntüleri. Hipertrofik adipositler (turuncu yıldız), kollajen alanları (siyah ok).

TARTIŞMA VE SONUÇ

Hem PKOS hem de obezite günümüzde dünyada büyük bir sağlık sorunu olarak görülmektedir. Obezite PKOS'un bir nedeni olmayabilir fakat PKOS fenotipinin birçok yönünü şiddetlendirir özellikle glukoz intoleransı ve dislipidemi gibi etkenlerin kardiyovasküler risk faktörlerini arttırdığı bilinmektedir. PKOS'lu obez kadınlar PKOS'suz obez kadınlarla benzer fenotiplere sahiptir. Daha önce yapılan çalışma verilerine bakıldığında PKOS'lu obez kadınların obez kadınlara benzer inflamatuar ve oksidatif stres fenotiplerine sahip olduğu gösterilmiştir (16-18). Normal vücut kitle indeksine sahip PKOS'lu kadınlarında olduğu unutulmamalıdır. İnsan ve kemirgen modelleri ile yapılan çalışmalarda obezitenin ovaryumun fonksiyonu üzerinde olumsuz etkileri olduğu gösterilmiştir. Örneğin yüksek yağlı bir diyetle beslenen kemirgenlerde östrus siklusunda düzensizliklerin olduğu gösterilmiştir (19-21). Obezite folikül gelişimi ve büyümesini değiştirmektedir. Primordiyal folikül havuzunda bir azalma ve buna bağlı olarak foliküllerin antral aşamaya ilerlemesinde artış olduğu gösterilmiştir. Ayrıca atretik folikül sayısında da bir artış olduğu belirtilmiştir (21-24). Obezitenin yumurtalık fonksiyonu ve oosit kalitesi üzerindeki olumsuz etkileri yapılan çalışmalar ile bildirilmiştir.

Çalışmamızda PKOS grubunda adiposit hiperplazi ve hipertrofisi mevcuttu. Obezite sırasında da beyaz yağ dokusu yeniden şekillenir. Bu durum genellikle adiposit hipertrofisi, immün hücre infiltrasyonu, fibrozis ve anjiyogenez ile karakterize edilir (25-27). Obezitenin neden olduğu beyaz yağ dokusunun kronik düşük dereceli inflamasyonu metabolik sendromdaki kronik inflamasyonun kaynağıdır. Disfonksiyonel adipositlerden gelen dengesiz adipositokin seviyelerinin adrenal ve ovaryumun steroidojenik hücreleri ile etkileşime girdiği gösterilmiştir. PKOS'daki hiperandrojenemi artmış abdominal visseral adipozite ve anormal karbonhidrat ve lipid metabolizması ile ilişkilidir (28, 29).

Çalışmamız yağ dokusundaki kollajen birikiminin PKOS grubunda artmış olduğunu göstermektedir. Beyaz yağ dokusu fibrozu aşırı ekstrasellular matriks (ESM) birikimi ile karakterizedir. ESM esas olarak proteoglikanlardan ve en bol bulunan kollajen olan lifli proteinlerden oluşan hücresel olmayan bir bileşendir. Kollajenin çoğu fibroblastlar, miyofibroblastlar, adiposit progenitörleri ve adipositler tarafından oluşturulur (30). Fizyolojik koşullar altında ESM'nin adipositlerin yapısal bütünlüğünü koruduğu ve hücre-hücre iletişimini modüle ettiği bilinir. Obezite kaynaklı yağ dokusu fibrozunda beyaz yağ dokusunu sertleştiren kollajen demetlerinin oluşumuna yol açan ESM birikimi vardır (31). Dahası beyaz yağ dokusu fibrozu adipositlerin aşırı genişlemesini sınırlayabilir adipositler üzerine mekanik stres uygulayıp beyaz yağ dokusunun yağ depolama kapasitesini inhibe edebilir ve ektopik lipit birikimine yol açabilir (32). Beyaz yağ dokusu inflamasyonu ve fibrozu birbirine bağlı süreçlerdir ve çeşitli biyolojik mekanizmalar yoluyla etkileşime girerek sonunda beyaz yağ dokusu işlev bozukluğuna ve sistemik metabolik bozukluklara yol açabilirler.

Sonuç olarak bu çalışmada DHEA ile indükleyerek oluşturulan PKOS fare modelinde adipoz doku üzerinde yapılan histolojik incelemede obezite ile ilgili yapılan çalışmalardakine benzer şekilde adipoz doku fibrozu, adiposit hipertrofisi ve adiposit hiperplazisinin varlığı gösterildi. PKOS karmaşık bir kadın endokrinopatisidir. PKOS tanısı konulan kadınların metabolik sendrom açısından değerlendirilmesi gerekir. Obezite muhtemelen PKOS'un bir nedeni değildir ve dünyanın birçok yerinde PKOS'lu kadınların çoğu normal kilodadır. Obezitenin varlığı PKOS semptomlarını şiddetlendirmektedir. Bu hastalarda obezitenin tedavi edilmesi/ kilo kaybı PKOS fenotipinde iyileşme sağlayabilir. PKOS'un gelişimi ve patogenezinde adipoz dokunun rolünü anlamak için daha fazla çalışmaya ihtiyaç vardır.

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A PRAGMATIC APPROACH TO THE WORTH AND VALUE OF THE HUMAN AND HEALTH CARE PROFESSIONAL

ABSTRACT

Nurses, who are healthcare professionals, are members of a discipline that focuses on protecting people and their lives with a humanistic and holistic approach. Life is a value gained through existential struggle. While biopsychosocial and spiritual investments made in life constitute its value, gains directly proportional to investments constitute the value of life. This study aims to analyze the value and worth of people and healthcare professionals with a pragmatic approach and in the light of current data. Materials and Methods: Current TÜİK, Health Statistics data and articles related to the study title were scanned and findings suitable for the purpose were analyzed.

Findings: The estimated total cost of raising children in Turkey is between 500,000 and 1,200,000 TL (2005-2022), depending on various factors such as educational preferences, access to healthcare, and lifestyle. The monthly income of an adult worker in Türkiye in 2023-2024 is approximately 15,000 to 20,000 TL for blue-collar workers and 25,000 to 35,000 TL for white-collar workers. The average annual workday loss per worker is around 10 to 15 days. The main reasons for the workday loss of employees in Türkiye are generally health-related problems, especially stress, workplace injuries, and illnesses. Cost of illness studies address the economic burden of a disease or the gains that could be achieved if the disease could be prevented, the amount of resources spent on medical goods and services used in its treatment, and the social productivity losses resulting from the disease. In the last year, a total of 56 million days were spent in hospital for treatment, and the total loss of workdays and the apparent economic losses calculated based on the daily earnings of employees in that year are around 67,887,000,000 TL. The cost of accommodation, medicine and therapy for a person's inpatient treatment can vary between 1,500 and 10,000 TL per day. The GDP per capita in our country is 13 thousand dollars in 2023. The total estimated cost for a four-year nursing education at a foundation university in Türkiye is between 32,000 and 113,800 dollars. The value of the nursing profession (monthly salary/2024; 47,000 TL) comes after a police officer, a teacher and an imam. The "value" of a nurse depends on the patient outcomes of their work, the quality of the healthcare they provide and the economic impact in reducing healthcare costs. Nurses often face emotional exhaustion/compassion fatigue due to stressful and long working hours and dealing with critically ill patients.

Conclusion The worth and value of the healthcare professional who protects and develops the value and worth of people should be supported.

Keywords; worth , value, health care professional

İNSANIN VE SAĞLIK BAKIM PROFESYONELİNİN EDERİNE VE DEĞERİNE PRAGMATİK BİR YAKLAŞIM

ÖZET

Sağlık bakım profesyoneli olan hemşireler, hümanistik ve holistik yaklaşımla insanı ve yaşamını korumaya odaklanan bir disiplinin üyesidirler. Yaşam varoluşsal mücadele ile kazanılan bir değerdir. Yaşama yapılan biopsikososyal ve manevi yatırımlar değerini oluştururken yatırımlarla doğru orantılı kazanımlar ise yaşamın ederini oluşturmaktadır. Bu çalışmayla insanın ve sağlık bakım profesyonelinin ederinin ve değerinin pragmatik bir yaklaşımla ve güncel veriler ışığında analizi edilmesi amaçlanmıştır.

Gereç ve Yöntem: Güncel TÜİK, Sağlık İstatistik verileri ve çalışma başlığına ilişkin makaleler taranarak amaca uygun bulgular analiz edilmiştir.

Bulgular: Türkiye'de çocuk yetiştirmenin tahmini toplam maliyeti, eğitim tercihleri, sağlık hizmetlerine erişim ve yaşam tarzı gibi çeşitli faktörlere bağlı olarak (2005-2022 yılları arası) ortalama 500.000 ila 1.200.000 TL arasındadır. Türkiye'de 2023 - 2024 yılı yetişkin çalışanın aylık geliri; mavi yakalı çalışanların ortalama geliri yaklaşık 15.000 ila 20.000 TL, beyaz yakalı çalışanların ise 25.000 ila 35.000 TL civarındadır. Yıllık iş günü kaybı, işçi başına ortalama 10 ila 15 gün civarındadır. Türkiye'de çalışanların iş günü kaybının başlıca nedeni genellikle sağlıkla ilgili sorunlar, özellikle de stres, iş yeri yaralanmaları ve hastalıklardır. Hastalık maliyeti çalışmaları bir hastalığın ekonomik yükünü veya bir hastalığın önlenebilmesi durumunda sağlanabilecek kazanımları, tedavisinde kullanılan tıbbi mal ve hizmetler için harcanan kaynak miktarını, hastalıktan kaynaklanan toplumsal verimlilik kayıplarını ele almaktadır. Son bir yılda tedavi için toplamda 56 milyon gün hastanede kalınmış olup toplam işgünü kaybı ile o yılki çalışanların günlük kazançları üzerinden hesaplanan görünür ekonomik kayıpların yükü 67.887.000.000 TL civarındadır. Bir kişinin yatarak tedavisinde konaklama, ilaç ve terapi masraflar günlük 1.500 ila 10.000 TL arasında değişebilmektedir. Ülkemizde kişi başı GSYİH 2023 yılında 13 bin dolardır. Türkiye'deki bir vakıf üniversitesinde dört yıllık bir hemşirelik eğitim için toplam tahmini maliyet ;32.000 doları ile 113.800 dolar arasındadır. Hemşirelik mesleğinin ederi (aylık maaşı/2024 ;47.000 TL olup) bir polisten, bir öğretmenden ve imamdan sonra geliyor Bir hemşirenin "değeri" yaptıkları işin hasta sonuçlarına, verdikleri sağlık hizmetinin kalitesine ve sağlık bakım maliyetlerinin azaltılmasındaki ekonomik etkiye bağlıdır. Hemşireler genellikle stresli ve uzun çalışma saatlerine ve kritik hastalarla uğraşmaya bağlı duygusal tükenmeyle/şefkat yorgunluğu ile karşı karşıyadır.

Sonuç İnsanın ederini ve değerine koruyan, geliştiren sağlık bakım profesyonelinin eder ve değerinin desteklenmesi gerekmektedir.

Anahtar kelimeler; eder, değer, sağlık bakım profesyoneli

GİRİŞ

Sağlık bakım profesyoneli olan hemşireler, hümanistik ve holistik yaklaşımla insanı ve yaşamını korumaya odaklanan bir disiplinin üyesidirler. Yaşam varoluşsal mücadele ile kazanılan bir değerdir. Yaşama yapılan fiziksel, duygusal, sosyal ve manevi yatırımlar değerini oluştururken yatırımlarla doğru orantılı kazanımlar ise yaşamın maddi ve manevi ederini oluşturmaktadır.

Yaşamda değer emekle kazanılır. Emek bireyin ailenin ve toplumun bilgi ve deneyimlerini düşünce, duygu ve davranışsal yatırımlarla sergilediği ve yararlılığı hedefleyen amatör ya da profesyonel bir çabadır. Başka bir deyişle; yeni doğanın yaşamını anlamlı ve değerli kılmak için ailenin onu iyi beslemesi, sevgi ve güven içinde hastalık ve kazalardan koruması , iyi bir eğitimle bilinçli, aidiyet duygusu gelişmiş ve yetişkin yaşamın sorumluluklarını üstlenecek bir birey olarak yetiştirmesi için yapılan maddi ve manevi tüm yatırımlar, yaşamın değerini oluşturmaktadır. Eder ise tüm bu yatırımlarla bireyin fiziksel ,zihinsel, duygusal ve manevi yönden sergilediği ya da sergileyemediği ;yeterli ya da yetersiz; doğru ya da yanlış performansıdır.

Değer kavramı, bireyin nesne ile ilişkisinden doğan nitelik olarak anlaşılır. Değer kavramı hem nesne alanında hem de ahlaksal alanda ortaya çıkar. Kültürümüzde olan ve cinsiyetçi olan ”Kaç paralık adamsın ” yerine kullanacağım ”Kaç paralık insansın” deyişi, insanın ederinden çok ahlaki yönünü/değerini anlatmaktadır. Değer, ister kişisel görüşlere dayalı ister se ölçülebilir olsun, önemi vurgular[1-2]

Eder kavramı ise değeri karşılığı, fiyat ya da paha anlamındadır. Bu konunun öznesi insan ve yaşamı olduğu için değere daha çok felsefi ve etik açıdan incelemek ve ederi de işletme ve ekonomi açısından tanımlamak gerekir.[1]

Türkiye’de İnsanın Ederi

Türkiye'de doğumdan yetişkinliğe kadar çocuk yetiştirmenin ortalama maliyetinin hesaplanmasında eğitim, sağlık, gıda, giyim ve barınma gibi çeşitli faktörler yer alıyor. Belirli rakamlar aile koşullarına ve bölgesel farklılıklara bağlı olarak büyük ölçüde değişiklik gösterse de mevcut verilere dayanarak genel bir bakışla; 1990’dan 2023’e kadar Türkiye’de çocuk yetiştirmenin tahmini toplam maliyeti, eğitim tercihleri, sağlık hizmetlerine erişim ve yaşam tarzı gibi çeşitli faktörlere bağlı olarak 500.000 ila 1.200.000 TL arasında olabilir (Kesin hesaplamalar için bölgesel farklılıklar ve enflasyon oranları da dahil olmak üzere daha ayrıntılı veriler gereklidir).[3]

Türkiye'de 2023 ve 2024 Yılı Yetişkin Çalışanın Aylık Geliri:

Mavi yakalı çalışanların aylık ortalama geliri yaklaşık 15.000 ila 20.000 TL,

Beyaz yakalı çalışanların ise 25.000 ila 35.000 TL civarındadır.

Yıllık iş günü kaybı, çeşitli faktörlere bağlı olarak genellikle işçi başına ortalama 10 ila 15 gün civarındadır. Parasal açıdan bu, ortalama günlük ücrete bağlı olarak birkaç bin liralık bir kayıp anlamına gelebilir.[3]

Türkiye'de çalışanların iş günü kaybının başlıca nedeni genellikle sağlıkla ilgili sorunlar, özellikle de stres, iş yeri yaralanmaları ve hastalıklardır. Bu faktörler üretkenliği ve çalışanların refahını önemli ölçüde etkiler .

Hastalık Ederi (Maliyeti):

Hastalık biopsikososyal ve manevi sağlığın bozulmasıdır. Hastalıkların ederi,bireyin hastalanmasının getirdiği tanılama, tedavi ve bakım sürecinin ya da erken ölümüyle oluşan ekonomik maliyeti olup hastalıkların ve erken ölümlerin topluma parasal yükünü gösterir. Hastalık ve ölüm oranlarında artış, kamuda insan gücünün hem sayısal hem de emek olarak azalması demektir. Hastalık maliyeti çalışmaları, bir hastalığın veya hastalıkların ekonomik yükünü veya hastalıklardan korunma ile sağlanabilecek kazanımları, bir hastalığın tedavisinde harcanan kaynak miktarını, hastalıktan kaynaklanan sosyoekonomik verimlilik kayıplarını ele almaktadır.[6]

Sağlık Bakanlığı (SB-2023) verilerine göre ;

Gençlik, yetişkinlik ve yaşlılık döneminde yüz bireyden dördünün hareket ve hijyen konusunda zorluk yaşadıkları ve bakım gereksinimi içinde oldukları görülmektedir. Son bir yılda sosyal yaşamın içinde olan, okuyan, çalışan insanımızın dörtte biri bel ve boyun bölgesi hastalıkları yaşamaktadır. [4]

Yetişkin yaşamın sorumluluklarını alan ve dolayısıyla ülke ekonomisine katkı sağlayacak yaşta olan (25 ile 65 yaş arası) her 100 bireyden beşi ile on üçünün genel sağlık durumunun yaş ilerledikçe bozulduğu görülmektedir.[4]

Ülke ekonomisine katkılarının tavan yapacağı yaşta olan bu insanlara ait verilen bu oranları küçümsemeden doğru okumak gerekir. Çalışan, üreten, karar verebilen ve sevebilen insan biyopsikososyal yönden sağlıklıdır ve değerlidir. Sağlığının bozulması halinde emeğini sunamayan bu insanlar, doğal olarak üretime katkıda bulunamamaktadır. Bunun sonucunda hem milli gelirde hem de bireysel gelirde düşüş yaşanmaktadır.[5]

Ülkemizde 100 bin kişiye 281 yatak düşmektedir ve Ülkemiz insanları yıl içinde SB hastanelerine daha fazla olmak üzere; 6 defa hastaneye başvurmuş,13 milyonu hastaneye yatmış, 6 milyonu ameliyat olmuştur.Son bir yılda tedavi için toplamda 56 milyon gün hastanede yatılmıştır.[4]

Erken tanı, tedavi ve bakımla önlenebilir ölümcül hastalık verilerine bakılınca en fazla kalp hastalığı, akciğer kanseri, Covid gibi salgınlar ve kronik alt solunum yolu hastalığı olduğu görülmektedir; Türkiye'de ölümlerin çoğunluğunun bulaşıcı olmayan hastalıklardan kaynaklandığı ve Türk ekonomisine toplam ekonomik maliyetinin de yüz milyar liranın üzerinde olduğu düşünülmektedir. [4]

Son verilere göre en fazla yapılan organ /doku nakil sayısı ; 5000 kemik iliği,4000 civarında böbrek nakli olup 23000 civarında böbrek ve 2500 civarında insanımız da karaciğer nakli beklemektedir. Dolayısıyla bu insanlarımız, çalışamayan ve üretemeyen tedavi ve bakım gerektiren grubu oluşturmaktadır.[4]

Toplam işgünü kaybı ile o yılki çalışanların günlük kazançları üzerinden hesaplanan görünür ekonomik kayıplara bakıldığında; son on yılda (2005-2014) iş kazaları ve meslek hastalıklarının ülke ekonomisine olan ekonomik maliyeti 67-68 milyar TL olarak belirlenmiştir.[4-7]

Muayene, tedavi ve bakımın maliyeti; tesise, konuma ve sağlanan spesifik hizmetlere bağlı olarak önemli ölçüde değişebilir. Genel olarak konaklama, ilaç ve tedavi dahil masraflar günlük 1.500 ila 10.000 Türk Lirası arasında değişebilmektedir (Daha doğru bir tahmin için, fiyatlar bireysel koşullara ve tedavi ihtiyaçlarına göre değişiklik gösterebileceğinden gerçekçi ederde Ülke ekonomisi, bireysel kazanç ve devlet ve özel hastane fiyatlaması dikkate alınmalıdır).[3]

İnsanların sağlıklarının bozulması, çalışamaması ve üretememesi demektir. Sağlığı koruyucu hizmetlere gereken önemin verilmemesi, teşhiste gecikme, yanlış tanılama ya da tedavi, kalitesiz bir bakım, bireylerin hastaneye yatış sıklığını ve hastanede kalış süresini arttıracağı bunun da bireyin, ailenin ve ülkenin ekonomisini olumsuz etkileyeceği unutulmamalıdır.[5]

Sağlık bakım profesyoneli bir hemşirenin ederi ve değeri;

Birey aile ve toplumun sağlığının korunması, geliştirilmesi hastalık halinde tedavisi ,bakım ve rehabilitasyonunda sağlık bakım profesyoneli olan hemşirelerin görev ve sorumlulukları oldukça önemlidir.

Türkiye'de son verilere göre hemşire sayısı 240.613 olup 354 bin kişiye bir hemşire düşmektedir. 2022-2023 öğretim yılı öğrenci kontenjanı da dahil edildiğinde hemşirelik programlarında öğrenim gören öğrenci sayısı 68.152'dir.[8-4]

Türkiye'de bir vakıf üniversitesinde okuyan bir hemşirelik öğrencisinin eğitim, konaklama, yemek ve eğlence masrafı ortalama 600.000-2.133.750 TL(32.000 -113.800 ABD Dolar / 2022 yılı) arasındadır.[3-5]

Hemşirelik mesleğinin ederi (aylık maaşı/2024 ;47.000 TL), bir polisten, bir öğretmenden ve imamdan sonra gelmektedir.[9]

Hemşirelik, tıbbi hizmetlerin belkemiği olarak hizmet veren ve hasta bakımının ayrılmaz bir parçasıdır. Hemşireler, hastaların biyopsikososyal ve manevi gereksinimlerini göz önünde bulunduran bütünsel bakım sunarlar.

Bir hemşirenin "değeri/ederi"; genellikle hasta sonuçlarına, sağlık hizmeti kalitesine ve sağlık sistemine yaptığı ölçülebilir katkılarla ifade edilir. Koruyucu bakım, kronik rahatsızlıkların yönetilmesi ve doğrudan hasta bakımının sağlanması yoluyla sağlık bakım maliyetlerinin azaltılmasındaki rolünü gösterir.. Olga Yakusheva ve Dr. Marianne Weiss tarafından geliştirilen 'Hemşirelik İnsan Sermayesi Değer Modeli' ne göre ; hemşireliğe yapılan yatırımların (mesleki gelişim, eğitim ve liderlik gibi) daha iyi hasta sonuçlarına, gelişmiş kurumsal performansa ve hatta sağlık hizmeti kuruluşları için finansal büyümeye nasıl yol açabileceğini gösteriyor.[10]

Hemşire, fiziksel tedavinin ötesinde duygusal ve psikolojik desteğe uzanan temel bakım sağlayan sağlık sisteminin temel bir direğidir. Hemşirelerin rolü, hastanın refahını sağlamada, halk sağlığını teşvik etmede ve sağlık kurumlarının verimliliğini korumada paha biçilmezdir.

Hemşireliğin önemi/değeri, hastane hizmetlerinden evde bakıma, toplum sağlığı programlarına ve rehabilitasyon merkezlerine kadar uzanmaktadır.

Sağlık bakım profesyonelinin değerliliğinin göstergeleri: Sağlığın korunması, hastanın iyileştirilmesi, hastaneye yeniden yatışların azaltılması, enfeksiyon kontrolü ve hasta memnuniyetinin arttırılması gibi hasta sonuçları; zamanında, dikkatli ve hastayı savunan iyi uygulamalara bağlılığı içeren kaliteli ve yüksek standartlarda bakım sağlama yeteneği; gereksiz prosedürlerin azaltılması, komplikasyonların önlenmesi ve hastanede kalış süresinin kısaltılması gibi uygun maliyetli bakıma katkılarıyla sağlanan verimlilik ve maliyet tasarrufu; hastaların durumları ve tedavileri hakkında verdikleri eğitimle onların uyumunu arttıran ve sağlık okuryazarlığını teşvik eden hasta eğitimi ve desteği; tıbbi gelişmeler ve en iyi uygulamalar konusunda güncel kalmak için sürekli eğitimle becerilerinin ve yeterliliklerinin geliştirilmesinde gösterdikleri performans; hastalarla, ailelerle ve sağlık ekibiyle etkili iletişim kurarak oluşturdukları işbirliği ve hasta odaklı yaklaşımı sağlama becerisi olarak sıralanabilir.[3-10]

Aiken ve ark. (2014), daha yüksek hemşire personel seviyelerinin daha iyi hasta sağkalım oranları ve daha düşük komplikasyonlarla ilişkili olduğunu bulmuşlardır. Bu, kaliteli sağlık hizmetlerinin sağlanmasında ve tıbbi tesisler üzerindeki yükü azaltmada hemşireliğin öneminin altını çizmektedir.[11-3]

Hemşireler genellikle yüksek stres ortamlarda, uzun çalışma saatleri ve kritik hastalarla uğraşmanın getirdiği duygusal tükenme ile karşı karşıyadır. Joinson (2019) tarafından yapılan bir araştırma, duygusal taleplerin arttığı acil durum ve yoğun bakım birimlerinde hemşireler arasında şefkat yorgunluğunun yaygın olduğunu göstermektedir.[12]

Hemşireler genellikle stresli ve uzun çalışma saatlerine ve kritik hastalarla uğraşmaya bağlı duygusal tükenmeyle/şefkat yorgunluğu ile karşı karşıyadır. Araştırmalar hemşirelerin işyeri stres faktörleri nedeniyle tükenmişlik, anksiyete ve depresyon belirtileri gösterdiklerini bildirmişlerdir. Yönetimle yaşanan çatışmalar veya algılanan destek eksikliği gibi stres faktörlerinin memnuniyetsizliği artırabileceğini, ekip içindeki destekleyici ilişkilerin ise iş memnuniyetini artırdığını ve duygusal tükenmeyi azalttığını göstermektedir.[13]

İş tatminini etkileyen temel faktörler arasında hemşirenin değerliliğinin de göstergesi olan ; hasta-hemşire ve ekip ilişkileri, tanınma ve kabul, çalışma koşulları yer alır. Bu alanlarda yaşanan sorunlar hemşirelerde strese yol açarak iş memnuniyetsizliğini arttırır..

Sunulan sağlık hizmetinin sonuçlarını izlemek için kullanılan kalite değerlendirmeleri; maliyet analizleri, tıbbi sonuçlar ve hasta memnuniyeti üzerinden yapılabilmektedir. Sağlık kurumlarında hasta memnuniyetini; kurumdaki tıbbı ve hemşirelik bakım hizmetleri, sağlık personelinin ilgisi, genel otelcilik hizmetleri, hizmete erişim hızı, yönetim anlayışı, tanılama,tedavi ve bakımın fiyatı etkiler.

Aldemir ve ark.(2018), cerrahi kliniklerde yatan hastaların hemşirelik bakımından memnuniyet araştırmasında hastaların hastanede kalış süresi ile memnuniyetleri arasında negatif yönde anlamlı ilişki saptamışlardır. [14]

Arslan Ve Kelleci (2011) çalışmalarında bir üniversite hastanesinde yatan hastaların yarıya yakınının hemşirelik hizmetlerini güvenilir ve doğru şekilde yapılmasına önem verdiklerini , verilen hemşirelik bakımından memnun olmadıklarını ve hemşirelik bakımı ile ilgili gereksinimlerinin yeterince karşılanmadığını bulmuşlardır.[15]

Öztürk Ruşen ve ark.(2013), hemşirelerin iş yaşam kalitesinin hastaların hemşirelik bakımından memnuniyet düzeylerine etkisi çalışmasında; hemşirelerin iş yaşam kalitesi arttıkça hasta memnuniyetinin de arttığını bulmuşlardır. [13]

Uğur ve Abaan(2008), bir devlet hastanesinde çalışan hemşirelerin yarıya yakınının iş yaşam kalitesini "iyi" olarak değerlendirdiklerini saptamışlardır. [16]

Brooks ve Anderson (2004) yoğun bakım ünitelerinde çalışan hemşirelerin iş yaşamı kalitesinin orta seviyede olduğunu saptamışlardır.[17]

Almalki ve ark. (2012) yaptıklar bir çalışmada, iş yaşam kalitesi puanını ortalamanın üzerinde bulurken 'yöneticilerle ilişkiler' ve 'destek hizmetler' alt boyutları ile hemşirelikten memnuniyet arasında pozitif yönde anlamlı bir ilişki saptamışlardır. [18]

Nayeri ve ark.(2011) İranlı hemşirelerin iş yaşam kalitelerinin orta düzeyde olduğunu; gündüz çalışan hemşirelerin, hem gündüz hem gece çalışan hemşirelere göre iş yaşam kalitelerinin daha yüksek olduğunu saptamışlardır. [19]

Bennett ve ark. (2001), yönetsel destek eksikliğinin, düşük moral ve iş tatmini düzeyi ile ilişkili olduğunu belirtmişlerdir. [20]

Yapılan çalışmalara bakıldığında hemşirelerin genel olarak iş yaşam kalitelerinin çok iyi olmadığı ve orta düzeyde değerlendirdikleri görülmektedir. Yine yapılan çalışmalar sağlık ortamında başarılı iş yaşam kalitesi, çalışanların moral ve örgütsel etkinliği ile artırabileceğini göstermektedir. Meslektaşların ve yöneticilerin sosyal desteğinin hemşireliğin olumsuz psikolojik etkilerini azalttığını göstermiştir. [21]

Bayrak ve Bostanoğlı'nun (2012), yoğun bakım ünitelerinde çalışan hemşirelerin hasta iletişimi konulu çalışmalarında; etkin iletişimin, hastaların tedavi ve bakım kalitesinin arttırılmasının yanında hastanede kalış süresini azaltmaya katkı sağladığını vurgulamışlardır .[22]

Cerit Ve Ark.(2020), hemşirelerin otonomi düzeyinin mesleki benlik saygısına etkisi çalışmasında hemşirelerin otonomisini ve mesleki benlik saygısını orta düzeyde saptamışlardır. [23]

Bu verilere göre; hemşirelerde bağımsız davranışın mesleki benlik saygısını yükselttiği ve değerliliğini arttırdığını; yöneticilerle olumlu ilişkinin yanı sıra hemşirelerin -hem tıbbi hem yönetsel hem de finansal- desteklenmesinin iş yaşam kalitesi üzerinde olumlu etkisi olduğu söylenebilir.

İş tatminini etkileyen temel faktörler arasında değerliliğin göstergesi olan ; kişiler arası ilişkiler, tanınma ve çalışma koşulları yer alır. İdari talepler, hasta denetimi ve olumsuz çalışma koşulları gibi konular yüksek düzeyde strese yol açtıklarında iş tatminini etkileyebilir. İşyeri ilişkileri ve destek sistemler, stresin azaltılmasında önemli bir rol oynamaktadır.

Sonuç olarak;

Bir hemşirenin "değeri" yaptıkları işin hasta sonuçlarına, verdikleri sağlık hizmetinin kalitesine ve sağlık bakım maliyetlerinin azaltılmasındaki ekonomik etkiye bağlıdır.

Hemşirelerin iş yaşam kalitesinin artırılması, verilecek bakım kalitesini de etkileyerek hasta memnuniyetinin artmasını sağlar. Hemşirelerin iyi bakım vermelerini sağlayacak koşulların oluşturulması iş yaşam kalitesini arttırır.

Yöneticilerle olumlu ilişkinin ve destek hizmetlerinin varlığı hemşirelerin iş yaşam kalitesini arttırır.

Hemşirelerin değerliliğinin göstergesi mesleki benlik saygısını artırmak için mesleki otonomilerinin desteklenmesi ve uygulamalarında yeterli özerkliğin tanınması önemlidir.

İnsanın ederini ve değerine koruyan, geliştiren sağlık bakım profesyonelinin eder ve değerinin destekleyecek düzenlemelerin ivedilikle hayata geçirilmesi gerekmektedir.

Hastalığın, iş görmezliğin getirdiği işgünü ve işgücü kayıplarının oluşturacağı; maliyet (eder) kaybı , hastalığa bağlı olarak bireyin anne,baba, eş, çalışan ve vatandaş olarak rol ve sorumluluklarını yerine getirememesi başka bir deyişle değerliliğini sergileyememesi/kendini gerçekleştirememesi söz konusudur.

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EFFECTS OF PDE5 INHIBITORS ON cGMP, PKG, AND PROTEIN METABOLISM IN SPERMATOGENESIS

ABSTRACT

Phosphodiesterases (PDEs) are enzymes involved in the metabolism of intracellular second messenger molecules. They catalyze the degradation of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), which play critical roles in cellular signal transduction, regulate various physiological processes.

PDE inhibitors prevent the activity of these enzymes, thereby halting the degradation of cAMP and cGMP and increasing the intracellular levels of these signaling molecules. Among PDE inhibitors, the most well known are PDE5 inhibitors. PDE5 is responsible for the degradation of cGMP, and its inhibition leads to increased cGMP levels. Elevated cGMP levels promote vasodilation and enhanced blood flow, making PDE5 inhibitors effective in the treatment of erectile dysfunction. In recent years, the beneficial effects of PDE5 inhibitors on spermatogenesis have also been recognized. These inhibitors enhance the effects of cGMP, improving sperm motility, structure, and function. PDE5 inhibitors particularly sildenafil, vardenafil, and tadalafil exert direct effects on sperm function by increasing cGMP levels.

cGMP regulates various cellular processes through protein kinase G (PKG), which plays a crucial role in spermatogenesis. PKG activation enhances protein synthesis in sperm cells, regulating the metabolic processes essential for spermatogenesis. Protein metabolism encompasses protein synthesis, folding, modification, and degradation within the cell, all of which are vital for sperm development. The activation of PKG accelerates and regulates these processes, supporting sperm cell maturation, development, and motility. Furthermore, by increasing the synthesis of essential proteins in sperm cells, it strengthens cellular structures and enhances the spermatogenesis process. The increased cGMP levels induced

by PDE5 inhibitors significantly improve protein metabolism, reinforcing the functional characteristics and structural integrity of sperm cells.

Consequently, PDE5 inhibitors exert positive effects on spermatogenesis through the cGMP-PKG pathway and present a potential therapeutic option for improving sperm production and quality.

Keywords: Autism, cGMP, PDE5, PKG, PPA

INTRODUCTION

PDEs are enzymes responsible for hydrolyzing the cyclic nucleotides cAMP and cGMP [1].

The signaling pathways involving cAMP and cGMP have been extensively studied across various fields because of their significant biological and therapeutic roles [2]. PDEs are enzymes involved in the metabolism of second messenger molecules within the cell. Second messengers transmit signals generated by receptor-ligand interactions at the cell surface to effector proteins. Effector proteins such as protein kinases activated by cAMP and cGMP mediate biological responses. Intracellular levels of second messengers are regulated by homeostatic mechanisms. The cyclic nucleotide signaling system includes adenylyl cyclase, guanylyl cyclase, and PDEs. Adenylyl and guanylyl cyclases are activated upon receptor-ligand binding and catalyze the conversion of ATP/GTP into 3'-5' cAMP and cGMP, respectively, while PDEs degrade these cyclic nucleotides, terminating the signal [2,3].

The PDE family consists of 11 subfamilies (PDE1–11) encoded by 21 distinct genes. PDE isoforms are classified based on their amino acid sequences, substrate specificity, cofactor dependency, catalytic activity, and kinetic characteristics. Some PDE subfamilies selectively hydrolyze cAMP (PDE4, 7, 8) or cGMP (PDE5, 6, 9), whereas PDE1, 2, 3, 10, and 11 regulate physiological functions by targeting both cyclic nucleotides [4].

Among the PDE family, PDE5 is one of the earliest identified subfamilies. It has three variants: PDE5A1, PDE5A2, and PDE5A3. These variants share common phosphorylation sites, allosteric cGMP binding sites, and catalytic domains. However, they differ in their N-terminal regions and tissue distribution. PDE5A3 is predominantly expressed in vascular smooth muscle cells, whereas PDE5A1 and PDE5A2 have a broader tissue distribution. PDE5 serves as a key regulator of cGMP signaling in various tissues [5-7].

The cGMP signaling pathway is initiated by ligand-mediated activation of the guanylyl cyclase (GC) enzyme, resulting in increased cGMP production. This activates effectors such as protein kinase G (PKG) and cGMP-regulated ion channels. The pathway regulates various physiological processes including cell growth, cell motility, anti-inflammatory activity, and apoptosis. It is regulated by PDE5, which is allosterically activated by the increased cGMP level through binding to its regulatory domain, leading to enhanced PDE5 activity that restores intracellular cGMP concentration to basal levels. PDE5 is expressed in multiple tissues, including lung, brain, kidney, cardiac myocytes, gastrointestinal tissue, vascular smooth muscle cells, platelets, and penile corpus cavernosum [5].

PDE5 Inhibitors

The first PDE5 inhibitor, sildenafil, received approval in 1998, followed by vardenafil and tadalafil in 2003. Avanafil was subsequently approved in 2012. Among these, sildenafil remains the oldest and most commonly used PDE5 inhibitor [8,9].

It is currently approved for clinical use in the treatment of erectile dysfunction (ED), pulmonary arterial hypertension (PAH), and lower urinary tract symptoms associated with benign prostatic hyperplasia [10].

PDE5 inhibitors function by inhibiting the degradation of cGMP, thereby elevating intracellular cGMP levels. Endothelial cells in the corpus cavernosum of the penile smooth

muscle release nitric oxide (NO), which activates GC and enhances cGMP synthesis. By preventing cGMP breakdown, these inhibitors prolong the duration of erection and are therapeutically used in the treatment of erectile dysfunction [11].

PDE5 inhibitors are utilized in the treatment of PAH due to their ability to induce pulmonary vasodilation. This effect counteracts the reduced nitric oxide (NO) release in the pulmonary vasculature, which leads to decreased cGMP levels. Additionally, PDE3, PDE4, and PDE5 contribute by increasing cAMP levels in the pulmonary vessels, promoting bronchial relaxation and reducing proinflammatory mediators [12].

The primary mechanism of PDE5 inhibitors involves the inhibition of the PDE5 enzyme located in vascular smooth muscle cells. By blocking this enzyme, the degradation of cGMP is prevented, leading to increased intracellular cGMP levels. Elevated cGMP activates protein kinase G (PKG), which induces relaxation of the vascular smooth muscle. The accumulation of cGMP results in vasodilation through the phosphorylation of various effector molecules. Consequently, PDE5 inhibitors prolong PKG activity by preventing cGMP breakdown [13].

Although PDE5 inhibitors are primarily used for treating erectile dysfunction, recent research has increasingly focused on their potential role in reproductive physiology, particularly regarding sperm production and quality. Their indirect effects on testicular microcirculation, hormonal homeostasis, and oxidative stress have generated hypotheses suggesting influence at various stages of spermatogenesis. Consequently, the possibility that PDE5 inhibitors may serve as supportive agents in male infertility treatment beyond symptomatic relief is gaining significant attention. This study aims to evaluate the impact of PDE5 inhibitors on spermatogenesis based on current literature.

NO-cGMP-PKG Pathway

NO is a key regulator of cGMP signaling. It binds to soluble sGC, catalyzing the conversion of guanosine triphosphate (GTP) into cGMP inside the cell. The produced cGMP modulates ion channels by decreasing calcium influx and activates PKG, which facilitates the release of intracellular calcium. This cascade ultimately results in smooth muscle relaxation [14,15].

The NO-cGMP-PKG pathway plays a key role in regulating blood flow to the testes, impacting nutrient delivery, oxygen supply, and hormonal signals essential for spermatogenesis. Additionally, it supports sperm transport and maturation by controlling contractions in the epididymis and efferent ducts. Peritubular myoid cells in the seminiferous tubules and contractions within the epididymal ducts regulate nonvascular smooth muscle activity. In vascular smooth muscle tissue, NO stimulates the production of cGMP, which subsequently activates PKG, leading to vasodilation. This effect is counterbalanced by PDE5, which breaks down cGMP. Within the male reproductive system, the NO-cGMP-PKG signaling axis and PDE5 activity coordinate essential processes such as fluid secretion in the seminiferous tubules, rhythmic contractions of the testis, and sperm transport along the reproductive tract.[14,16].

Scipioni and colleagues identified PDE5 expression in both Leydig and peritubular cells of prepubertal and adult rat testes. Their research emphasized the importance of cGMP-mediated pathways in regulating testosterone synthesis in Leydig cells and supporting sperm

transit via relaxation of myofibroblasts. Additionally, PDE5's role in modulating cGMP levels within peritubular myoid cells is essential for maintaining Sertoli cell functions, ensuring germinal epithelium integrity, and facilitating vitamin A metabolism, all of which contribute to effective spermatogenesis [17]. An investigation using Sprague-Dawley rats explored the effects of sildenafil, a PDE5 inhibitor, and found marked improvements in sperm motility and concentration, confirming its positive effect on epididymal sperm parameters [18]. The NO/cGMP system is widely recognized for its role in ejaculation regulation. Sildenafil has also been evaluated for its effectiveness in addressing premature ejaculation by influencing the contractile behavior of the vas deferens and enhancing overall reproductive system function [19]. In diabetic infertile men, daily intake of 5 mg tadalafil over three months led to improved ultrasound findings in the seminal vesicles and better semen discharge parameters [20]. Moreover, zinc-rich antibacterial substances within prostatic fluid are crucial for maintaining seminal osmotic balance and promoting sperm motility. Sildenafil and vardenafil treatments are associated with increased prostatic secretions, suggesting a link between these drugs and improved sperm mobility [21].

FDE5 Inhibitors and Semen Quality

PDE5 inhibitors are best known for enhancing erectile function by preventing cGMP degradation in the corpus cavernosum. However, PDE5 isoforms and other phosphodiesterase enzymes are also present in sperm cells, hinting at both direct and indirect effects on sperm function. These agents may enhance secretory activity in accessory sex glands like the prostate and seminal vesicles, enriching seminal plasma with components that support sperm motility, vitality, and fertilization ability [22,23].

By blocking cGMP breakdown, PDE5 inhibitors raise intracellular cGMP levels and trigger a secondary increase in cAMP, which activates key enzymes like PKA and PKG. These kinases influence ion channels and intracellular signaling pathways essential for sperm movement, capacitation, and the acrosomal reaction. Thus, these medications can help maintain acrosome structure and improve fertilization potential [24,25].

Emerging data suggest that PDE5 inhibitors also guard against oxidative damage, bolster mitochondrial function, and promote ATP production, all of which aid in sperm viability and motility. Like the nonselective PDE inhibitors pentoxifylline and caffeine, PDE5 inhibitors exert regulatory effects on molecular targets crucial to sperm health. They also stimulate Leydig cell testosterone production and enhance Sertoli cell secretory function, creating an environment conducive to spermatogenesis. Furthermore, by modulating smooth muscle contractions in the testis and epididymis, these drugs support efficient sperm transit [26-28].

Moderate dosing of PDE5 inhibitors may enhance sperm parameters, while excessive doses risk adverse effects due to inhibition of PDE11 isoenzymes, which are vital to spermatogenesis [29].

Meta-analyses confirm improvements in sperm motility and morphology among infertile men using PDE5 inhibitors, although benefits are limited in men with already normal semen profiles [30].

Evidence supports the role of PDE5 inhibitors in improving semen collection, reducing stress during fertility treatments, and aiding sperm transfer by maintaining post-ejaculation penile

rigidity. Studies on diabetic rat models reveal that sildenafil enhances reproductive organ blood flow, positively impacting fertility. Additionally, sildenafil significantly increases the number of sperm undergoing the acrosomal reaction, likely due to cGMP-mediated calcium influx mechanisms. Glenn et al. observed that exposing sperm to 0.67 μmol/L sildenafil significantly enhanced the percentage exhibiting this acrosomal change [30-36].

CONCLUSION

Originally developed for the treatment of erectile dysfunction, PDE5 inhibitors have since emerged as pharmacological agents with multifaceted effects on male reproductive physiology. By modulating the cGMP signaling cascade specifically through activation of the cGMP dependent PKG pathway these compounds exert regulatory control over several critical testicular processes. Their influence extends to various stages of spermatogenesis, including cell proliferation, differentiation, and maturation, thereby promoting overall testicular function.

In addition to their effects on testicular tissue, PDE5 inhibitors have demonstrated benefits in enhancing sperm motility and capacitation, which are crucial for successful fertilization. Several studies also suggest a positive modulatory effect on Leydig cell activity, resulting in improved testosterone synthesis and hormonal homeostasis both of which are indispensable for optimal spermatogenesis. Moreover, PDE5 inhibitors may improve the secretory functions of accessory glands, such as the prostate and seminal vesicles, thereby creating a more favorable biochemical environment for sperm maturation and survival.

Despite these promising findings, the current body of literature remains limited in scope. The majority of studies to date have been conducted on healthy volunteers or men diagnosed with erectile dysfunction, limiting the generalizability of the results to subfertile populations. The impact of PDE5 inhibitors on sperm morphology, motility, DNA integrity, and epididymal function in subfertile men remains inadequately investigated. Furthermore, while short-term studies report various beneficial outcomes, data regarding long-term safety and efficacy are notably scarce. Given the approximately 74-day cycle of human spermatogenesis, short duration interventions fail to capture the full spectrum of reproductive dynamics, particularly those involving testicular histology, endocrine function, and epididymal transit.

To fully elucidate the reproductive implications of PDE5 inhibition, future research must prioritize large-scale, multicenter, and longitudinal clinical studies. These investigations should not be limited to standard semen parameters but should also encompass molecular assessments, such as gene expression profiling, oxidative stress markers, apoptosis indices, and comprehensive hormonal panels. Additionally, variability in individual treatment responses potentially influenced by genetic, epigenetic, or lifestyle factors should be addressed through integrative, systems-based research methodologies.

In conclusion, PDE5 inhibitors represent a promising avenue in the pharmacological modulation of male fertility. However, translating this potential into clinical practice necessitates the resolution of existing knowledge gaps through robust experimental and clinical investigations. Expanding the evidence base in this manner will not only clarify the therapeutic role of PDE5 inhibitors in male fertility but also support the development of novel treatment strategies for reproductive dysfunction.

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CORE ASPECTS OF ENHANCING THE CAPABILITIES AND VERSATILITY OF DEGRADABLE TRIAZOLE 'CLICK' OF POLYMER LIBRARIES FOR BROAD BIOMEDICAL APPLICATIONS: PROGRESS, OBSTACLES, STRATEGIES FOR FUTURE DEVELOPMENT AND INNOVATIVE PRACTICAL SOLUTIONS

ABSTRACT

A series of new aliphatic AA-BB-type poly(ester ether amide)s (PEEAs) and poly(ester ether)s (PEEs) containing 1,2,3-triazole rings in the main chain were successfully obtained. The synthesis of the “click” polymers was performed *via* Cu(I)-catalyzed click step-growth polymerization (SGP) employing the efficient one pot/two-step synthetic approach that we had previously developed. The structure of the polymers was confirmed by FT-IR and NMR spectroscopy. The newly synthesized materials were extensively characterized, including assessments of their yield, solubility, film-forming properties, molecular weights, and molecular weight distribution. The obtained PEEAs and PEEs exhibited a quite satisfactory degree of polymerization, good film-forming properties, and favorable solubility behavior. The reported materials enlarge a library of available degradable triazole click polymers promising for a wide range of biomedical applications. The results validate once again the applicability of our innovative synthetic strategy for designing various classes of triazole-backbone degradable click polymers. Degradable triazole-based “click” polymers have emerged as a versatile and indispensable class of materials in biomedical innovation. Their unique properties, such as biocompatibility, tunable degradability, and ease of synthesis via “click” chemistry, have made them highly attractive for diverse applications, ranging from drug delivery systems to tissue engineering scaffolds. Expanding their scope and functionality remains a pivotal goal to meet the growing demands of advanced biomedical technologies. This article explores the advances, challenges, opportunities, future development strategies, and emerging practical implementation approaches for these polymers. The field of degradable triazole "click" polymers is poised for significant advancements in biomedical innovation. As the library of these polymers expands, it is important to balance the opportunities they offer with the challenges they present. By focusing on controlled synthesis, enhanced biological interactions, and scalable production, researchers and clinicians can harness the full potential of these materials. With continued development and collaboration, these polymers could become a cornerstone of next-generation biomedical therapies, leading to improved patient outcomes and more sustainable healthcare solutions. The study successfully demonstrates the synthesis of new poly(ester ether amide)s (PEEAs) and poly(ester ether)s (PEEs) incorporating 1,4-disubstituted 1,2,3-triazole rings in their backbone. The materials exhibit promising properties that make them potential candidates for a variety of biomedical applications, particularly in controlled drug delivery and tissue engineering. However, further research is needed to fully explore their clinical potential, optimize their properties, and address challenges related to their large-scale production and biological interactions.

Keywords: Poly(ester ether amide)s, (PEEAs) poly(ester ether)s, (PEEs) copper(i), catalyzed azide-alkyne cycloaddition, (CuAAC) step growth polymerization (SGP) 1,2,3-triazole ring.

INTRODUCTION

Degradable triazole-based "click" polymers have emerged as a versatile and indispensable class of materials in biomedical innovation. Their unique properties, such as biocompatibility, tunable degradability, and ease of synthesis via "click" chemistry, have made them highly attractive for diverse applications, ranging from drug delivery systems to tissue engineering scaffolds. Expanding their scope and functionality remains a pivotal goal to meet the growing demands of advanced biomedical technologies. This article explores the advances, challenges, opportunities, future development strategies, and emerging practical implementation approaches for these polymers.

Advances in Degradable Triazole "Click" Polymers

1. **Synthetic Innovations**:

- Introduction of novel monomers and polymerization techniques has significantly broadened the library of triazole-based polymers.

- Controlled polymerization strategies enable precise tailoring of molecular weights and architectures, including linear, branched, and network structures.

2. **Functional Diversity**:

- Integration of functional groups has allowed for enhanced interaction with biological systems, enabling applications in targeted drug delivery and imaging.

- Multi-stimuli-responsive systems have been developed for controlled degradation under specific physiological conditions.

3. **Biomedical Applications**:

- **Drug Delivery**: High loading capacities and tunable release profiles make these polymers ideal carriers for chemotherapeutics, antibiotics, and gene therapies.

- **Tissue Engineering**: Biodegradable scaffolds support cell attachment, proliferation, and differentiation while degrading into non-toxic byproducts.

- **Diagnostics**: Functionalized triazole polymers serve as contrast agents in imaging and biosensing applications.

Challenges in Expanding the Scope and Functionality

1. **Synthetic Complexity**:

- Achieving scalable, cost-effective synthesis of highly functionalized triazole polymers remains a significant hurdle.

2. **Biocompatibility and Safety**:

- Comprehensive in vivo studies are required to ensure long-term biocompatibility and to understand degradation pathways and byproducts.

3. **Regulatory Hurdles**:

- The stringent regulatory requirements for biomedical materials pose challenges for clinical translation.

4. **Integration with Emerging Technologies**:

- Compatibility with advanced biomedical tools such as 3D bioprinting and microfluidics is still underexplored.

Opportunities for Innovation

1. **Interdisciplinary Collaboration**:

- Partnerships between chemists, biologists, engineers, and clinicians can accelerate innovation and application.

2. **Customization for Personalized Medicine**:

- Tailoring polymer properties to meet individual patient needs in drug delivery and tissue engineering.

3. **Green Chemistry Approaches**:

- Development of sustainable, eco-friendly synthetic methods for triazole polymers.

4. **Integration with Smart Materials**:

- Combining triazole polymers with stimuli-responsive or bioactive materials to create multifunctional systems.

Future Development Strategies

1. **Advanced Synthesis Techniques**:

- Leveraging automation, artificial intelligence, and machine learning for the design and synthesis of complex polymer architectures.

2. **Comprehensive Characterization**:

- Employing state-of-the-art analytical tools to study polymer structure, functionality, and degradation mechanisms.

3. **Enhanced Biocompatibility Testing**:

- Long-term in vitro and in vivo evaluations to ensure safety and efficacy.

4. **Clinical Translation**:

- Establishing partnerships with industry and regulatory bodies to streamline the transition from laboratory research to practical applications.

Emerging Practical Implementation Approaches

1. **3D Printing and Bioprinting**:

➢ Utilization of triazole-based polymers as bioinks for creating customized biomedical devices and tissue constructs.

2. **Nanotechnology Integration**:

➢ Designing nanoscale polymeric systems for precision medicine applications.

3. **Hybrid Systems**:

➢ Developing composite materials that combine the benefits of triazole polymers with other biomaterials for enhanced performance.

4. **Digital Health and Monitoring**:

➢ Incorporating triazole polymers into wearable biosensors and diagnostic tools for real-time health monitoring.

The Copper(I) catalyzed azide-alkyne cycloaddition (CuAAC) stands as a prominent tool within the realm of "click" reactions, showcasing its widespread utility across diverse domains in contemporary polymer and material science. This reaction has gained significant recognition due to its exceptional attributes, including rapid reaction kinetics, high efficiency, precise regioselectivity, tolerance towards diverse functional groups, and mild reaction conditions. Consequently, CuAAC click reactions have found extensive application in the synthesis of various polymer architectures, such as block-copolymers, cyclic polymers, dendrimers, hyper-branched macromolecules, star-shaped polymers, and cross-linked polymeric networks [1-11]. Furthermore, this technique has been instrumental in functionalizing and modifying the surfaces of polymeric materials.

Intrigued by its potential, synthetic polymer chemists have sought to leverage CuAAC for the synthesis of polytriazoles through step-growth polymerization (SGP) since 2004 [12-15]. Despite notable advancements, this field remains in a state of continuous development, beset by numerous challenges and obstacles [14-15]. Specifically, there is a paucity of reports detailing the synthesis of aliphatic main-chain triazole degradable polymers through CuAAC-based click SGP. Noteworthy contributions include the pioneering work of Nagao and Takasu [16], who successfully synthesized degradable polyesters (PEs), and the efforts of Galbis et al. [17], who produced click PEs on the basis of erythritol, bearing free hydroxyl groups. Beyond these achievements, click polymerization has also been harnessed for the fabrication of various other biomedical materials [18-24].

It should be noted that click polymers with 1,2,3-triazole rings in the backbone have some important advantages. To commence with, the triazole rings are known to be low-toxic moieties [25,26] with a high level of mimicry of the amide bond of native peptides: the 1,2,3-triazole ring is structurally similar to the amide bond of proteins in terms of configuration, distance, and planarity [27]. So, the incorporation of the triazole units in the polymeric chains is anticipated to enhance the biocompatibility of the materials. Furthermore, the insertion of rigid triazole fragments in the polymeric structure can notably improve the thermal characteristics of the polymers [28]. It is known that triazole's derivatives demonstrate a wide range of biological activities, including anti-inflammatory, antioxidant, antiviral,

antimicrobial, antifungal, anticancer, analgesic, etc. [29,30]. Therefore, the click polymers with triazole rings in the backbone are expected to reveal some biological activities, and such polymers can be promising for creating new bioactive materials. It is worth noting that 1,2,3-triazoles are widely used in the design of various high-performance organic coatings such as anti-microbial, anti-fouling, anti-corrosive, self-healing, etc. [31]. Thus, the triazole-enriched click polymers can be considered as perspective materials for creating effective polymeric coatings as well.

Moreover, an important advantage of click polymers lies in the quaternizable nature of 1,2,3-triazole rings, as documented in prior studies [32,33]. This characteristic facilitates subsequent post-polymerization functionalization of these polymers. The process of quaternization, involving the modification of triazole rings with diverse quaternizing agents such as halo-alkyls and polyethylene glycol (PEG) derivatives, presents opportunities for creating cationic systems featuring 1,2,3-triazolium moieties within the polymer backbone. This includes the development of cationic polymers and amphiphilic surfactants (e.g., when employing PEG-bromides as quaternizing agents) and the formation of cross-linked hydrogels (when utilizing bifunctional quaternizing agents like dibromo-PEGs, for instance). These approaches hold significant promise for a multitude of biomedical applications.

To synthesize new high-molecular-weight 1,2,3-trialoze containing degradable polymers, we have previously elaborated a new synthetic strategy of CuAAC-based click SGP [28]. Our innovative approach could be considered as more versatile compared to existing strategies and allows to synthesize different types (AB and AA-BB) and classes (PEs, poly(ester amide)s, poly(ester urea)s, their co-polymers, etc.) of aliphatic hetero-chain click polymers, avoiding the utilization of potentially explosive organic azides through safe and facile one-pot/two-step procedure. In the mentioned work [28], we successfully synthesized a series of novel linear AA-BB type 1,2,3-triazole rings-containing click PEs following the new strategy. Obtained on the basis of non-toxic building blocks (fatty diols and dicarboxylic acids), the new polymers possessed high molecular weights, improved thermal characteristics, good solubility in organic solvents, film- and nanoparticles-forming properties. Very recently, we demonstrated the suitability of the new synthetic approach for designing novel hydrolytically degradable AB-type click PEs and Co-PEs as well [34].

In the present work, we report on the successful synthesis of two other classes of new linear AA-BB-type degradable click polymers *via* our efficient synthetic strategy: poly(ester ether amide)s (PEEAs) and poly(ester ether)s (PEEs). The key homo-bifunctional diyne monomers were synthesized by the interaction of sebacoyl chloride with propargyl alcohol or propargylamine according to Figure 1.

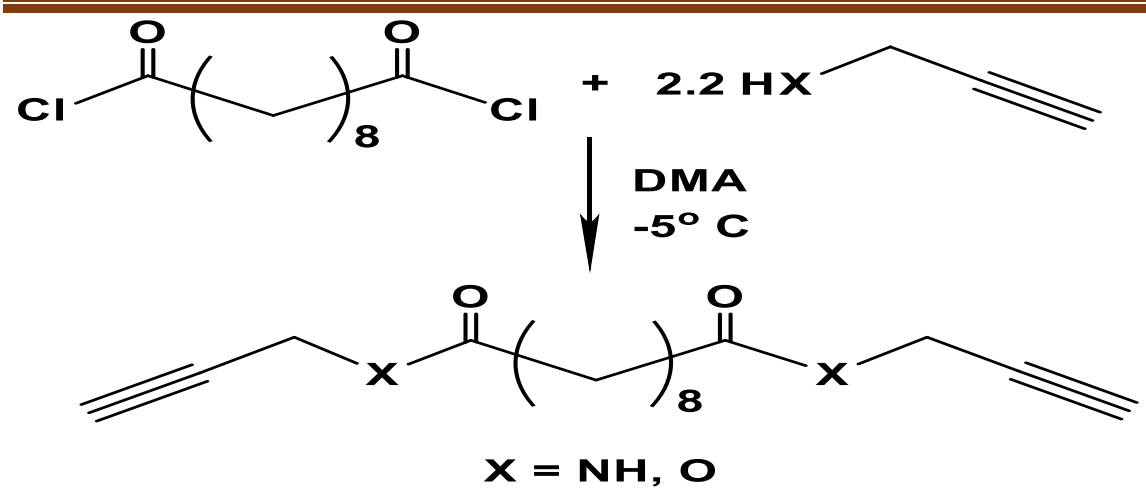


FIGURE 1. Synthesis of diyne monomers

The synthetic precursors of target diazide monomers (bis-bromoacetyl derivatives) were obtained by the interaction of bromoacetyl bromide with di-, tri-, and tetra-ethylene glycol (Figure 2).

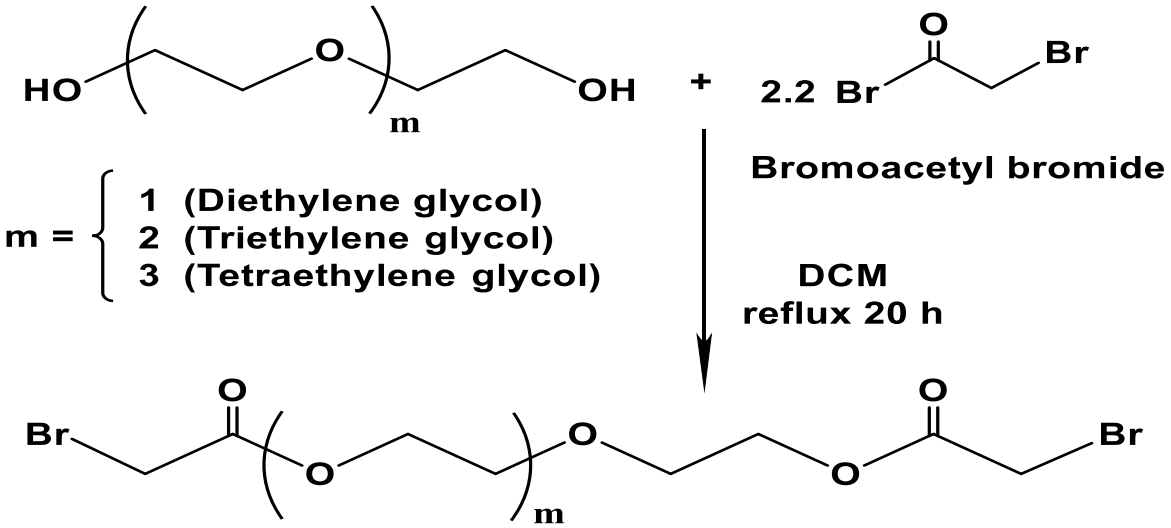


FIGURE 2. Synthesis of bis-bromoacetyl derivatives

The synthesis of the new click polymers with triazole rings in the backbone was realized by one-pot/two-step SGP of the homo-bifunctional monomers in the presence of sodium azide using copper(I) iodide/triethylamine (CuI/NEt_3) as a catalytic system (Figure 3).

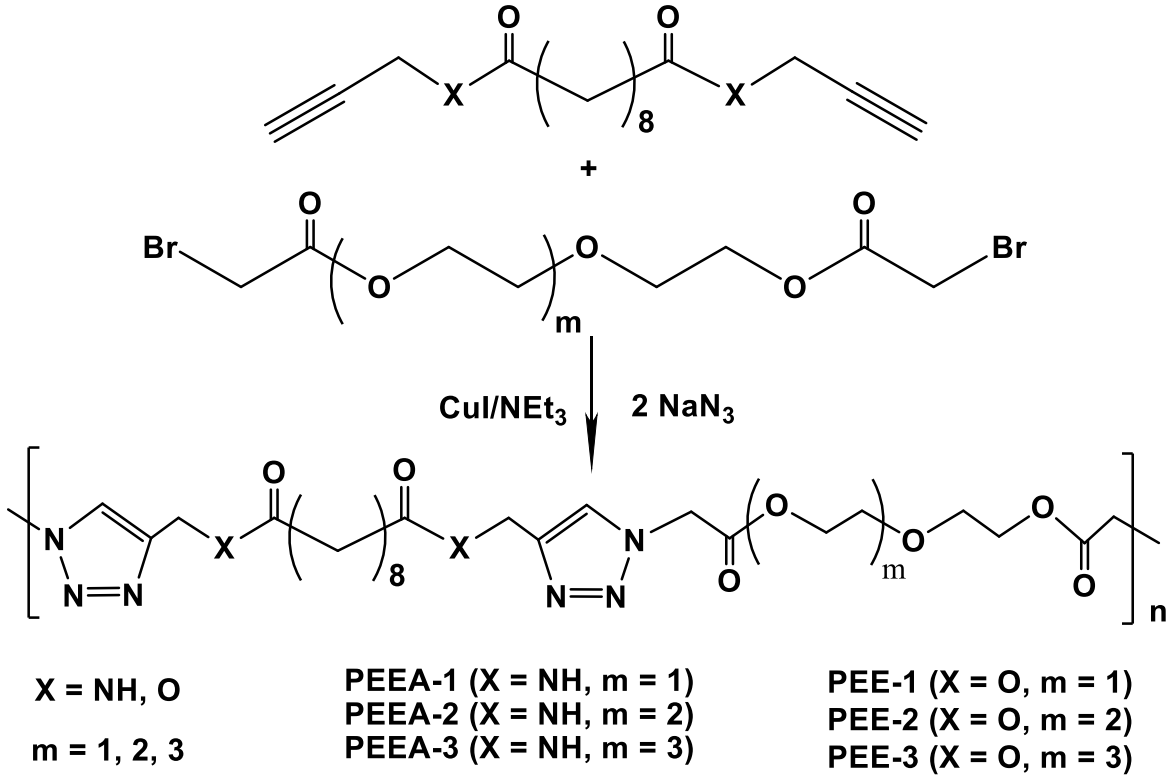


FIGURE 3. Synthesis of PEEAs (X=NH) and PEEs (X=O)

The confirmation of monomer and polymer structures was performed through the use of FT-IR and NMR spectroscopic techniques. Comprehensive polymer characterization encompassed the assessment of yield, solubility in organic solvents, film-forming attributes, determination of molecular weights, and evaluation of molecular weight distribution. The introduction of novel AA-BB-type PEEAs and PEEs serves to enrich the existing repository of degradable click polymers, broadening the spectrum of materials available for a diverse array of biomedical applications.

EXPERIMENTAL METHODS AND MATERIALS

Materials

Broboacetyl bromide, propargyl alcohol, propargylamine, sodium azide, anhydrous sodium sulfate, copper(I) iodide, lithium bromide, aluminum oxide (alumina) (activated, basic, Brockmann I), acetone, ethanol, methanol, hexane, ethyl acetate, dichloromethane (DCM), N,N-Dimethylformamide (DMF), N,N-dimetyl-acetamide (DMA), and 1,1,1,3,3,3-hexa¬fluoro¬isopropanol (HFIP) were purchased from Sigma-Aldrich (Germany). N-methylpyrrolidone (NMP) was purchased from Carl Roth, Karlsruhe (Germany). Triethylamine (TEA) was purchased from Lancaster (UK). All the starting materials, chemicals, and solvents purchased from the commercial sources were used without further purification.

Characterization

The polymers synthesized were characterized by Fourier-transform infrared spectroscopy (FT-IR), 1H nuclear magnetic resonance (NMR) spectroscopy, and gel permeation chromatography (GPC).

The IR analysis of samples was performed on Thermo Nicolet Avatar 370 FT-IR spectrophotometer coupled with EZ OMNIC software measuring between wavelength range of 4000 and 400 cm^{-1}. The FT-IR spectra of monomers were recorded using Avatar Multi-Bounce Flat Plate 45 degree Ge. To obtain the spectra of polymers, the thin films were cast from HFIP solution on KBr plates, the solvent was evaporated at room temperature and films were dried in a vacuum at 40° C to a constant weight.

The 1H and NMR spectra were recorded at 300 K on a JEOL ECP 500 NMR spectrometer operating at 400 MHz. DMSO-d_6 was used as solvents and internal standards. The chemical shifts (δ) in the spectra are conventionally expressed in parts per million (ppm).

The weight-average (M_w), number-average (M_n) molecular weights, and molecular weight distribution (Dispersity, $Đ$) of the polymers were determined on a GPC machine (Waters Associates, Inc., Milford, United States) comprising two Styragel columns in DMF: HR4 and HR3 (7.8 mm × 300 mm) and equipped with a high-pressure liquid chromatography pump (Waters 1525 Binary HPLC) and a Waters refractive index detector 2414 and UV-detector (Waters 2487 dual absorbance detector, λ = 240 nm). A solution of LiBr (0.05 M) in DMF was used as an eluent. Injected volume 100 µL, flow rate 1.0 mL min^{-1}. The columns were calibrated with poly(methyl methacrylate) standards (M_n = 500 – 500, 000 g mol^{-1}). Polymer sample solutions with concentration 5 mg ml^{-1} were prepared in the GPC eluent and filtered with PTFE filters (0.45 µm) prior to injection.

Synthesis of diyne monomers

The key homo-bifunctional diyne monomers (di-propargyl amide/ester of sebacic acid) were synthesized by the interaction of sebacoyl chloride with propargylamine or propargyl alcohol according to Figure 1. The synthesis was carried out in DMA solution without using tertiary amine as HCl acceptor. In a typical procedure, propargylamine/propargyl alcohol (0.159 mol – an excess) was dissolved in 260 mL of DMA, the solution was chilled to –5° C and 17.30 g of sebacoyl chloride (0.072 mol) was added dropwise upon stirring using a magnetic stirrer. The reaction solution was stirred for 30 min at -5 °C and then was continued at room temperature for 24 h. Afterwards, the solution was poured into water and the vessel with precipitated white powder was placed overnight in a refrigerator. The obtained solid product was filtered off, dried under reduced pressure at room temperature, and recrystallized from the ethanol/hexane mixture.

Di-propargyl amide of sebacic acid. Yield: 68 %. FTIR (cm^{-1}): 3280 (-NH-, amide, stretching vibr.), 2132 (C≡C), 1642 (-CO-, amide), 1552 (NH-, amide, bending vibr.). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 1.28-1.32 (8H, m, C$\underline{H_2}$); 1.54 (4H, m, C$\underline{H_2}$CH_2CO); 2.16 (4H, t, C$\underline{H_2}$CO); 3.04 (2H, t, sp-C$\underline{H}$); 4.11 (4H, d, NHC$\underline{H_2}$), 8.12 (2H, N$\underline{H}$).

Di-propargyl ester of sebacic acid. Yield: 75 %. FTIR (cm^{-1}): 3238 (≡C–H), 2128 (C≡C), 1732 (-CO- ester), 1217 (C-O-C). ^{1}H NMR: (400 MHz, DMSO-d_6, δ): 1.29-1.35 (8H, m, C$\underline{H_2}$); 1.59 (4H, m, C$\underline{H_2}$CH_2CO); 2.30 (4H, t, C$\underline{H_2}$CO); 2.93 (2H, t, sp-C$\underline{H}$); 4.61 (4H, d, OC$\underline{H_2}$).

Synthesis of bis-bromoacetyl derivatives (precursors of diazide monomers)

The synthetic precursors of target diazide monomers (bis-bromoacetyl derivatives) were synthesized by the interaction of bromoacetyl bromide with di- (DEG), tri- (TEG), and tetra-ethylene glycol (TTEG) according to Figure 2 above. The brief synthetic procedure is described here on the example of DEG-based bis-bromoacetyl derivative: to a solution of 6.09 g (0.057 mol) of DEG in 315 mL of DCM, 25.52 g (0.126 mol) of bromoacetyl bromide was added. The resulting yellow solution was refluxed for 20 h and the solvent was removed in a vacuum on a rotary evaporator yielding a brownish viscous liquid. The obtained crude product was dissolved in 40 mL of methanol and the solution was washed with 40 mL of hexane. The mixture was separated using a separated funnel and the procedure was repeated twice (i.e. methanol solution of the crude product was washed 3 times with hexane). After the last separation of the mixture, the methanol solution of the monomer was dried over anhydrous sodium sulfate, then it was filtered and the organic solvent was removed in a vacuum on a rotary evaporator, yielding a brownish viscous liquid. DEG- and TTEG-based bis-bromoacetyl derivatives were synthesized according to the same procedure.

DEG-based bis-bromoacetyl derivative. Yield: 69 %. FTIR (cm^{-1}): 1740 (-CO-, ester), 1282 (C-O-C, ester), 1123 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 3.51 (4H, C$\underline{H_2}$-O-C$\underline{H_2}$), 4.11 (4H, COO-C$\underline{H_2}$), 4.21 (4H, CO-C$\underline{H_2}$).

TEG-based bis-bromoacetyl derivative. Yield: 76 %. FTIR (cm^{-1}): 1736 (-CO-, ester), 1278 (C-O-C, ester), 1115 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 3.21-3.63 (8H, C$\underline{H_2}$-O-C$\underline{H_2}$-C$\underline{H_2}$-O-C$\underline{H_2}$), 4.12 (4H, COO-C$\underline{H_2}$), 4.22 (4H, CO-C$\underline{H_2}$).

TTEG-based bis-bromoacetyl derivative. Yield: 73 %. FTIR (cm^{-1}): 1744 (-CO-, ester), 1282 (C-O-C, ester), 1116 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 3.13-3.47 (12H, C$\underline{H_2}$-O-C$\underline{H_2}$-C$\underline{H_2}$-O-C$\underline{H_2}$-C$\underline{H_2}$-O-C$\underline{H_2}$), 4.09 (4H, COO-C$\underline{H_2}$), 4.20 (4H, CO-C$\underline{H_2}$).

Polymer synthesis

The target PEEAs and PEEs were synthesized according to the one-pot two-step synthetic strategy that we had previously developed [28,34] (Figure 3). The synthetic procedure is similar to the one applied for the AB-type click PEs reported in our recent work [34]. The brief synthetic procedure for the click SGP of the PEEAs and PEEs is described here for PEEA-1 as an example: 1.902 g (5.46 mmol) of DEG-based bis-bromoacetyl derivative and 0.782g (12.03 mmol) of sodium azide were dissolved in 8.35 mL of NMP and stirred at room temperature for 3 h. Then, 1.511 g (5.46 mmol) of a di-propargyl amide of sebacic acid, 31.24 mg (0.16 mmol) of catalyst CuI (3 mol %), and 0.114 mL (0.82 mmol) of NEt_3 as a ligand were added to the reaction solution. The reaction solution was stirred at room temperature for 24 hours. After completion of the reaction, the solution was diluted with 8 mL of NMP, and the copper catalyst was removed by passing the crude polymer solution through a small column of activated basic alumina. Then, the obtained polymer solution was precipitated in water, filtered, thoroughly washed with water, and dried under vacuum at room temperature. Then, the polymer was twice precipitated from NMP solution (at a concentration of 10% w/v) to water, filtered, and dried under vacuum at room temperature to a constant weight. All the other polymers were synthesized employing the same synthetic procedure.

PEEA-1. Yield: 73 %. FTIR (cm^{-1}): 3297 (-NH-, amide, stretching vibr.), 3068 (C=C-H of the 1,2,3-triazole), 1752 (-CO-, ester), 1638 (-CO-, amide), 1544 (NH-, amide, bending vibr.), 1217 (C-O-C, ester), 1135 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 1.01 (12H, CH_2-(CH_2)$_6$-CH_2), 1.85 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.24-3.50 (4H, CH_2-O-CH_2), 4.02-4.11 (8H, COO-CH_2 and NH-CH_2-, stack), 5.17 (4H, CO-CH_2-N), 7.68 (2H, -C=CH of triazole), 8.16 (2H, NH).

PEEA-2. Yield: 94 %. FTIR (cm^{-1}): 3293 (-NH-, amide, stretching vibr.), 3063 (C=C-H of the 1,2,3-triazole moiety), 1744 (-CO-, ester), 1638 (-CO-, amide), 1544 (NH-, amide, bending vibr.), 1217 (C-O-C, ester), 1131 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 1.07 (12H, CH_2-(CH_2)$_6$-CH_2), 1.82 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.23-3.65 (8H, CH_2-O-CH_2-CH_2-O-CH_2), 4.03-4.12 (8H, COO-CH_2 and NH-CH_2-, stack), 5.18 (4H, CO-CH_2-N), 7.70 (2H, -C=CH of triazole), 8.14 (2H, NH).

PEEA-3. Yield: 89 %. FTIR (cm^{-1}): 3297 (-NH-, amide, stretching vibr.), 3076 (C=C-H of the 1,2,3-triazole), 1752 (-CO-, ester), 1638 (-CO-, amide), 1543 (NH-, amide, bending vibr.), 1225 (C-O-C, ester), 1127 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 0.99 (12H, CH_2-(CH_2)$_6$-CH_2), 1.84 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.14-3.45 (12H, CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2), 3.93-4.08 (8H, COO-CH_2 and NH-CH_2-, stack), 5.13 (4H, CO-CH_2-N), 7.66 (2H, -C=CH of triazole), 8.07 (2H, NH).

PEE-1. Yield: 93 %. FTIR (cm^{-1}): 3145 (C=C-H of the 1,2,3-triazole), 1744 (-CO-, ester), 1213 (C-O-C, ester), 1164 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 0.87 (12H, CH_2-(CH_2)$_6$-CH_2), 1.90 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.29 (4H, CH_2-O-CH_2), 3.91 (4H, COO-CH_2-CH_2), 4.78 (4H, COO-CH_2-C), 5.10 (4H, CO-CH_2-N), 7.83 (2H, -C=CH of triazole).

PEE-2. Yield: 87 %. FTIR (cm^{-1}): 3141 (C=C-H of the 1,2,3-triazole), 1740 (-CO-, ester), 1213 (C-O-C, ester), 1168 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 0.99 (12H, CH_2-(CH_2)$_6$-CH_2), 2.07 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.30 (8H, CH_2-O-CH_2-CH_2-O-CH_2), 4.02 (4H, COO-CH_2-CH_2), 4.91 (4H, COO-CH_2-C), 5.20 (4H, CO-CH_2-N), 7.93 (2H, -C=CH of triazole).

PEE-3. Yield: 85 %. FTIR (cm^{-1}): 3145 (C=C-H of the 1,2,3-triazole), 1752 (-CO-, ester), 1209 (C-O-C, ester), 1164 (C-O-C, ether). ^{1}H NMR (400 MHz, DMSO-d_6, δ): 0.97 (12H, CH_2-(CH_2)$_6$-CH_2), 2.04 (4H, CO-CH_2-(CH_2)$_6$-CH_2-CO), 3.26 (12H, CH_2-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_2), 4.02 (4H, COO-CH_2-CH_2), 4.88 (4H, COO-CH_2-C), 5.17 (4H, CO-CH_2-N), 7.91 (2H, -C=CH of triazole).

RESULTS AND DISCUSSION

Synthesis of diyne monomers

The detailed procedure of the synthesis of key homo-bifunctional diyne monomers (di-propargyl amide/ester of sebacic acid) was discussed above. The AA-BB-type monomers were synthesized by the interaction of sebacoyl chloride with propargylamine or propargyl alcohol (Figure 1). The yields of the obtained di-propargyl amide of sebacic acid and di-propargyl ester of sebacic acid were 68 and 75 %, respectively. The presumed structure of the diyne monomers was proved by FT-IR and ^{1}H NMR spectroscopies.

Synthesis of bis-bromoacetyl derivatives (precursors of diazide monomers)

The synthesis of bis-bromoacetyl derivatives – precursors of diazide monomers, was described above (see Materials and methods). Three bis-bromoacetates were obtained by the interaction of bromoacetyl bromide with di- (DEG), tri- (TEG), and tetra-ethylene glycol (TTEG) (see Figure 2 above). The yields of the obtained bis-bromoacetyl derivatives were in the range of 69 – 76 %. Their structure was confirmed by FTIR and ^{1}H NMR spectroscopies.

Synthesis of the click PEEAs and PEEs

Six new triazole click polymers (three PEEAs and three PEEs) were synthesized *via* one-pot/two-step synthetic strategy that we had previously [28,34] developed. The detailed procedure of the synthesis of target click polymers was discussed above (see *Experimental Methods and Materials*).

The polymers were obtained with quite high yields (73 – 94 %). The molecular weight characteristics of the new click polymers such as weight-average (M_w), number-average (M_n) molecular weights, and molecular weight distribution ($Đ$) were determined using the GPC system with PMMA standards. Due to the insolubility of the PEEA-1 in DMF, it was not characterized by the GPC technique. According to the obtained data, given in Table 1, the new click polymers possess average molecular weights (M_w is in the range of 14,500 – 34,800 g mol^{-1}) and display moderately wide molecular weight distribution ($Đ$ = 1.47 – 1.60). The degree of polymerization of the polymers is quite satisfactory for step-growth polymers (the DP is in the range of 16 - 42).

TABLE 1. Characteristics of the obtained click PEEAs and PEEs

Polymer	M_w (g mol^{-1})	M_n (g mol^{-1})	$Đ$	DP
PEEA-2	14,500	9,300	1.55	16
PEEA-3	16,600	11,400	1.47	18
PEE-1	34,800	23,100	1.51	42
PEE-2	28,300	17,800	1.60	30
PEE-3	27,100	17,200	1.58	27

$Đ$ - Dispersity (M_w/M_n); DP - degree of polymerization

To assess the film-forming abilities of the new polymers, the thin films were cast from HFIP solutions on polytetrafluoroethylene dishes, the solvent was allowed to evaporate at room temperature, and the generated films were finally dried in a vacuum at room temperature to a constant weight. With the exception of PEEA-1 and PEE-1, which formed brittle films, all the other click polymers revealed good elastic film-forming properties. The poor elasticity of the films produced by DEG-based polymers PEEA-1 and PEE-1 can be attributed to the highest rigidity of their molecular structure stipulated by the shortness of their monomeric units (only two –CH_2-CH_2-O- fragments per monomeric unit).

Spectral studies

The structure of the click PEEAs and PEEs was investigated using FT-IR and NMR spectroscopy. Both methods confirmed the presumed structure of the new click polymers. The FT-IR study proved the presence of all IR-detectable functional moieties of the polymers. All the expected absorption bands were observed: 3297 - 3293 cm^{-1} attributed to the stretching vibration of amide NH, 3145 – 3063 cm^{-1} corresponding to stretching vibration of C=C–H of the 1,2,3-triazole ring, 1752 - 1740 cm^{-1} ascribed to ester C=O, 1638 – 1636 cm^{-1} distinctive for amide CO, 1544 – 1543 cm^{-1} expected for the bending vibration of amide NH, 1225 - 1209 cm^{-1} characteristic of ester C-O-C moiety, and 1168 - 1127 cm^{-1} typical for ether C-O-C. The detailed ^{1}H NMR studies of the PEEAs and PEEs demonstrated precise regioselectivity of Cu(I) catalyzed click SGP: single signals of 1,2,3-triazole protons (C=C–H) at 7.66 – 7.93 ppm in the ^{1}H NMR spectra of the polymers confirmed the presence of exclusively 1,4-disubstituted 1,2,3-triazole rings in the macromolecular chains.

Solubility of the click PEEAs and PEEs

The solubility of the new click PEEAs and PEEs in ten common organic solvents (10.0 mg in 1.0 mL) is presented in Table 2. All the new polymers were insoluble in common solvents such as DCM, ethanol, acetone, acetonitrile, and ethyl acetate even upon heating. Overall, PEEs revealed better solubility as compared to PEEAs. All the PEEs displayed good solubility in polar solvents such as DMSO, NMP, DMF, DMA, and HFIP at room temperature. Expectedly, the best solubility among the PEEAs was demonstrated by TTEG-based PEEA-3 which was readily soluble in DMSO and HFIP at room temperature and in NMP, DMF, and DMA upon heating. The poorest solubility of the PEEA-1, which was soluble only in DMSO, NMP, and HFIP, may be attributed to the increased rigidity of the molecular architecture conditioned by the shortness of the monomeric unit (only two $–CH_2-CH_2-O-$ fragments per monomeric unit). The poor solubility behavior of PEEAs compared to PEEs can presumably be ascribed to the increased rigidness of the macromolecular backbone and stronger intermolecular forces stipulated by the robust amide bonds.

TABLE 2. Solubility of the click PEEAs and PEEs (10 mg of polymer in 1 mL of solvent)

Polymer	DMSO	NMP	DMF	DMA	HFIP	DCM	EtOH	Acetone	CH_3CN	EtAc
PEEA-1	+t	+t	-	-	+	-	-	-	-	-
PEEA-2	+t	+t	+t	+t	+	-	-	-	-	-
PEEA-3	t	+t	+t	+t	+	-	-	-	-	-
PEE-1	+	+	+	+	+	-	-	-	-	-
PEE-2	+	+	+	+	+	-	-	-	-	-
PEE-3	+	+	+	+	+	-	-	-	-	-

+ Soluble at room temperature; +t soluble upon heating; - insoluble

Three new linear AA-BB-type poly(ester ether amide)s (PEEAs) and three poly(ester ether)s (PEEs) containing 1,4-disubstituted 1,2,3-triazole rings in the main chain were successfully synthesized through Cu(I)-catalyzed click step-growth polymerization (SGP) using homo-bifunctional monomers following one-pot/two-step synthetic strategy we have previously elaborated. The presumed structure of the new polymers was confirmed by FT-IR and NMR techniques. The click polymers with average molecular weights (M_w = 14,500 – 34,800 g mol^{-1}) and moderately wide molecular weight distribution (1.47 – 1.60) were obtained in quite good yields (73 – 94 %). The degree of polymerization of the materials was quite satisfactory for step-growth polymers (DP = 16 – 42), allowing most of them to form elastic films. The click polymers reported in this work expand a library of available degradable polymers with functionally interesting 1,2,3-triazole moieties in the backbone. The new polymers obtained can be considered as having a potential for various biomedical applications.

The development of new polymers with tailored properties is crucial for advancing various industrial and biomedical applications. This study explores the synthesis of three novel linear poly(ester ether amide)s (PEEAs) and poly(ester ether)s (PEEs) that incorporate 1,4-disubstituted 1,2,3-triazole rings in their main chains. The synthesis is achieved through Cu(I)-catalyzed click step-growth polymerization (SGP), employing a one-pot/two-step strategy previously outlined by the research team. Here, we discuss the significance of these newly synthesized polymers, their potential for biomedical applications, and the implications for future developments.

Synthesis and Structural Confirmation

The synthesis of these polymers using a click chemistry approach ensures that the desired 1,4-disubstituted 1,2,3-triazole units are efficiently integrated into the polymer backbone. The use of Cu(I)-catalyzed click polymerization provides several advantages, including high selectivity, mild reaction conditions, and the ability to precisely control the polymer's structure. The resulting polymers were confirmed via FT-IR and NMR techniques, which validate their structure and the incorporation of the triazole ring.

The synthesis of PEEAs and PEEs with molecular weights ranging from 14,500 to 34,800 g/mol and moderately wide molecular weight distributions (1.47 – 1.60) highlights the feasibility of producing high-quality, functional materials. The degree of polymerization (DP) of the materials, ranging from 16 to 42, indicates that these polymers are well-suited for step-growth polymerization, a key feature for developing materials with predictable and reproducible properties.

Properties and Characterization

The new polymers demonstrated desirable properties such as good yield (73 – 94 %) and the ability to form elastic films. This suggests that the incorporation of 1,4-disubstituted 1,2,3-triazole units enhances the mechanical flexibility of the polymers, making them suitable for applications where elasticity and toughness are required. The molecular weight distribution and the degree of polymerization indicate that these materials have a good balance of processability and performance, essential for practical uses in biomedical devices.

Biomedical Application Potential

The incorporation of 1,2,3-triazole rings in the polymer backbone provides significant functional diversity, which is a promising feature for biomedical applications. Triazole units are known for their biocompatibility, stability, and ability to engage in various chemical interactions, making them ideal candidates for use in drug delivery systems, tissue engineering, and other medical devices. These polymers' degradability, an essential feature for many biomedical applications, further enhances their potential for use in medical implants and controlled-release systems.

Given their tunable properties and functional groups, these polymers could be developed for specific applications in drug delivery, where the degradation rate can be tailored to match the therapeutic needs. Additionally, the flexibility of these polymers could be leveraged in applications such as tissue scaffolds, where mechanical properties and biocompatibility are crucial for supporting tissue regeneration.

Future Development and Challenges

While the synthesis and properties of these polymers are promising, further optimization is required to fully realize their potential in biomedical applications. Future work could focus on improving the control over polymer architecture, which may further enhance the properties of the materials. Additionally, a more in-depth study of the degradation kinetics and in vivo biocompatibility of these polymers is necessary to assess their performance in biological environments.

Challenges remain in scaling up the synthesis for industrial applications while maintaining the material's performance and reproducibility. Moreover, the interaction of these new polymers with biological systems, such as immune responses, cytotoxicity, and long-term degradation behavior, will need to be carefully evaluated.

Expanding the scope and functionality of degradable triazole “click” polymers holds immense promise for driving biomedical innovation. By addressing current challenges and leveraging emerging opportunities, researchers can unlock the full potential of these materials. Future advancements will depend on interdisciplinary collaboration, integration with cutting-edge technologies, and a commitment to sustainability and safety. The continued evolution of triazole polymers will undoubtedly pave the way for transformative breakthroughs in healthcare and beyond

The use of degradable triazole "click" polymers in biomedical applications has gained significant attention due to their unique properties, such as biocompatibility, degradability, and tunability. The expansion of this polymer library promises to offer new opportunities for a variety of biomedical innovations, but also presents a number of challenges. In this discussion, we will explore the recent advances, challenges, opportunities, future development strategies, and emerging practical implementation approaches related to these polymers.

Advances in Degradable Triazole "Click" Polymers

Recent studies have significantly expanded the library of triazole-based polymers, enabling better control over their physical, chemical, and biological properties. The introduction of degradable "click" chemistry has allowed for more precise and efficient polymer synthesis, leading to the development of materials with specific degradation profiles, ideal for targeted

drug delivery, tissue engineering, and implantable devices. These polymers can be engineered to degrade under physiological conditions, minimizing the long-term environmental and toxicological risks associated with traditional synthetic polymers.

Challenges in Expanding the Scope and Functionality

Despite these advances, there are several challenges in expanding the scope and functionality of these polymers. The complexity of developing polymers with both controlled degradation rates and appropriate biological activity requires deeper understanding and innovative techniques. Issues such as reproducibility in polymer synthesis, scalability for mass production, and the optimization of degradation rates to match tissue healing or drug release requirements remain significant hurdles. Furthermore, understanding the interactions between these polymers and the biological systems they are intended to interact with—such as immune response, tissue compatibility, and potential cytotoxicity—is crucial for ensuring their safe use in clinical settings.

Opportunities for Biomedical Innovation

The expanding library of degradable triazole "click" polymers presents numerous opportunities for biomedical applications. These polymers could revolutionize fields like personalized medicine, wound healing, and regenerative medicine by enabling the development of highly tailored biomaterials. Their potential use in controlled drug release systems, particularly in targeted therapies for cancer, diabetes, and cardiovascular diseases, offers promising pathways to improve patient outcomes and reduce side effects. Additionally, the use of these polymers in 3D-bioprinted tissue scaffolds could pave the way for creating more efficient and biologically relevant tissue structures for implantation.

Future Development Strategies

Moving forward, the development of novel synthetic strategies that allow for greater control over the polymer’s structure and properties will be critical. Incorporating bioactive molecules into the polymer matrix to enhance cellular interactions and tissue regeneration will also be a key area of focus. Further integration of these polymers with cutting-edge technologies, such as CRISPR-based gene editing and advanced biomaterials, could lead to highly effective combination therapies that address complex medical challenges. Additionally, the improvement of degradation pathways to match specific clinical needs, alongside the use of more sustainable raw materials, will likely play an important role in the future direction of this field.

Emerging Practical Implementation Approaches

The practical implementation of degradable triazole "click" polymers in real-world biomedical applications will require collaboration across multiple disciplines, including materials science, molecular biology, and clinical medicine. Pilot clinical trials and collaborations between academia and industry will be key to moving from theoretical advancements to functional, market-ready products. Innovations such as injectable hydrogels, which can rapidly form in situ and degrade as needed, as well as smart polymers that respond to environmental stimuli, could drive the next wave of biomedical devices and therapeutics. Regulatory challenges and the need for standardized testing protocols will also play a significant role in accelerating the adoption of these materials.

The field of degradable triazole "click" polymers is poised for significant advancements in biomedical innovation. As the library of these polymers expands, it is important to balance the opportunities they offer with the challenges they present. By focusing on controlled synthesis, enhanced biological interactions, and scalable production, researchers and clinicians can harness the full potential of these materials. With continued development and collaboration, these polymers could become a cornerstone of next-generation biomedical therapies, leading to improved patient outcomes and more sustainable healthcare solutions.

CONCLUSION

The field of degradable triazole "click" polymers is poised for significant advancements in biomedical innovation. As the library of these polymers expands, it is important to balance the opportunities they offer with the challenges they present. By focusing on controlled synthesis, enhanced biological interactions, and scalable production, researchers and clinicians can harness the full potential of these materials. With continued development and collaboration, these polymers could become a cornerstone of next-generation biomedical therapies, leading to improved patient outcomes and more sustainable healthcare solutions. The study successfully demonstrates the synthesis of new poly(ester ether amide)s (PEEAs) and poly(ester ether)s (PEEs) incorporating 1,4-disubstituted 1,2,3-triazole rings in their backbone. The materials exhibit promising properties that make them potential candidates for a variety of biomedical applications, particularly in controlled drug delivery and tissue engineering. However, further research is needed to fully explore their clinical potential, optimize their properties, and address challenges related to their large-scale production and biological interactions.

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INVESTIGATING THE DEEP ENVIRONMENTAL IMPACT OF MEDICATION WASTE, THEIR EFFECTS ON NATURAL SYSTEMS: PUBLIC HEALTH THREATS, INTRICATE RELATIONSHIPS, RISK ANALYSIS, HOLISTIC SOLUTIONS, AND THE NEED FOR ADVANCED HAZARD ASSESSMENT

ABSTRACT

The pervasive presence of pharmaceutical residues in the environment has emerged as a critical issue, with far-reaching consequences for ecosystems and human health. This study delves into the extensive contamination caused by these residues, examining their detrimental effects on ecological balance and biodiversity. It highlights the complex interactions between pharmaceutical compounds and environmental matrices, which exacerbate their persistence and toxicity. The research underscores the significant health risks posed to both wildlife and human populations, particularly through bioaccumulation and the disruption of endocrine systems. Furthermore, the study evaluates current methodologies for assessing environmental and health risks, emphasizing their limitations and the need for more robust evaluation frameworks. To address these challenges, comprehensive mitigation strategies are proposed, ranging from improved wastewater treatment technologies to policy interventions aimed at reducing pharmaceutical waste at its source. The findings stress the urgent necessity for enhanced risk evaluation protocols and global cooperation to mitigate the environmental and public health impacts of pharmaceutical contamination. Pharmaceutical contaminants have become a critical environmental concern, infiltrating water bodies, soil, and air, leading to widespread

ecological disruptions and public health risks. These persistent pollutants interfere with aquatic and terrestrial ecosystems, affecting biodiversity, altering microbial communities, and contributing to antimicrobial resistance. Their complex interactions with environmental systems make risk assessment challenging, necessitating a deeper understanding of their long-term consequences. This study explores the intricate pathways through which pharmaceutical residues impact ecosystems and human health, emphasizing the need for comprehensive mitigation strategies. Advanced wastewater treatment technologies, stricter regulatory policies, and sustainable pharmaceutical disposal practices are essential to minimize contamination. Moreover, enhancing risk evaluation frameworks with improved analytical methods and predictive models is crucial for safeguarding environmental and public health. The widespread presence of pharmaceutical contaminants in the environment has raised significant concerns due to their persistent nature and far-reaching ecological and health implications. These pollutants, originating from pharmaceutical production, improper disposal, and wastewater discharge, infiltrate aquatic and terrestrial ecosystems, disrupting biodiversity, altering biochemical cycles, and fostering antimicrobial resistance. Their accumulation in water bodies threatens aquatic organisms, bioaccumulates in the food chain, and poses risks to human health through prolonged exposure. The intricate interactions between pharmaceutical residues and environmental systems complicate risk assessment, making it essential to develop more advanced analytical techniques and predictive models. This study delves into the extensive impact of pharmaceutical contamination, analyzing the mechanisms through which these compounds affect ecosystems and public health. It highlights the urgent need for holistic mitigation strategies, including the enhancement of wastewater treatment technologies, the development of green pharmaceuticals, stricter regulatory frameworks, and public awareness campaigns. Furthermore, a refined risk evaluation approach integrating multidisciplinary research, innovative monitoring tools, and comprehensive toxicity assessments is imperative for mitigating contamination risks effectively. Addressing this escalating issue requires a collaborative global effort to ensure environmental sustainability and protect human and ecological well-being.

Keywords: Drug, pharmaceuticals, medicine, ecology, environment, human health.

Introduction

Aim of the research was to study the profound environmental contamination by pharmaceutical residues, their action on ecosystems: risks, complex interactions, assessing risks, comprehensive mitigation strategies and the imperative for enhanced risk evaluation. Pharmaceutical residues in the environment have become a growing concern due to their potential impact on ecosystems and human health. These contaminants, often originating from human and veterinary medicine, are found in water, soil, and air, and pose significant risks through their complex interactions with other environmental pollutants. Despite their widespread presence, current environmental risk assessments typically focus on individual substances, potentially underestimating the broader ecological implications. This study explores the profound environmental contamination caused by pharmaceutical residues, emphasizing their effects on aquatic and terrestrial ecosystems. It also discusses the risks associated with the accumulation of these substances, their interactions with other pollutants, and the potential for synergy or additive effects. Furthermore, it highlights the urgent need for more robust and comprehensive risk assessments, including the consideration of transformation products, indirect effects, and the long-term consequences of pharmaceutical exposure.

The paper advocates for the development of improved mitigation strategies, such as enhanced waste treatment technologies, better pharmaceutical disposal systems, and more effective regulatory frameworks. Ultimately, this research calls for a multidisciplinary approach to address the environmental challenges posed by pharmaceutical contamination, aiming to safeguard both ecological and human health in the face of growing global concerns. Pharmaceutical contamination of the environment is an increasingly significant concern that demands urgent attention. The presence of pharmaceutical residues in natural systems, primarily from human and veterinary drug use, leads to contamination of water, soil, and air, where their persistence can disrupt ecological balance and potentially harm human health. Current environmental assessments often fail to consider the complex interactions between pharmaceutical residues and other pollutants, leaving many potential risks overlooked. A key issue is the difficulty in predicting the cumulative effects of these contaminants, especially when pharmaceuticals are mixed with other toxic substances in the environment. The impacts are not limited to direct toxicity but may include indirect effects, such as changes to microbial communities and disruptions in ecological processes, like nutrient cycling. Moreover, the transformation products of pharmaceuticals, which may be more persistent or toxic than the original compounds, remain poorly understood and under-researched. Given these challenges, the existing risk assessment frameworks, which often focus on single-substance exposures, are insufficient. A more holistic approach is necessary to account for the interactions, transformations, and cumulative risks posed by pharmaceutical residues.

Effective mitigation strategies will require a combination of improved waste management practices, targeted regulatory policies, and advanced treatment technologies. Understanding the full scope of pharmaceutical contamination and its ecological and human health implications is essential for developing proactive, sustainable solutions. The uncontrolled release drugs into the environment may be wastewater and atmospheric emissions from enterprises producing finished drugs and pharmaceutical substances. the environmental safety of such production is usually regulated by law. However, accidental releases of drugs into the environment or those that violate existing norms and regulations that occur in industry, are nevertheless not systematic. Moreover, there is a general trend towards a

reduction in the environmental load on the part of pharmaceutical production, primarily in developed countries of the world, due to a consistent increase in the technological effectiveness and organization of the production process, the introduction of increasing quality standards and environmental safety, and control by authorized government bodies . It is also necessary to take into account that pharmaceutical production is localized geographically, and if an accident occurs at the enterprise or there are violations of environmental legislation, then such emissions are exclusively local in nature and pose a danger only to specific regions. For all the reasons listed above, such sources are not the subject of analysis in this review, although they contribute to environmental pollution. Other sources of drugs that are practically uncontrollable and are formed mainly by people who use drugs for medical purposes, as well as in animals, pose a great danger to the environment.

The contamination of the environment by pharmaceutical residues presents a critical challenge to both ecosystem health and human well-being. The widespread presence of these substances in water, soil, and air underscores the need for a more comprehensive understanding of their environmental fate and effects. Current risk assessment approaches, which often examine individual compounds in isolation, are inadequate in addressing the complex interactions and cumulative risks posed by pharmaceutical pollutants, especially when combined with other environmental contaminants. Furthermore, the potential dangers of pharmaceutical transformation products, which may exhibit greater toxicity or persistence, remain underexplored. To address these concerns, a paradigm shift is required in environmental risk assessment, incorporating multi-substance interactions, long-term ecological impacts, and the effects of transformation products. The development of robust mitigation strategies—such as advanced waste treatment technologies, improved pharmaceutical disposal practices, and more stringent regulatory frameworks—must be prioritized. By adopting a more integrated, precautionary approach to pharmaceutical contamination, we can better protect ecosystems and human health from the growing threat posed by these persistent pollutants. Future research and policy initiatives should focus on improving our understanding of these substances, developing innovative solutions to reduce their environmental impact, and ensuring sustainable management practices for pharmaceuticals.

The presence of pharmaceutical residues in the environment has emerged as a significant global concern, as these substances increasingly contaminate water, soil, and air systems. The widespread use of pharmaceuticals in human and veterinary medicine, along with improper disposal practices, has led to the accumulation of pharmaceutical compounds in various environmental compartments. These residues, often detected in trace amounts, are not only persistent but can also have profound ecological and human health implications. The environmental impact of pharmaceuticals extends beyond direct toxicity, as they can disrupt ecosystems, alter microbial communities, and interfere with natural processes such as nutrient cycling and waste decomposition [1-2].

Current environmental risk assessments often focus on single substances, neglecting the combined effects of pharmaceuticals in the environment. This approach may overlook the potential for greater toxicity when multiple substances interact or the unanticipated consequences of transformation products, which can be more persistent or toxic than their parent compounds. For example, the breakdown products of some pharmaceuticals may persist in the environment for extended periods, increasing the long-term ecological risks. Moreover, the potential for these transformation products to migrate through the food chain and impact human health remains largely unexamined [13-15].

The lack of comprehensive understanding of pharmaceutical pollution in the environment is further compounded by inadequate data on the long-term effects of low-level, chronic exposure to these compounds. Despite significant advances in detecting pharmaceutical residues in environmental matrices, only a small fraction of the thousands of active pharmaceutical ingredients used globally have been adequately studied. This gap in knowledge makes it difficult to assess the full scope of the risks posed by pharmaceutical contamination [16-18].

To address this growing environmental challenge, there is an urgent need for an integrated, precautionary approach to risk assessment that considers the complex interactions between pharmaceuticals and other pollutants. A more nuanced understanding of how pharmaceuticals degrade in the environment, how they interact with other chemicals, and how these compounds affect ecological functions and biodiversity is essential. This requires an expansion of ecotoxicity testing to incorporate a broader range of subtle biological effects, such as behavioral changes, physiological disruptions, and alterations in biochemical processes. Advanced technologies, including genomics, proteomics, and high-throughput screening, could play a pivotal role in improving the assessment of pharmaceutical pollutants.

Moreover, effective mitigation strategies must be developed to reduce pharmaceutical releases into the environment. These strategies could include improved waste management practices, such as source control, better disposal systems for unused pharmaceuticals, and more advanced wastewater treatment technologies. Additionally, regulatory frameworks must be strengthened to ensure that pharmaceutical contaminants are adequately managed and that new drugs are evaluated for their environmental risks before they are widely used. Such efforts would require collaboration among scientists, policymakers, and the pharmaceutical industry to develop sustainable solutions that minimize the environmental impact of pharmaceutical residues [19-21].

This paper aims to delve deeper into the environmental contamination caused by pharmaceutical residues, exploring their ecological impacts, the complexity of their interactions with other pollutants, and the urgent need for more comprehensive and integrated risk assessments. Furthermore, it will highlight the critical role of advanced mitigation strategies, innovative treatment technologies, and regulatory measures in addressing the growing environmental threat posed by pharmaceuticals. By fostering a greater understanding of pharmaceutical pollution, we can better protect ecosystems, safeguard human health, and mitigate the long-term risks associated with pharmaceutical contamination in the environment [22-24].

While some studies have identified individual pharmaceuticals in the environment, the complexity of interactions between multiple contaminants—such as pharmaceuticals, pesticides, and industrial chemicals—remains insufficiently understood. Current risk assessment frameworks primarily focus on single-substance exposure, which may fail to account for the cumulative or synergistic effects that arise when pharmaceuticals interact with other environmental pollutants. Additionally, the potential risks associated with transformation products, which may be more persistent or toxic than the parent compounds, have been largely overlooked [3-5].

Given these concerns, there is a pressing need for a more integrated approach to the study and management of pharmaceutical residues in the environment. This includes the development of more robust risk assessment models that consider multiple substances, the

environmental behavior of transformation products, and their potential long-term ecological impacts. Furthermore, effective mitigation strategies, including improved waste management, disposal practices, and regulatory measures, are essential to address the growing issue of pharmaceutical contamination. This paper aims to explore the environmental contamination caused by pharmaceutical residues, assess their risks and interactions, and highlight the need for improved frameworks to better understand and mitigate their impact on both ecosystems and human health [6-8].

The environmental contamination caused by pharmaceutical residues is an increasingly complex and critical issue that threatens the health of ecosystems and poses risks to human well-being. The widespread use of pharmaceuticals in both human and veterinary medicine, combined with inadequate disposal practices, has led to the persistence of these substances in various environmental media, including water, soil, and air. While pharmaceuticals are essential for human health, their unintended release into the environment raises concerns due to their potential ecological impacts. These compounds, often present in trace amounts, can accumulate over time and exhibit a range of adverse effects on aquatic and terrestrial organisms, including the disruption of microbial communities, alterations in biodiversity, and interference with critical ecosystem processes such as nutrient cycling and soil fertility [9-10].

Pharmaceutical residues in the environment are particularly concerning because they can have multiple modes of action, which can interfere with the natural functioning of ecosystems. Some pharmaceutical compounds, such as antibacterial, have been shown to affect soil microbes that play an essential role in processes like pesticide degradation and manure decomposition. The potential for synergistic or additive effects among pharmaceuticals and other environmental pollutants, such as pesticides, biocides, and industrial chemicals, adds further complexity to the issue. While individual pharmaceuticals have been studied in isolation, little is known about how they interact with other chemicals in the environment, which may lead to underestimated risks [11-12].

Goal

Aim of the research was to study and analyzed the deep environmental impact of medication waste, their effects on natural systems: public health threats, intricate relationships, risk analysis, holistic solutions, and the need for advanced hazard assessment.

Methodology

The material of the article was the data from scientific publications, which were processed, analyzed, overviewed and reviewed by generalization and systematization. Research studies are based on a review/overview assessment of the development of critical visibility and overlook of the modern scientific literature. Use the following databases: (for extensive literature searches to identify the the deep environmental impact of medication waste, their effects on natural systems: public health threats, intricate relationships, risk analysis, holistic solutions, and the need for advanced hazard assessment.). PubMed, Medline, Web of Science, Scopus, Web of Knowledge, Clinical Key, Tomson Reuters, Google Scholar, Cochrane library, and Elsevier foundations, national and international policies and guidelines were also reviewed and as well as grey literature.

Results and Discussion

Medicines play an important role in the treatment and prevention of diseases in humans and animals. But it is due to the very nature of drugs that they can also have unintended effects on animals and micro-organisms present in the environment. Although side effects on human and animal health are typically studied in extensive safety and toxicology studies, the potential environmental impacts of drug manufacturing and use are less well understood and have only become recently a topic of research interest. Some of the effects of various compounds, including veterinary anthelmintics and antibacterial therapeutics, are already known, but there are many other substances that can affect organisms in the environment. The situation is further complicated by the fact that some pharmaceuticals can have effects on bacteria and animals well below the concentrations usually used in safety and effectiveness testing. Additionally, degradation products and the combination of different biologically active compounds can have unexpected effects on the environment. Although it is reasonable to assume that these substances do not significantly harm humans, we have only recently begun to investigate whether and how they affect a wide range of organisms in the environment and what this means for health environmental [39-42].

The scale of this potential problem should not be underestimated. More than several million women use oral contraceptives, which eventually end up in the environment. A wide range of human drugs are produced and used, including antibiotics, statins, and cytotoxins used to treat cancer, some of which are produced in quantities of several thousand tons per year. Information on the quantities of drugs used by humans is difficult to obtain, but recent data from Canada indicate that the most commonly used drugs include acetaminophen, aspirin, ibuprofen, naproxen, and carbamazepine. Large quantities of veterinary drugs, such as antibacterials, antifungals, and parasiticides, produced in aquaculture and agriculture can also contribute to environmental stress, especially because they are often found directly in soil and surface water, unlike human drugs, which typically pass through wastewater treatment plants first [43-45].

Human and veterinary drugs enter the environment through a variety of pathways. Residues generated during manufacturing may eventually end up in surface waters. After administration, human medications are absorbed, metabolized, and then discharged to sewers. They typically pass through wastewater treatment plants before ending up in water or on land through the application of sewage sludge. Antibacterial agents used to treat fish or shrimp in aquaculture end up directly in surface waters. Veterinary drugs used to treat grazing animals end up in soil or surface waters. When intensively treated livestock are treated, these drugs may end up indirectly in the environment through the application of slurry and manure as fertilizer. Other minor pathways include air emissions and disposal of unused medications and containers [46-47].

Pharmaceuticals have been entering the environment for decades, and researchers have only recently begun to quantify their levels in the environment. Using information from different countries and uses, several prioritization exercises have identified pharmaceutical products that are most likely to end up in the environment. Annual veterinary drug use was combined with information on routes of administration, metabolism and ecotoxicity to identify drugs that should be monitored under a national recognition programme. New analytical techniques such as liquid chromatography coupled with tandem mass spectrometry (LC-MS-MS) have provided a better understanding of the behaviour of drugs in the environment and

have determined their concentrations in wastewater treatment plants, soil, surface water [48-49].

Once released into the environment, pharmaceuticals will be transported and distributed by air, water, soil or sediment. Their distribution will be influenced by a number of factors, such as the physicochemical properties of the compound and the characteristics of the receiving environment. The extent to which a pharmaceutical product is transported between different environmental media depends primarily on the sorption behavior of the substance in soils, sludge and wastewater systems, and wastewater treatment plants, which varies considerably between products. pharmaceuticals. Additionally, unlike other organic substances such as pesticides and industrial chemicals, the sorption behavior of many pharmaceuticals cannot be simply inferred from the hydrophobicity of the substance or the organic carbon content of the material. solid. Pharmaceutical substances can also be degraded by biological organisms in processing systems, water bodies and soils, as well as by abiotic reactions. Typically, these processes reduce the effectiveness of medications; however, some degradation products have the same toxicity as their original compounds. Additionally, degradation varies considerably depending on chemistry, biology and climatic conditions. For example, the half-life of the antiparasitic ivermectin is six times longer in winter than in summer, and the compound breaks down more quickly in sandy soils than in sandy loam soils. The natural estrogens 17β-estradiol and estrone are degraded in both aerobic and anoxic reservoirs of activated sludge systems, while 17α-ethinylestradiol is only degraded under aerobic conditions. All of this adds to the complexity of the problem and requires customized solutions for individual pharmaceuticals and applications[50-51].

In some studies have found low levels of a wide range of pharmaceuticals, including hormones, steroids, antibiotics and parasiticides, in soils, surface waters and waters. underground. Reported concentrations are generally low, but what is even more alarming is that many therapeutic substances have been found under a wide range of hydrological, climatic and land use conditions, and many substances have been detected throughout of the year. The study results raised questions about how this mixture of veterinary and medicinal drugs, abundant in soil and surface waters, affects beneficial organisms in the environment and human health [52-54].

Comparison of these data with information on therapeutic doses, drinking water restrictions, and health advisories shows that concentrations of therapeutic compounds in surface waters are well below levels of concern to human health. Therefore, indirect exposure to pharmaceuticals through the water supply is unlikely to pose a risk to humans. However, risks from other exposure routes, such as ingestion of crops through soil and biomagnification through the food chain, have not yet been quantified and cannot be completely excluded. Environmental health effects are more difficult to assess. Human and veterinary drugs are required by law to undergo an environmental risk assessment for their effects on aquatic and terrestrial organisms before a product can be marketed, and the EU has introduced similar requirements. These environmental impact studies examine the potential adverse effects of manure on fish, daphnia, algae, bacteria, earthworms, plants, and invertebrates. Most of the data are publicly available (many environmental assessments are posted on the FDA website) and provide a reasonable data set for further study. However, legitimate questions arise about the real value of these studies. Risk assessments typically use standard ecotoxicity tests, which are often short-term and focus primarily on mortality as an endpoint. In addition, aquatic tests typically focus on the aquatic environment and do not take into account pharmaceuticals present in sediment. In general, the effects observed

in these studies occur at concentrations significantly higher than those measured in the environment. Less well known are the more subtle effects that therapeutically active substances may have on organisms in the environment, such as growth, fertility, or behavior. Pharmaceutical compounds are designed to be either highly active and receptor-reactive in humans and animals, or toxic to many infectious organisms, including bacteria, fungi, and parasites. However, this does not mean that they affect only these life forms. Many lower animals have receptor systems similar to those of humans and animals used in agriculture. In addition, numerous groups of organisms that affect human and animal health, and to which pharmaceutical products are directed, play a critical role in the functioning of ecosystems. It is therefore possible that pharmaceuticals have subtle effects on aquatic and terrestrial organisms that are not detected in standard tests. And because human drugs are released almost continuously into the environment, wild organisms are exposed for much longer periods than those used in standard tests. Researchers have therefore begun to study some of the more subtle effects caused by long-term, low-dose exposure to pharmaceuticals. A wide range of subtle effects have been reported, including effects on oocyte and testis maturation, effects on insect physiology and behavior, effects on faecal decomposition, inhibition of growth or stimulation of aquatic plant and algal species, and the development of antibacterial resistance in soil. There is strong suspicion that steroids in contraceptives affect the fertility and development of fish, reptiles, and aquatic invertebrates. Similarly, human and veterinary antibiotics have effects on soil microbes and algae [55-57].

Macrocyclic lactones can affect invertebrate larvae in faeces at relatively low concentrations; earthworms appear sensitive to parasiticides used in veterinary medicine, and plants may be sensitive to many antibiotics. In addition, macrocyclic lactones have been shown to cause numerous sublethal responses in dung-feeding invertebrates, such as reduced feeding, water imbalance, decreased growth rate, inhibition of pupation, and impaired mating. Since livestock faeces contain a diverse fauna and provide a fruitful habitat for other species, macrocyclic lactones may therefore indirectly affect other species by depleting the quality and quantity of their food source. Sediment-related effects of pharmaceutical products have also been considered. Carbamazepine affects the emergence of chironomid midges [58-60].

Additionally, pharmaceuticals are not the only pollutants of environmental systems. Aquatic and terrestrial organisms are exposed to a mixture of drugs and other substances, including pesticides, biocides and common industrial chemicals. A recent study discovered the antibacterial agent lincomycin in combination with other additional chemicals. The study focused only on selected compounds, so many other synthetic substances could be present. Therefore, interactive effects are possible, such as the additivity of substances with similar modes of action and synergy. Because current environmental risk assessments focus on individual substances, it is possible that these assessments underestimate exposure. It is also possible that the environmental behavior of a substance changes in the presence of other substances. For example, antibacterials have been shown to affect soil microbes that play an important role in the breakdown of pesticides. For example, research shows that veterinary antibacterial medications can influence the reduction of sulfates in soil and inhibit the decomposition of manure. If an antibacterial veterinary drug was applied as a slurry to an agricultural field prior to pesticide application, it is possible that the environmental impact of the pesticide would be dramatically altered [61-63].

Because very little is known about the effects of pharmaceuticals on environmental health and the interactions of various compounds, some workers are taking a precautionary approach and developing methods to reduce releases of these substances into the

environment . Various approaches have been proposed, including source control of pharmaceuticals, source separation, waste treatment to remove pharmaceutical compounds, implementation of breeding practices, and improvement of drug disposal systems. expired medicines and waste containers. Source control includes marking, controlled disposal and separation of urine. Separating sources of pharmaceuticals, such as hospital wastewater, which are likely to be heavily contaminated with pharmaceuticals and antibiotic-resistant bacteria, should allow treatment resources to be focused on the most contaminated waters [64-66].

Pharmaceuticals may be removed by treatment with physical processes such as sorption or volatilization, biodegradation, or chemical reactions such as ozone treatment. The significance of the different options is likely to be very specific to each substance. For example, the antibiotic ciprofloxacin is removed by strong sorption to suspended solids in sewage sludge, whereas diclofenac and 17α-ethinyl estradiol undergo significant biodegradation in aged activated sludge. A range of measures to reduce emissions is therefore likely to be required. Many treatment methods that eliminate pharmaceuticals may also produce transformation products that are more persistent and more mobile than the parent compounds, some of which may also have similar or increased toxicity. Little work has been done to assess the environmental impacts of these transformation products. Clearly, a wealth of data on the levels of pharmaceuticals in the environment and their effects on aquatic and terrestrial organisms has become available in recent years. However, many issues remain to be resolved before it can be determined whether residues in the environment pose a threat to human health and the environment. First, there are risks associated with substances that have not yet been studied. Due to resource limitations, only a small proportion of pharmaceuticals in use today have been studied, and there is an urgent need to understand how other substances affect the environment. Second, we can better assess ecotoxicity. Current standard ecotoxicity tests are likely inadequate to assess the effects of many pharmaceuticals. The use of more subtle parameters such as behavioral changes, physiology, and biochemistry is of particular interest. Further work is needed to identify these subtle effects. It is likely that many of the technologies currently used by molecular biologists, such as proteomics and genomics techniques or large-scale DNA or protein microarrays, can make a significant contribution to this task. Third, ecotoxicity data are relevant to the real world. Although many subtle effects have been demonstrated following exposure to pharmaceuticals at environmentally realistic concentrations, we need to establish the significance of these data in terms of ecological functioning. Fourth, there are risks associated with mixtures. Pharmaceuticals are unlikely to occur alone in the environment, so the current single-substance risk assessment approach may underestimate environmental impacts. This also includes potential indirect effects. Little has been done to determine the absorption of pharmaceuticals into organisms and throughout the food chain. Such studies are critical to determining the potential indirect impacts of environmental exposure on the ecology and human health. A related question is: should we be concerned about transformation products? Much of the work to date has focused on the parent compounds; however, we know that transformation products are produced in the environment and during processing. It is important that we begin to understand the potential impacts of these substances. Future work should therefore focus on understanding the biotic and abiotic processes underlying the release, fate, and environmental impacts of pharmaceuticals. Finally, certain environmental exposures lead to greater resistance to antibacterial drugs. A wide range of antibacterial agents have been found in water and soil, many of which persist for some time. It is possible that such exposures could lead to the development of resistant microbes that could pose a serious threat to human and animal health [67-70].

The future work should focus on understanding the biotic and abiotic processes underlying the release, environmental fate, and effects of pharmaceuticals. Such an understanding should ultimately enable the development of new modeling approaches. A comparative plasma concentration model linking mammalian and fish species, which could provide useful information on the likely effects of pharmaceuticals on fish. Other modeling approaches, such as quantitative structure-activity relationships, could help estimate the environmental impacts of pharmaceutical products based on their chemical structure. Read-across approaches, in which data from closely related compounds are used to determine the effects of an untested compound, can also help improve environmental assessment. Improved tools should provide a better understanding of the environmental impacts of pharmaceutical products. At the same time, we must strive to improve the way we use, handle and process medicines to minimize their release into the environmen [71-72]t.

The contamination of various components of the environment (water, soil and air) by pharmaceutical residues poses an environmental problem. Human consumption of medicines ranges from 50 to 150 g per person per year in the EU. Veterinary drugs are used in smaller quantities, but pets are a growing segment of the veterinary drug market. In most EU Member States, around 50% of unused human medicines (3-8% of total sales) are not collected [73-74].

The problem is that we do not have a comprehensive understanding of what happens when these drugs are released into the environment, and further characterization of possible pathways of human exposure is needed. Residues of different types of drugs (hormones, anti-cancer drugs, antidepressants, antibiotics, etc.) have been found in various environmental elements, raising the question of whether this poses a risk to exposed plants, animals and microbes or to the man [75-76].

This study characterizes the extent of the environmental impact of pharmaceutical products outside of personal care products. The aim was to identify non-legislative and legislative reasons for their presence in the environment and to suggest ways to adapt legislation to address this problem. 30 to 90% of an orally administered dose of the drug is generally excreted as active substance in the urine of animals and humans. A large proportion of medicines are flushed down sinks and toilets and end up in the environment. Inappropriate and excessive consumption can also lead to unnecessary emissions [77-78].

In the EU, the contribution of manufacturing facilities to emissions of medicines and/or their residues is generally considered negligible.

Once in the environment, drugs are transformed and transferred between its different parts (surface and groundwater, soil, air). Highly fat-soluble drugs also have the ability to accumulate in the fatty tissues of animals and can thus be introduced into the food chain. These products can be broken down either through digestion and metabolism by organisms or through physicochemical processes in soil and water. Some degradation products may persist even after wastewater treatment and cause concern [79-81].

For a number of pharmaceutical products, the environmental risks can be quite minor because they do not remain in the environment for long and are low in toxicity. However, it is increasingly clear that certain drugs, notably antiparasitics, antifungals, antibiotics and (xeno)estrogens, which can have ecotoxicological effects, in some cases present environmental risks. For example, the vulture population in the Indian subcontinent has declined due to poisoning with diclofenac, a painkiller found in the carcasses the vultures

fed on. For humans, the possible consequences are less obvious than for the environment. Residue levels in drinking water or food are very low and are not considered to pose a risk to humans, but long-term exposure to low levels may occur through these routes [82-83].

There are currently no legal restrictions on human medicines potentially present in products of animal origin, this route of exposure being considered minor, even if it is currently not well characterized. For example, in Europe, only very low concentrations of veterinary antibiotics are found in dairy products [84-85].

Until 2005, the registration process for medicines did not include an environmental risk assessment (ERA), and therefore much relevant information was missing. Even for new products, the ERA was often incomplete. A number of regulatory frameworks for chemicals marketed and used in Europe now include an assessment of the potential for persistence, bioaccumulation and toxicity (PBT), but there is no specific guidance for veterinary and human medicinal products [86-87].

There are currently no European regulations covering the assessment of risks associated with contaminated soils and product residues transferred to animals, including fish, or present in wastewater sludge from wastewater treatment plants.

Key legislative steps to address these limitations include, among others, strengthening environmental risk assessments, which could also target “old” pharmaceuticals. The Water Framework Directive could explicitly take into account the results of the ERA for active pharmaceutical ingredients. Relevant legislative instruments could also establish a special label for the “green” pharmacy. The main non-legislative solutions focus on consumption and waste management through a better understanding of the ecotoxicity of medicines and encouraging the recruitment of ecotoxicology-trained staff to regulatory agencies. At the same time, training sections for doctors could be organized, a better match between consumer needs and packaging sizes could be considered, while increasing the role of pharmacists in collecting unused medicines and organizing public information campaigns. The main improvements in waste management could focus on more efficient collection systems for unused human and veterinary medicines and on monitoring their effectiveness [88-91].

Impact of climate change on the use of medicinal pharmaceuticals in the Northern Hemisphere. As climate change alters environmental conditions, the prevalence and global distribution of human diseases will change. Climate-related environmental changes are associated with an increase in chronic diseases already common in the Northern Hemisphere, such as cardiovascular disease and mental illness. The increase in these diseases is leading to an increase in the use of already widely used Western drugs. People with respiratory diseases may experience a worsening of symptoms due to changing environmental conditions, such as increased pollen counts, leading to an increase in the demand for drugs used to control these symptoms. Toxic substances and respiratory, waterborne, and foodborne infections, including vector-borne infections, may become more common in Western countries, Central and East Asia, and across North America. As new disease threats emerge, a significant increase in the use of pharmaceuticals seems inevitable, particularly for pharmaceuticals not currently in wide use (e.g., antiprotozoal drugs). This study found that the use of drugs to treat common symptoms, such as painkillers, may also increase. Understanding which diseases, and therefore which drugs, may be used in the future is important so that toxicologists, environmental scientists, policymakers and legislators can

focus their efforts, implement mitigation measures and plan training, education and treatment [92-93].

The chemical pollutants such as pesticides, biocides or industrial chemicals, the release of pharmaceuticals into the environment must be regulated to ensure adequate information and transparency about the environmental impacts of pharmaceuticals; adequate and reliable assessment of environmental risks of pharmaceutical products; prevent pharmaceutical products from entering the environment throughout their entire life cycle and control releases of pharmaceuticals into the environment when prevention is not possible [94-96].

Consumption of medicinal products for human and veterinary purposes has impacts on terrestrial and marine environments and ecosystems. Increased environmental awareness regarding pharmaceutical activities has led to the development of policies and measures aimed at mitigating negative environmental impacts. Various measures have been taken to promote environmentally friendly production and practices, leading to the development of alternative methods and processes benefiting both the environment and industry. Distributors and pharmacists can make a difference by effectively managing daily operations, including improving inventory and rotation, consolidating supplies and reducing unused medications [97-98].

Pharmaceutical products are essential to human health, but they become an environmental problem when they enter the environment, which occurs when residues are excreted from the body after consumption or when unused pharmaceutical products are improperly disposed of. Although no method has been developed to detect all drugs entering an ecosystem, certain groups have been shown to have negative impacts on ecosystems, including increased mortality of aquatic species and changes in physiology, behavior, or reproduction. Particular attention is paid to these groups of drugs and their impact on the environment. In this review, the authors propose measures to reduce the amount of unused pharmaceutical products in the environment, with a focus on prevention. Various policy measures are recommended throughout the life cycle, including source-oriented, user-oriented and waste management measures, to prevent the generation of household pharmaceutical waste and ensure environmentally sound disposal of household pharmaceutical waste. Preventive measures include rational drug consumption, prescribing more environmentally friendly drugs or developing safe and easily biodegradable drugs, better disease prevention, personalized medicines, better packaging sizes and markets for the redistribution of unsafe drugs. The next step is to prevent inevitable waste from entering the environment. Therefore, it is extremely important to collect and properly dispose of unused medicines. Finally, education of healthcare professionals and the public, as well as partnerships between environmental scientists and clinicians, are essential at all stages of the pharmaceutical life cycle. Reducing drug levels in the environment will benefit human life [99-100].

Demographic, epidemiological and lifestyle changes, such as the aging of the population, the increase in chronic diseases, the availability of cheap generic treatments and easy access to a large number of over-the-counter medications, have become key factors in the growth of the pharmaceutical industry. The global increase in drug consumption has led to greater international awareness of the problem of unused pharmaceuticals (UPs) in households and the harmful environmental and health consequences of their improper disposal. Drugs in the environment are challenging because they are designed to interact with a living system and produce a pharmacological response at low doses, making them dangerous to the

environment even at low concentrations. Secondly, drugs are designed to be stable in reaching and interacting with their target molecules, meaning that they degrade very slowly or that their continued use results in a constant, slower release into the environment, that is, as quickly like decomposition. In addition, conventional wastewater treatment plants are not designed to completely remove pharmaceuticals from wastewater [101-103].

Pharmaceutical products enter the environment through two main routes: excretion and insufficient elimination. In both cases, pharmaceuticals end up in sewage treatment plants, which are generally not designed to remove these pollutants from wastewater. Drugs have been found mainly in surface water, but also in groundwater, soil, manure and even drinking water. The presence of drugs in freshwater and terrestrial ecosystems can lead to the release of drugs into wildlife with the possibility of bioaccumulation. People are then exposed to drugs through drinking water and their residues in crops, fish, dairy products and meat. The effects of pharmaceuticals entering aquatic environments are of increasing concern, with impacts ranging from molecular changes to population-level effects [104-105].

The environment is everything that surrounds us: the air we breathe, the water we drink, and the land on which all living creatures live, the plants we use for food thrive. Development is what we do with these resources to improve lives. Our actions to make our lives more comfortable change the environment

One of the achievements of the United Nations in the field of environmental protection is the Kyoto Resolution on the Climate Change Convention (1997). In 2004, it passed into law, requiring countries to reduce emissions of dangerous greenhouse gases by 5.2% by 2012. The United Nations Convention on Biological Diversity (1992) obliges states to preserve the rich diversity of plants and animals necessary for human existence.

Environmental pollution leads to the increase of toxic substances in the human body and its environment - air, water, soil, animal and plant world - beyond the permissible norm, which is followed by a sharp increase in various chronic diseases [106-108].

The interaction between the organism and the environment takes place in two main directions. One of them refers to those biochemical changes in human organisms that are caused by the demands of environmental conditions or arise in the process of human impact on the environment. It is necessary to specify the impact processes of men, women, children and entire groups. The environment is that part of living and non-living nature that surrounds organisms and directly or indirectly affects their existence, development and reproduction [109-111].

Pharmaceutical and personal care products (PPCP) in the environment are a hot topic. Veterinary antibiotics, prescription drugs and cosmetic products are discarded from a variety of sources and regularly enter the environment, where they occur in small quantities in wastewater, surface and ground water, silt-laden agricultural soils, aquatic and terrestrial biota, and wet drinks Water. The public should become aware of this and is calling on the scientific and regulatory community to assess the potential risks to human health and the environment and take appropriate action if necessary [112-114].

Chemical pollutants are known to have specific effects on organisms, for example: Organotin compounds (used in anti-fouling paints on ships) affect marine life. However, there is another very diverse group of chemical compounds that can be harmful but have

received relatively little attention as potential environmental pollutants. These include drugs, including drugs for humans and animals, as well as illegal (recreational) drugs.

Thousands of tons of pharmacologically active substances are used worldwide every year, but surprisingly little is known about the fate of most drugs after their intended use. Most of the administered dose is excreted unchanged from the body, and metabolites can be converted back into the active ingredient by bacteria. In addition, the public often throws unused medicines down the drain. Based on published prevalence data, it is likely that a significant portion of municipal wastewater is contaminated with narcotic compounds that vary only in the type and content of substances present [115-117].

Modern research has shown that many drugs are not completely eliminated from the body in wastewater treatment plants. The presence of drugs in surface systems, soil and even marine systems has been confirmed in concentrations ranging from high ng/liter to low mg/liter, which are similar to the concentrations of some pesticides. Pharmaceutical compounds discarded in household waste can end up in landfills and pose a risk to surface and ground water. Additionally, unlike more regulated contaminants, which often have a longer half-life in the environment, pharmaceuticals can become pseudopersistent due to prolonged exposure to wastewater, with unknown consequences for aquatic organisms that may be continuously exposed [118-119].

The potential consequences of the presence of pharmaceuticals in aquatic systems are unknown and have therefore received increasing attention as potential pollutants in recent years. The fact that an industrial chemical can end up in the environment is not surprising in itself. What's interesting about drug contamination is that it does not primarily arise from manufacturing, but rather from the widespread and ongoing use, isolation, and improper disposal of drugs for human and veterinary use [120-121].

Pharmaceuticals are potentially ubiquitous pollutants as they are present in all human environments. There is currently little evidence that pharmaceuticals are present in the environment in sufficient quantities to cause significant harm, although their use is expected to increase as the Human Genome Project is completed and the population ages. Drugs and their metabolites are increasingly being found in water bodies in areas adjacent to anthropogenic activities [122-123].

The biggest concern at the moment is that antibiotics in wastewater treatment plants may lead to increased resistance of natural bacterial populations. There are many isolates of microorganisms resistant to antibiotics in the environment, and although the issue remains controversial, the significant increase in the number of bacterial strains resistant to multiple antibiotics is often attributed to the misuse of antibiotics and the increase in their discharge into wastewater. Three known mechanisms of gene transfer (conjugation, transduction, and transformation) are thought to occur in aquatic environments; As a result, streams and rivers can become a source and reservoir of resistant genes, as well as a means of their dissemination. In addition, some non-target organisms (eg cyanobacteria) may be exposed to antibiotics, which may have indirect negative effects on the aquatic food [123-124].

The problem is further complicated by the fact that exposure to only one drug or toxic substance at a time is likely to be a rare event. Laboratory studies have shown that mixtures of just a few compounds have effects on ecosystems, but it is unknown what happens in the wider environment. Most organisms are constantly exposed to various substances, the concentrations of which vary little in time and space. Therefore, the limits of your tolerance

depend on the duration of exposure to chemical and non-chemical stressors, many of which have the same mechanism of action and whose effects can result in additive effects. Thus, risk estimates that ignore possible cumulative drug effects will almost certainly lead to significant underestimation of risk [125-126].

Increasing demand for global water sources will likely lead to increased indirect and direct water reuse in the future. Drinking water is a direct route to the human body, including drugs and other contaminants that may be present there. Advanced water treatment technologies such as granular activated carbon (GAC) and reverse osmosis (RO) can remove drugs from drinking water until they are invisible, but these processes are not widely used. Due to the lack of appropriate technology and the need for significant economic investment, municipal wastewater is never treated in this way. In addition, large-scale monitoring programs to test these compounds would be extremely expensive and time-consuming due to the large number of different compounds and the diversity of their properties and effects [128-128].

Given that the extent and consequences of the presence of drugs in aquatic environments is largely unknown, more research is needed before a clear picture of the true nature and importance of the problem can be formed. Therefore, it would be unwise to claim that these compounds have significant environmental impacts until convincing evidence is available. To this end, future emphasis should be on adequate and sufficient scientific knowledge to determine occurrence, exposure, sensitivity and consequences in order to make informed decisions regarding human health and the environment [129-130].

When evaluating drugs, benefits to human health must take precedence over potential harm to the environment. Therefore, it may be beneficial to focus on reducing or eliminating problems at their source by developing clearer drug labeling and more effective guidelines for the disposal of pharmaceutical compounds by patients and healthcare professionals. The potential benefit of this approach would be improved consumer health (by minimizing the consumption of active substances) as well as reduced healthcare costs. Given the enormous importance of the pharmaceutical industry to both human health and the economy, any increased control could have serious economic and social consequences. If pharmaceuticals turn out to be problematic contaminants, collaboration between health professionals and environmentalists will be mutually beneficial, as much research remains to be done before the problem can be fully understood [131-132].

Ecology, which directly affects the health of society, is one of the most important factors in the modern era of civilization. Factors affecting population health are the biggest social problem. The health and illness of society are determined by the environment in which a living organism is located and develops. Man is a biosocial being. Environmental factors affect organisms in different ways. It can be irritating, limiting or determining the existence of the organism in specific conditions; the danger of disturbing the natural balance is associated with pollution of the atmosphere, water, soil and food products with nitrates, pesticides, radionuclides and other harmful substances. The environment is saturated with psychotoxins, chemical waste, biological damaging agents (drug-resistant bacteria, fungi, viruses, parasites resulting from mutations). causing death of plants and animals and illness in humans. Therefore, it is clear what a great danger an environmental disaster poses [133-134].

An environmental disaster has a direct impact on public health. Society and the environment are in constant relationship. Therefore, the health and illness of society are determined by

the environment in which a living organism is located and develops. Factors affecting population health are the biggest social problem.

There is a danger of disturbing the natural balance. Pollution of the atmosphere, water, soil and food products with nitrates, pesticides, radionuclides and other harmful substances leads to the death of plants and animals and diseases of people. Therefore, it is clear what a great danger ecological disaster causes [135-136].

The most serious consequence of biosphere pollution is the manifestation of genetic disorders. As a result of increased radioactive background and chemical pollution of the environment, the number of pathologies, malignant tumors, mental disorders, etc. increases. number. Mutagens in the form of chemical compounds, ionizing radiation penetrate the cell and cause disruption of the genetic program, causing mutations in somatic cells [137-138].

Diseases and conditions caused by climate change will also impact demand in the healthcare system and pharmaceutical industry. The pharmaceutical industry may see a change or increase in demand for drugs. For example, an increase in temperature can trigger asthma due to increased pollen levels. This increase in asthma cases will, in turn, lead to an increase in demand for medications to control asthma. Changing demand for medicines could create opportunities for the pharmaceutical industry to make the most of climate change and incorporate green chemistry principles into the development of new medicines [139-140].

The production and consumption of pharmaceuticals results in the presence of active pharmaceutical ingredients (APIs) in the ecosystem. Active ingredients enter the marine and terrestrial environment through release from manufacturing facilities, into wastewater after consumption of the drug in question, or through improper disposal of expired or unused drugs. The use of medicinal products in veterinary medicine may also result in the release of active substances into the environment, for example through the use of wastewater for irrigation, agriculture, aquaculture or the disposal of animal carcasses treated with veterinary drugs. The presence of APIs in the ecosystem can have a number of side effects, such as: Bacterial resistance to antibiotics and changes in the activity of digestive glands in marine life, reproductive toxicity in amphibians and feminization of fish. Another striking example of the impact of APIs on the ecosystem is the sharp decline in vulture populations due to the presence of diclofenac residues in cattle carcasses [141-142].

Based on data from the World Health Organization, an analysis of the impact of environmental factors on human health was published, which revealed large differences between countries and showed that human health can be improved by reducing exposure to environmental factors such as: pollution, ultraviolet radiation, noise, climate, ecosystem change and dangerous work environment. More than 10% of deaths in 23 countries of the world are related to the environment with two risk factors: 1) polluted air and water; 2) low sanitary and hygienic indicators.

The industrial agriculture, municipal wastewater treatment, and the introduction of municipal sewage sludge (biosolids) as major sources of pharmaceuticals and personal care products in the environment. To compensate for this, indicators of veterinary antibiotic use are provided by both the agricultural industry and interested scientists. Personal care products are divided into fragrances and musks, cleansers and disinfectants [143-144].

Pharmaceutical products intended for human use are included in the UNESCO list of emerging pollutants. Their identification and elimination represent a decisive step towards

achieving the goals of the Sustainable Development Program. Concentrations of drugs found in the environment are below therapeutic levels. In waters receiving treated wastewater, drugs are found at concentrations below 100 ng/L. These low concentrations make it difficult to assess their toxic effects on ecosystems and human health. The vast majority of pharmaceutical products have not been adequately studied regarding their long-term toxic effects, presence and fate in the environment. However, certain classes of drugs, such as beta blockers, antibiotics, anticancer drugs, and endocrine disruptors, have been shown to have devastating effects on the ecosystem, including increased mortality and disruption of the physiological and reproductive functions of aquatic species. Moreover, since it is impossible to separate humans from nature, this has devastating consequences for human health. However, the extent of the problem remains largely unknown due to the large number of drugs available and difficulties in assessing the risks associated with exposure to multiple compounds at low doses over long periods of time. The drugs on the market pose a potential risk to the environment. Although there is no established method for detecting all pharmaceuticals entering an ecosystem, some are widespread and have been shown to have negative impacts on ecosystems. These groups include hormones, antibiotics, antidepressants, anti-inflammatory and pain relievers, beta blockers and anti-cancer drugs [145-146].

Antibiotic resistance is a global public health problem, especially given the increased use of antibiotics during the COVID-19 pandemic, which has led to the exhaustion of the last line of antibiotics. It has been established that the use of antibiotics in medicine, veterinary medicine and agriculture is associated with pollution of various parts of the environment, which has contributed to increased antibiotic resistance and the occurrence of ecotoxicological effects. Failure to properly dispose of antibiotics through sewers by patients also poses a growing environmental threat to public health. Additionally, high levels of antibiotic contamination after long-term exposure can negatively impact human health, especially in patients with chronic diseases such as obesity, diabetes and asthma [147-149].

Antidepressant contamination has increased significantly worldwide during the COVID-19 pandemic. To this day, antidepressants can be found in urban and suburban water supplies. Many aquatic animal species bioaccumulate various antidepressants in their tissues, resulting in cytotoxicity, genotoxicity, impaired stress response, weight and length gain/loss, and liver and kidney damage. Because there is significant overlap between human and animal environments, exposure to antidepressants (sertraline, fluoxetine) in the environment also affects human neurological development and various mental illnesses. Although psychotropic drugs are usually present in wastewater at subtherapeutic levels, they can have biological effects at low doses, and combinations of multiple psychotropic drugs are often present, especially in the environment, increasing the risk of toxic effects [149-150].

Pharmaceutical compounds are used in modern society for various beneficial purposes, but at the same time, the pharmaceutical industry releases highly toxic pollutants into the environment either directly or after chemical modification. Additionally, pharmaceutical compounds can enter the environment through various routes such as treated wastewater discharge, seepage into landfills, sewer pipes, animal waste, etc. Although a number of physical and biological processes occur in an aquatic ecosystem, they can lead to depletion of many lead to pharmaceutical compounds. Traces of human and veterinary drugs and their metabolites were found in several bodies of water. Objects such as surface water, groundwater and drinking water sources. Several industries, including pharmaceuticals, chemicals, paints, etc., are rapidly developing in India, with wastewater being discharged

into water bodies either directly or after partial treatment. Pharmaceutical compounds have been found to be released into the environment and may be considered environmental pollutants. Several pharmaceutical plants have been found to be sources of much higher concentrations in the environment than those resulting from drug use. Typically, the pharmaceutical industry generates a large amount of waste during production and service. Drugs have been found in sewage treatment plant wastewater and drinking water. Trace amounts of drugs in drinking water can have serious adverse effects on human health and aquatic life over long periods of time, even when drug concentrations in drinking water (in the nanogram per liter range) are orders of magnitude below the minimum therapeutic dose [151-152].

Pathways through which drugs may be exposed to the environment include manufacturing plants and hospital wastewater, land use (eg, biosolids and water reuse), etc. Wastewater treatment services are not always successful in removing active chemicals from wastewater. Therefore, drugs enter the aquatic environment, where they have a direct effect on aquatic organisms and can be absorbed into the food chain.

Higher concentrations of antibiotics can lead to changes in microbial community structure and ultimately affect food chains. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen and diclofenac, are widely used and therefore often found in wastewater systems, both surface and groundwater. Ibuprofen, ketoprofen, naproxen, indomethacin, diclofenac, acetylsalicylic acid and phenazone were detected in the surface water system. However, after clofibric acid, the most common drugs found in aquatic environments are diclofenac, ibuprofen and propyphenazone. Diclofenac has also been shown to be highly toxic to vultures and livestock. NSAIDs such as ibuprofen, naproxen, and aspirin are the most commonly used medications and are often found in effective amounts in municipal wastewater [153-154].

Many pharmaceutical companies are responsible for the generation of toxic wastewater during their operations. The wastewater generated from these facilities contains solids, biodegradable and non-degradable organic compounds, etc. Pharmaceutical wastewater provides basic information about the reliability of the aquatic environment of the rivers and streams into which it is discharged. An important indicator of industrial wastewater contamination is the oxygen content of chemical oxygen demand (COD) and biological oxygen demand (BOD), with nutritional status measured by the amount of nitrogen and phosphorus in the wastewater.

Long-term exposure of coastal biota to lower concentrations of complex drug mixtures can result in acute and chronic damage, behavioral changes, tissue accumulation, reproductive impairment, and inhibition of cell proliferation. Several studies have shown that fish exposed to sewage may experience reproductive problems. In addition, fish exposed to trace amounts of contraceptive drugs in the concentration range found in the environment show dramatic reductions in reproductive success, suggesting that population-level effects may be possible [155-156].

Around the world, the drug residues in the environment poses risks to humans, aquatic animals and wildlife and is becoming a major concern for both regulatory authorities and the pharmaceutical industry. Significant progress on this issue is simply not possible with the current limited knowledge about the transport, fate, and environmental impact of pharmaceuticals. It is necessary to take into account the possible potentiating effects of different drugs acting on the same receptors. Risk assessment of pharmaceutical chemicals

involves identifying the hazards associated with each step and assessing the risks associated with those hazards.

Currently, pharmaceutical compounds are regularly released into the environment in extremely large quantities, and the current emission control system is unable to control untreated or partially treated pharmaceutical wastewater. The effects of drugs permeate and impact ecosystems, biota and humans. Adverse health effects on humans, aquatic animals and livestock should be investigated through careful toxicological and safety studies. Serious efforts are needed to reduce this problem, and appropriate regulations are needed to monitor and control it. Water quality guidelines in India should include analysis of the most commonly used pharmaceutical compounds in drinking water sources. In addition, pharmaceutical industrial wastewater treatment plants need to implement new corrective measures to prevent long-term environmental and health risks [7, 83,105].

Water sources contaminated with pharmaceutical contaminants are found in agricultural lands, surface water, groundwater, and drinking water. Water flows to plants, which affects the quality of soil and crops grown using this contaminated water. Pharmaceutical contaminants are considered external environmental factors that affect crop quality. Drugs enter plants as pollutants, either through the soil or the air. Pollutants enter the plant from the soil through the roots and are transported through the stem. Plants also absorb pollutants from the air, and leaves can absorb pollutants from the atmosphere. Pharmaceutical contaminants such as B-lactams, aminoglycosides, macrolides, tetracyclines, sulfonamides, herbicides including sulfonylureas, triazines, imidazolinone, phenylurea and bisphenol (BPA) have been found to cause toxicity in plants. Polychlorinated biphenyls (PCBs) affect plant growth, reproduction and productivity [8,39,67].

Most pharmaceuticals we use are excreted via urine and feces in unchanged form or as metabolites and eventually end up in the drain. The pharmaceutical residues can then reach lakes, the sea and groundwater, despite passage through wastewater treatment plants, as the wastewater treatment plants are not built to clear pharmaceuticals. Pharmaceuticals affect biological processes. They are also often designed to withstand biodegradation and can therefore remain in the environment for a long time. There are reports of effects on fish, as well as that measured concentrations of antibiotics in wastewater treatment plants can select for antibiotic resistance.

Chemicals play an important role in healthcare as they can be used as disinfectants, cleaning agents, laboratory reagents, sterilants, pesticides, pharmaceuticals, and in medical devices and equipment. They also offer great animal welfare benefits. However, there is growing awareness and concern about the consequences of mishandling drugs and chemicals on human health and the environment [9,47,88].

Pharmaceuticals are also biologically active substances specifically designed to provide pharmacological effects on living organisms. They affect the health of wildlife and ecosystems if not managed in an environmentally sound manner.

Active pharmaceutical ingredients (APIs) are the biologically active components of a drug. These APIs are sold to pharmaceutical companies that manufacture end products for patients around the world. More than 5,000 active pharmaceutical ingredients are used in prescription, over-the-counter and veterinary products worldwide.From a chemical and waste management perspective, environmental and health issues in this sector are mainly related to the release of pharmaceuticals into the environment: Waste ends up in rivers, lakes

and underground aquifers. In addition, when used in livestock production and when manure is used as fertilizer, veterinary drugs end up in the soil and environment. This leads to soil contamination and biomagnification due to leaching of drugs into food crops [12,58,79].

Sources of drug release into the environment include direct emissions from drug manufacturing, patient and animal feces, aquatic agriculture, and disposal of unused or expired drugs. Medicines designed to degrade slowly, or even non-degradate to resist chemical breakdown as they pass through the human or animal body, pose a particular risk if ingested, stored, or distributed into the environment. When released into the environment, the biological activity of persistent pharmaceutical pollutants in the environment can have direct negative effects on non-target organisms such as wildlife and have long-term impacts on the health and sustainability of ecosystems. The latter occurs through population-level reproductive effects that persist into future generations of non-target organisms. Pharmaceutical contaminants that are persistent in the environment are frequently and increasingly used in consumer products. However, significant gaps remain in knowledge about the environmental and health impacts of these pollutants [41,48,95].

Some pharmaceuticals have been found in low concentrations in drinking water, which is a warning sign that the current handling of pharmaceuticals may lead to health and environmental problems in the future.

Access to healthy water is a prerequisite for good health. Since society's use of chemicals, including pharmaceuticals, is continuously growing, the risk is also increasing that these chemicals will return to us in our food and water supply through nature's ecocycle.

There are little knowledge of the long term effects that continuously supplied trace quantities of pharmaceuticals and other chemicals could have on our development, our ability to resist disease and wellness in general. Therefore caution is advisable. The pharmaceuticals in nature can cause health problems. According to the precautionary principle, measures can be taken if there is reason to believe that a product or a method of production involves unacceptable risks to the health of human beings, animals, plants and the environment – even if there is no definitive scientific proof of such an effect [9, 65,79].

Drug residues are found in various environmental components around the world, and there is growing concern about the harm they may cause to human health and the environment. In nature, drug residues were found in urban wastewater, rivers and lakes. Effective measures must be taken to prevent further contamination of the environment by drugs. First of all, it is necessary to create a system for collecting drug waste from the population. Undoubtedly, drugs enter the environment during the production process through wastewater from pharmaceutical plants, municipal wastewater through natural human excretion, wastewater and manure from the use of veterinary drugs and as a result of improper handling of drug waste [19,36,77].

The review defines each of these sources and steps that can be taken to reduce drugs' environmental impacts. In the European Union, since 2004, the obligation to organize a system for collecting drug waste from the population has been established. For the successful operation of such a system, information work with the population about how drugs affect the environment and how to properly dispose of them is important. Residents of all European countries can bring drug waste to a pharmacy or hazardous waste collection point. However, in some countries there is a lack of widespread awareness-raising, which leads to inefficient collection systems and most waste ends up in the trash or drained into sewers. In some

countries, drug waste generated by medical and pharmaceutical organizations is neutralized in pharmacies, clinics, hospitals and manufacturers. At the same time, pharmacies and hospitals have the right to transfer expired medicines to the manufacturer [36,57.81].

In most countries where the system operates successfully, the costs of collecting and neutralizing drug waste are shared by pharmaceutical companies, drug manufacturers and local authorities. The main problem is the very existence of unused drugs. So, generally many patients buy more medicines than they need. The best way to reduce their number is seen in optimizing the practice of prescribing drugs, so that only the necessary amount of drugs is prescribed, giving preference to more environmentally friendly ones, as well as improving information interaction between doctors and patients. The pharmaceutical industry must also provide for the production of drug packaging adapted to various treatment regimens [10, 19, 64].

Every participant in the drug supply chain, from the pharmaceutical industry to the patient, plays an important role in reducing the environmental impact of pharmaceutical activities. The International Pharmaceutical Federation has highlighted the different roles that each person plays in the pharmaceutical supply chain to minimize the environmental impact of pharmaceutical products. The pharmaceutical industry plays an important role in the environmental impact of pharmaceutical products.

Educating pharmaceutical personnel and the public is an important aspect of helping to create a healthy environment and reduce activities that contribute to climate change. The implementation of green practices in the pharmaceutical sector is already included in the curricula of EU Countries countries universities. Pedagogical input helps to recognize the importance of such practice early in professional development.

Consumer education is also important as it plays an important role in reducing the amount of drugs in the environment. Consumers should be discouraged from storing medications to avoid wasting them when not in use. They should also be taught how to properly store and dispose of unused and expired medications that may end up down the drain [13, 28, 39].

The world's population is aging, which will lead to an increase in drug use. Various measures need to be taken to minimize the release of active pharmaceutical ingredients into the environment and reduce the carbon footprint of the pharmaceutical sector. Small contributions from many people can synergistically have a positive impact on the environment [7, 18,48].

There are several sources of release of active pharmaceutical ingredients (APIs) into the environment. The main ones are: wastewater from cities, hospitals, pharmaceutical plants and landfills. The vast majority of the active pharmaceutical ingredients (API) of drugs taken orally is excreted in the urine of animals and humans. Some pollution comes from the use of veterinary drugs in livestock and fish farming. However, it is not yet possible to evaluate this contribution, because there is no control and accessible reporting of the use of veterinary drugs. The most vulnerable to the effects of active pharmaceutical ingredients (APIs) are amphibians, fish, some animals and birds [48,54,69].

The main source of drugs entering the environment is wastewater from pharmaceutical enterprises (from product washing, waste acidic and alkaline wastewater, wastewater from cleaning equipment and production facilities, etc.) and liquid waste that is allowed to be discharged into the sewer system. Currently monitored parameters in pharmaceutical

wastewater are biological oxygen demand (BOD), chemical oxygen demand (COD), total suspended solids, ammonia and ammonium ions, phosphates, chlorides, sulfates, petroleum products, iron, anionic surfactants and pH value. This list may include other chemical compounds, including active pharmaceutical ingredients (APIs), but their content is not regulated or controlled at this time. Currently, the countries of the European Union have prioritized the most environmentally stable active pharmaceutical ingredients (APIs) - diclofenac, hormonal drugs of the estrogen group (ethinyl estradiol), antibiotics of the macrolide class (erythromycin, clarithromycin, azithromycin) and etc [29,57,68].

Assessment of environmental risks of both original and generic drugs. In European countries, for some drugs such an assessment is carried out, as well as an assessment of the level of resistance, bioaccumulation potential and toxicity. Currently, providing information about environmental hazards when registering drugs in the countries of the European Union is voluntary. In some countries has been created an online database of drugs, which describes their environmental risks and expanding the responsibility of drug manufacturers throughout the entire cycle from production to neutralization [84,88,95].

After drugs enter the body, they are destroyed, neutralized, metabolized and converted into new compounds. However, some of them are excreted unchanged or in the form of metabolites, ending up in the sewer system. Municipal wastewater treatment does not involve removal of APIs. Some of them are concentrated in sewage sludge from treatment plants, which is stored in filtration fields, while the rest ends up in rivers. The Challenges in this matter are also hospitals, where there is a high level of drug consumption. In the absence of an established system for collecting drug waste generated by the population, it either ends up in the sewer or is thrown into the trash. From landfills, drugs can be carried by animals, birds, or migrate into the soil and groundwater.

To raise animals and fish on an industrial scale, hormonal drugs, antibiotics and other drugs can be used, which can be excreted from the animal's body naturally. Hormones can be used in veterinary medicine and animal husbandry to stimulate the development and growth of animals, improve fertility, digestibility of feed, accelerate puberty, regulate the timing of pregnancy, etc. According to studies in some countries, antibiotic residues were found in manure, in plants grown in fields fertilized with manure, in soils, and in small quantities in groundwater. The use of veterinary drugs in should be regulated by veterinary and sanitary rules for the use, sale and storage of veterinary drugs.

European experience in collecting hazardous waste from the population shows that waste collection is carried out effectively if such collection is organized by a company specializing in the collection of hazardous waste. The same practice works in our country. In the EU, pharmacies are considered only as an area for the installation of appropriate containers and containers for collecting hazardous waste from the population. The containers themselves are installed by specialized companies interested in collecting hazardous waste. It is inappropriate to oblige pharmacies, healthcare institutions or other trade organizations to organize the collection of drug waste from the population [47,59,76].

Pharmacies and medical institutions are places where consumers can obtain the most complete information about drug waste, since these organizations employ personnel with the relevant knowledge. In the country, many pharmacies themselves are located on the territory of various retail facilities, so there may not be places in pharmacies to install a special container for collecting drug waste. When determining places for collecting waste from the population, it is necessary to comply with the criterion of step-by-step accessibility of such

places from the places of residence of citizens. In this regard, retail facilities should also be considered as places for installing special containers for collecting drug waste. The decision to organize collection points for drug waste from the population in pharmacies should be made by Health care institutions in every countries.

In the vast majority of countries, all drug waste collected from the population is sent for incineration. At the same time, pharmacies, for example, in Sweden and Lithuania, can only accept medications without packaging, because it belongs to secondary resources and must be sent for recycling. Low-temperature, medium-temperature (up to 850°C) and high-temperature (at least 1200°C) combustion is used for waste. Hazardous waste, which includes most drugs, cannot be burned at low temperatures. At medium temperatures it is possible in limited quantities and in the absence of high-temperature combustion technology. Cytostatic drugs for cancer treatment can only be burned at temperatures above 1200°C, but the generation of such waste in household use is unlikely. Currently, there is a steady trend towards a decrease in the number of thermal installations for the neutralization of pharmaceutical waste. Incineration of waste is contrary to three principles of international law: precaution, prevention and limitation of transboundary effects. In Europe, resistance to waste incineration manifests itself in the form of the introduction of alternative technologies. Any combustion method requires monitoring of pollutant emissions and the resulting ash. An alternative to conventional methods of thermal treatment of pharmaceutical waste are technologies that provide for the preliminary decomposition of the organic component of the waste in an oxygen-free atmosphere (pyrolysis). When carrying out microwave pyrolysis with heating using microwave waves, toxic gaseous products are converted into less dangerous ones.

In countries where there are no incineration plants or their use is limited geographically, drug waste is disposed of. The main disadvantage of this method is the high probability of soil and groundwater contamination. According recommendations of the World Health Organization, only non-hazardous drug waste (vitamins, herbal-based drugs, biodegradable drugs) can be sent to the landfill. Hazardous waste, including cytotoxic drugs, must be pre-sealed, i.e. placed in a metal capsule and filled with plaster and cement [46,62,85].

Liquid waste of drugs classified as non-hazardous (syrups, herbal preparations, solutions based on salts, amino acids, lipids or glucose) can be poured into the sewer after diluting with water. It is necessary to prevent the discharge of large quantities of disinfectants into the sewer system, because they can affect the quality of biological wastewater treatment. Discharge of drugs that are persistent in the environment, capable of biological accumulation and have toxic properties into the sewer system leads to environmental pollution with active pharmaceutical ingredients. According to studies conducted in many countries, existing wastewater treatment systems do not eliminate such pollution and drug residues are found in wastewater cleaning sludge, and to a greater extent in water after cleaning, which is discharged into natural watercourses.

Some drugs pass through the human body, exit unchanged or in the form of metabolites, while maintaining their stability in wastewater and the environment for a long time. In addition, improper disposal of medications and disposing of them down the drain increases the concentration of hazardous APIs in water. Wastewater from pharmaceutical plants is also discharged into the city sewer system after local treatment. The active pharmaceutical ingredients are present in municipal wastewater above detection limits. Traditional mechanical and biological wastewater cleaning methods are unable to neutralize the active

pharmaceutical ingredients in water. The issue of purification efficiency, the formation of drug metabolites and their behavior, the interaction of some drugs with others is still under study. Among the methods being developed and implemented in the countries of the European Union one can highlight physicochemical methods, aerobic/anaerobic biological cleaning in membrane bioreactors. Effective technologies for purifying wastewater from medicinal components include oxidation with ozone or hydrogen peroxide and the use of carbon filters. However, such technologies are currently expensive to implement and use. At the same time, more and more attention is being paid to preventing the entry of drugs into wastewater, including during production. The main problem is the very existence of unused drugs [15,19,22,58].

One of the most obvious sources of uncontrolled release of drugs into the environment may be wastewater and atmospheric emissions from enterprises producing finished drugs and pharmaceutical substances. The environmental safety of such production should be usually regulated by law. However, accidental releases of drugs into the environment or those that violate existing norms and rules that occur in industry, are nevertheless not systematic. Moreover, there is a general trend towards a reduction in the environmental load on the part of pharmaceutical production, primarily in developed countries of the world, due to a consistent increase in the technological effectiveness and organization of the production process, the introduction of increasing standards of quality and environmental safety, and control by authorized government agencies. It is also necessary to take into account that pharmaceutical production is localized geographically and if an accident occurs at the enterprise or there are violations of environmental legislation, then such emissions are exclusively local in nature and pose a danger only to specific regions. Other sources of drugs that are practically uncontrollable and are formed mainly by people who use drugs for medical purposes, as well as in animals, pose a great danger to the environment [55,62,84].

For the most part, drugs are xenobiotics, and many of them are metabolized in the human body. The task of metabolism, as a rule, is to impart polarity to lipophilic substances in order to facilitate subsequent excretion. Metabolic parameters are individual for each substance and depend on gender, race, age and physiological state of the human body. There are two phases of metabolism, the numbering of which does not necessarily reflect their actual sequence. In the first phase of metabolism, a redox or hydrolytic transformation of the molecule occurs, increasing its polarity. In the second phase of metabolism, the xenobiotic is conjugated with endogenous molecules that improve the transport properties of the metabolite. During metabolism, inactivation of the active substance often occurs, which can lead to its inability to further exert a biological effect. However, many drugs are either not subject to metabolism or are subject to it only to some extent. And this leads to the fact that the active molecule of the active substance is excreted unchanged either in the urine or in the feces and is capable of further exerting a biological effect. In addition, as research results show, glucuronide transport complexes of active molecules of some drugs, formed during the second phase of metabolism, are easily destroyed during sewage treatment processes and release unchanged active substance into the aqueous phase or sewer sludge. We can also mention the route of release of drugs into aquatic environments due to their transport through the skin or leaching of drugs for external use during swimming in open waters. But from the point of view of quantitative indicators, this path is of little significance [39,49,83].

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The increasing the availability of drugs, for the general development of health care systems, the consumption of drugs for medical purposes increases and, as a result, their content in the environment increases. This process is poorly managed and poses a potential danger to human health and other biological organisms. Contamination of the environment with drug residues has a global character and is actively studied in the developed countries of the world. However, this problem remains insufficiently worldwide [26,39,57,72].

The best ways to reduce their number are to optimize the practice of prescribing drugs, so that only the required amount of drugs is prescribed, giving preference to the least environmentally hazardous ones, as well as improving information interaction between doctors and patients. The pharmaceutical industry must also consider producing drug package sizes tailored to different treatment regimens. One key measure is to encourage the pharmaceutical industry to develop harmless drugs that quickly break down into harmless compounds in the environment. For example, currently in European countries, when registering a new drug, environmental characteristics such as ecotoxicity, biodegradability are indicated.

The comparing drugs that are equally safe and well suited for treating a patient, it is recommended to take into account, in addition to their pharmaceutical properties, their environmental impact. To do this, recommend using environmental drug classifiers.

Large quantities of nonsteroidal anti-inflammatory drugs, including acetaminophen, acetylsalicylic acid, ibuprofen, diclofenac, and naproxen, are significant contributors to environmental pollution, especially because they have been detected in nanogram and microgram quantities in soil, wastewater, surface water, and drinking water, groundwater. These drugs have chronic ecotoxic effects because their stable chemical structure makes them very resistant to biological changes in the environment. It is now known that they primarily damage the organs of invertebrate and vertebrate animals, cause oxidative stress and interfere with the activity of detoxification enzymes. These drugs may also cause cardiovascular effects, hepatotoxicity and affect oocyte maturation through unknown mechanisms [5,19,42,49].

Beta blockers are very long-acting drugs that are toxic to the environment. Although there is no data on their adsorption in the environment, these drugs are known to have moderately high water solubility and are present in surface waters at µg/L concentrations. These compounds are extremely resistant to hydrolysis, bioavailable and mobile in the environment. Therefore, its accumulation in the environment can have unexpected consequences for many living organisms. According to European Union Directive, metoprolol and propranolol are compounds harmful to aquatic organisms. This is evidenced by the results of tests with green algae.

Anticancer drugs interfere with cell growth and division, and when released into the environment, they disrupt the ecosystem, impair fertility and cause significant genetic changes in living organisms. Anticancer drugs are prescribed in smaller quantities, but their effects are destructive even at concentrations in the ng/L range and include mutagenic, carcinogenic and teratogenic effects on aquatic life. Cytostatics are frequently found in the pharmaceutical industry and hospital wastewater due to improper use and disposal. The detection rate of anti-cancer drugs in oncological hospitals wastewater is big amount and cisplatin is considered one of the most dangerous drugs. The presence of cisplatin in water, even at concentrations of ng/l, can have a toxic effect on aquatic flora and fauna [28,47,59,74].

Environmental pollution caused by pharmaceuticals is a complex public health problem that is scientifically controversial and affects multiple stakeholders with different interests and at different organizational levels: governments, non-governmental organizations, academic institutions, manufacturers, industries and families.

In keeping with the idea of protecting the environment, the pharmaceutical industry must develop promising concepts to minimize secretions while still ensuring sufficient pharmacologically effective concentrations in the patient. The potential of developing new pharmaceutical products that are more biodegradable and less harmful to the environment. There are already some examples of the development of greener pharmaceuticals, such as glufosfamide and green drug delivery systems. Scientists are currently developing an effective and environmentally friendly version of the antibiotic ciprofloxacin, a very stable drug. Using computer modeling, an existing active ingredient is analyzed and theoretically modified to improve biodegradability and reduce toxicological effects. The most promising candidates have been synthesized and tested in vitro [37,46,81,89].

Limited consumer awareness of best recycling practices weakens their influence on recycling practices in many countries. Information campaigns can increase awareness and use of environmentally friendly pharmaceutical waste disposal methods in households. A good example is the Meds disposal campaign, a European initiative jointly coordinated by several European health and supply chain organizations and supported by media campaigns in different languages. The aim of the initiative was to combat the negative impact of mishandling of pharmaceutical products on the environment, raising consumer awareness of correct disposal routes and collection systems in a number of European countries.

In addition, greater awareness and behavior change can be achieved through specific recycling instructions on the product's outer packaging or information leaflet, which are mandatory in EU countries. In addition, eco-labels that reflect the environmental impact of various pharmaceutical products can influence consumer choice and awareness, as well as help physicians make prescribing decisions. Instructions on how to properly dispose of medications should also accompany medication dispensing at regular intervals. Pharmacists can play a key role in educating their patients about proper medication disposal.

Human activity has the most negative impact by releasing pollutants. Pollutants are considered to be all those substances that enter the atmosphere, soil, natural waters and cause disruption of the biological, physical or chemical processes taking place there. Radiation and thermal radiation are also pollutants. As a result of human activities, carbon dioxide (CO_2), carbon dioxide (CO), sulfur dioxide (SO_2), methane (CH_4), nitrogen oxides NO_2, NO, N_2O are released into the atmosphere. As a result of aerosol use, chlorofluorocarbon enters the atmosphere, and hydrocarbons from transport emissions. Water bodies are polluted not only

by waste from industrial production, but also by organic and mineral fertilizers and pesticides used in agriculture. In the same way, sea water is being polluted. Rivers carry millions of tons of chemical waste into the sea every year. Millions of tons of oil spill into the oceans every year as a result of tanker and oil rig accidents, killing marine animals. Burial of nuclear waste at the bottom of the sea, sunken ships with nuclear reactors and weapons also pose a danger [7,19,28].

Radioactive contamination of the soil creates a great danger, since radioactive substances from the soil enter plants, and from there into the body of humans and animals, where they accumulate and cause various diseases. Chemicals pose a particular danger, specifically, organic compounds used in agriculture to control weeds, pests and diseases.

The uncontrolled release drugs into the environment may be wastewater and atmospheric emissions from enterprises producing finished drugs and pharmaceutical substances. the environmental safety of such production is usually regulated by law. However, accidental releases of drugs into the environment or those that violate existing norms and regulations that occur in industry, are nevertheless not systematic. Moreover, there is a general trend towards a reduction in the environmental load on the part of pharmaceutical production, primarily in developed countries of the world, due to a consistent increase in the technological effectiveness and organization of the production process, the introduction of increasing quality standards and environmental safety, and control by authorized government bodies . It is also necessary to take into account that pharmaceutical production is localized geographically, and if an accident occurs at the enterprise or there are violations of environmental legislation, then such emissions are exclusively local in nature and pose a danger only to specific regions. For all the reasons listed above, such sources are not the subject of analysis in this review, although they contribute to environmental pollution. Other sources of drugs that are practically uncontrollable and are formed mainly by people who use drugs for medical purposes, as well as in animals, pose a great danger to the environment [14,55,69].

For the most part, drugs are xenobiotics, and many of them are metabolized in the human body. The task of metabolism is generally to impart polarity to lipophilic substances in order to facilitate subsequent excretion. Metabolic parameters are individual for each substance and depend on gender, race, age and the physiological state of the human body. There are two phases of metabolism, the numbering of which does not necessarily reflect their actual sequence. In the first phase of metabolism, a redox or hydrolytic transformation of the molecule occurs, increasing its polarity. In the second phase of metabolism, the xenobiotic is conjugated with endogenous molecules that improve the transport properties of the metabolite [25,29,37].

The impact of pharmaceuticals on the ecology and human health. Currently, increasing attention is being paid to the presence and fate of active pharmaceutical ingredients, solvents, intermediates and raw materials that may be present in water and wastewater, including pharmaceutical wastewater. Traditional wastewater treatment methods, such as activated sludge, are insufficient to completely remove active pharmaceutical ingredients and other wastewater components from these waters. Pharmaceutical wastewater has direct and indirect impacts on the environment and health, especially near pharmaceutical industrial sites. Although pharmaceutical factories produce untreated or partially treated wastewater, drinking water sources are contaminated. Various classes of pharmaceutical compounds such as analgesics, antidepressants, antihypertensives, contraceptives, antibiotics, steroids,

hormones, etc. To protect the environment and lifestyles from health risks, the concentration of pharmaceutical compounds in medical wastewater entering drinking water sources should be regularly monitored. This article highlights the toxicity, health risks, and environmental risk assessments associated with pharmaceutical contaminants. To reduce contamination levels when consuming medicines should be: Creation of a system for collecting drug waste generated by the population; Conducting awareness-raising work with the population, employees of healthcare institutions and other target groups on the topic of environmental pollution by drug waste; Taking into account environmental factors when choosing and prescribing treatment. At the same time, there is no need to put environmental protection above the human need for treatment; Development and implementation of wastewater treatment systems. It should be taken into account that urban wastewater has an unstable composition in terms of names and concentrations of drugs. A higher priority is to prevent drug residues from entering the city sewer system [45,67,95].

Incorporating green practices into the pharmacy curriculum provides future pharmacists with the skills and competencies needed in the field to reduce the environmental impact of processes and medications. A more environmentally conscious workforce in the pharmaceutical industry is creating the necessary ripple effect for the adoption and implementation of green principles across various pharmaceutical environments. Patients should also learn to avoid accumulating medications and disposing of them safely and correctly. Adopting environmentally friendly practices leads to a reduction in the use of chemicals and waste generation, which in turn leads to a reduction in the pollutants that contribute to climate change.

The increasing production and use of pharmaceutical and veterinary products has had an impact on the environment over time. Drug production processes have a significant impact on the environment, which affects the value of chemistry to society. The pharmaceutical industry impacts the environment through the carbon footprint generated during the production of pharmaceutical products and throughout the supply chain, which can lead to climate change. Climate change may alter the incidence of vector-borne diseases by altering the population of species that act as disease vectors. Another consequence of climate change is the emergence of infectious diseases caused by pathogens that would otherwise be dormant [33-35].

Currently, increasing attention is being paid to the presence and fate of active pharmaceutical ingredients, solvents, intermediates and raw materials that may be present in water and wastewater, including pharmaceutical wastewater. Traditional wastewater treatment methods, such as activated sludge, are insufficient to completely remove active pharmaceutical ingredients and other wastewater components from these waters. Pharmaceutical wastewater has direct and indirect impacts on the environment and health, especially near pharmaceutical industrial sites. Although pharmaceutical factories produce untreated or partially treated wastewater, drinking water sources are contaminated. Various classes of pharmaceutical compounds such as analgesics, antidepressants, antihypertensives, contraceptives, antibiotics, steroids, hormones, etc. were detected in water samples ranging from mg/L to μg/L. Although the quantities detected are very small, they are highly toxic to humans, animals and aquatic life. To protect the environment and lifestyles from health risks, the concentration of pharmaceutical compounds in medical wastewater entering drinking water sources should be regularly monitored. This article highlights the toxicity, health risks, and environmental risk assessments associated with pharmaceutical contaminantsm [36-38].

Residues of many pharmaceutical products can be found in drinking water, plants and fruits, as well as in the tissues of fish and shellfish. Thus, people are exposed to these residues when they drink contaminated water and eat contaminated food. Pharmaceuticals in the environment can also influence the provision of important ecosystem services and have indirect effects on human health and well-being. Found the evidence that drug residues in drinking water and food affect human health, as well as the indirect effects of drugs on human health. Available evidence suggests that the risks of direct toxicity are low, but there are scenarios in which indirect effects are possible. Much remains to be done regarding the wider range of drugs and exposure pathways, and the links between the presence of drugs in the environment and the provision of ecosystem services.

Human drugs, hormones, antibiotics, analgesics, antidepressants and anticancer drugs indicate environmental risks. When it comes to veterinary products, hormones, antibiotics and parasiticides are often considered environmentally sensitive. These results are consistent with findings from the open scientific literature on approaches to environmental drug prioritization. Promising approaches such as environmental risk assessment of pharmaceuticals play an important role in minimizing the problems caused by pharmaceuticals in the environment. However, the regulatory framework for environmental risk assessment can be improved by integrating the environment into the risk-benefit analysis of drugs for human use, (ii) improving risk management capabilities, collecting data on existing drugs, and improving the availability of data for environmental risk assessment. In addition, more general and integrative stages of regulation, legislation and research have been developed and presented in this article. To minimize the amount of pharmaceuticals in the environment, they should strive to improve existing pharmaceutical legislation, prioritize pharmaceuticals present in the environment, and (iii) improve the availability and collection of pharmaceutical data.So, the presence of pharmaceuticals in the environment has received increasing attention. Medicines are released into the environment and can have harmful effects [25-27].

It is clear that priority must be given to environmentally relevant pharmaceutical substances. Existing pharmaceutical substances for which environmental data are lacking, as well as substances being considered for monitoring campaigns, need to be given priority attention to identify and minimize their environmental risk. According to the World Health Organization, concentrations of pharmaceuticals in water systems are expected to increase as the use of pharmaceuticals is expected to increase as they become more accessible to a growing world population. To be proactive, it is necessary to identify and prioritize the most important substances for the environment, which has become a challenge in recent years. Depending on the chemical properties of the substances, different approaches have been proposed. Most often, a combination of exposure and exposure data is used to prioritize environmentally significant chemicals. Several approaches have proposed using toxicological data to predict adverse effects on aquatic organisms (comparisons of several, but not all, approaches are included). Most published approaches to prioritization indicate the high environmental potential of various drug classes. Human medicines are often a priority, with all attention paid to hormones, antibiotics, psychotropic, anti-inflammatory and cytostatic substances, as well as beta blockers. In addition to hormones, antibiotics and parasiticides have proven to be environmentally important in veterinary medicines [28-30].

The origin and possible effects of human and veterinary drugs on aquatic and terrestrial organisms are relatively new topics. However, in recent decades, a large number of studies have been published indicating the varied effects of drugs on organisms and the occurrence

of drugs in different environmental areas on a global scale. It is now recognized that the environmental impact of pharmaceuticals is a global issue and not just a problem in developed countries. The general public, industry, research or regulatory authorities, do not want bioactive drugs to end up in the environment and therefore potentially in their drinking water. Therefore, the amount of pharmaceuticals in the environment needs to be minimized using all available strategies. Promising approaches such as ERA play an important role in minimizing problems before drugs enter the environment. These strategies need to be strengthened and adapted to minimize the amount of pharmaceuticals entering the environment [31-32].

The contamination of the environment by pharmaceutical residues presents a critical challenge to both ecosystem health and human well-being. The widespread presence of these substances in water, soil, and air underscores the need for a more comprehensive understanding of their environmental fate and effects. Current risk assessment approaches, which often examine individual compounds in isolation, are inadequate in addressing the complex interactions and cumulative risks posed by pharmaceutical pollutants, especially when combined with other environmental contaminants. Furthermore, the potential dangers of pharmaceutical transformation products, which may exhibit greater toxicity or persistence, remain underexplored. To address these concerns, a paradigm shift is required in environmental risk assessment, incorporating multi-substance interactions, long-term ecological impacts, and the effects of transformation products. The development of robust mitigation strategies—such as advanced waste treatment technologies, improved pharmaceutical disposal practices, and more stringent regulatory frameworks—must be prioritized. By adopting a more integrated, precautionary approach to pharmaceutical contamination, we can better protect ecosystems and human health from the growing threat posed by these persistent pollutants. Future research and policy initiatives should focus on improving our understanding of these substances, developing innovative solutions to reduce their environmental impact, and ensuring sustainable management practices for pharmaceuticals.

Regarding environmental risk assessment, (i) include the environment in the risk-benefit analysis of pharmaceutical products for human use, (ii) improve risk management capabilities, (iii) collect data on existing pharmaceutical products, and (iv) improve environmental availability risk These assessments represent some important next steps. The biological effects to environmental exposures promise interesting results, although very few studies have been conducted on wild animals or caged organisms, such as in the wild or in ecologically significant environments. This may be due to the lack of analytical method protocols as well as the variety of pharmaceutical structural features that are not easy to handle but need to be taken into account.

Various policies need to be implemented throughout the life cycle of pharmaceutical products, including source-oriented, consumer-oriented and waste management-oriented activities. The most effective solutions must be implemented at the source, before drugs enter the environment. These measures include rational drug consumption, prescribing more environmentally friendly drugs and developing harmless and easily biodegradable drugs. Improved disease prevention, personalized medicine, improved package sizes, and PC redistribution markets may go some way to avoiding drug waste. The next step is to prevent unavoidable waste from entering the environment. Therefore, correct collection and disposal of is critical and must be adapted to national and local conditions. Finally, education of health care professionals and the public, as well as partnerships between environmental scientists

and clinicians, paharmacists are important at all stages of the pharmaceutical product life cycle. All joint efforts must be guided by a One Health approach to combat pharmaceutical waste and improve the health of people, animals and the environment, which are closely linked. To reduce contamination levels when consuming medicines should be: Creation of a system for collecting drug waste generated by the population; Conducting awareness-raising work with the population, employees of healthcare institutions and other target groups on the topic of environmental pollution by drug waste; Taking into account environmental factors when choosing and prescribing treatment. At the same time, there is no need to put environmental protection above the human need for treatment; Development and implementation of wastewater treatment systems. It should be taken into account that urban wastewater has an unstable composition in terms of names and concentrations of drugs. A higher priority is to prevent drug residues from entering the city sewer system.

The widespread contamination of the environment by pharmaceutical residues represents a significant and escalating global concern. These pollutants infiltrate water bodies, soil, and even air, leading to severe ecological disruptions, biodiversity loss, and potential long-term health risks for humans and wildlife. Their persistence, bioaccumulation, and role in fostering antimicrobial resistance further complicate their impact, demanding urgent and comprehensive intervention. Despite growing awareness, existing mitigation measures remain insufficient, necessitating a paradigm shift toward more sustainable pharmaceutical production, improved waste disposal, and enhanced regulatory frameworks.

To effectively address this crisis, a multi-pronged approach is essential. Advanced wastewater treatment technologies, such as membrane filtration, bioremediation, and oxidation processes, must be widely implemented to reduce pharmaceutical contaminants before they enter natural ecosystems. Strengthening regulations and global policies is critical to ensuring stricter controls on pharmaceutical manufacturing, prescription practices, and disposal methods. Additionally, promoting public awareness and responsible medication disposal can play a key role in minimizing environmental contamination at its source.

Risk assessment frameworks must also be refined to better understand the complex interactions of pharmaceutical residues within ecosystems. Integrating cutting-edge analytical techniques, predictive models, and interdisciplinary research will enable more accurate hazard evaluation and inform targeted mitigation strategies. Furthermore, the development of green pharmaceuticals—biodegradable drugs designed to minimize environmental impact—offers a promising long-term solution to this issue.

Addressing pharmaceutical pollution requires collective action from governments, researchers, healthcare providers, industries, and the general public. By adopting a proactive, science-driven approach, we can mitigate the adverse effects of pharmaceutical contamination, protect ecological integrity, and safeguard public health for future generations. The time to act is now—delaying intervention will only exacerbate the environmental and health consequences of unchecked pharmaceutical pollution.

CONCLUSIONS

The pervasive presence of pharmaceutical contaminants in the environment presents a growing threat to ecosystems and public health. These pollutants disrupt biodiversity, alter ecological functions, and contribute to antimicrobial resistance, posing long-term risks that

require urgent attention. Given their persistence and complex interactions within natural systems, conventional mitigation approaches are insufficient. Addressing this challenge necessitates a multifaceted strategy that integrates advanced wastewater treatment technologies, stricter regulatory measures, sustainable pharmaceutical production, and responsible disposal practices. Furthermore, enhancing risk assessment methodologies through improved analytical techniques, predictive modeling, and interdisciplinary research is essential for accurately evaluating the hazards posed by pharmaceutical residues. Collaborative efforts between policymakers, scientists, healthcare professionals, and the public are critical to developing and implementing effective solutions. By prioritizing proactive environmental management and strengthening global regulatory frameworks, we can mitigate the detrimental effects of pharmaceutical pollution and safeguard both ecological integrity and human well-being for future generations.

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THE ACADEMIC DISCOURSE ON PHARMACY PROFESSIONALS' CAREER OUTLOOKS: INSIGHTS AND ASSESSMENTS OF CRITICAL FACTORS SHAPING OCCUPATIONAL GROWTH FOR PHARMACISTS IN GEORGIA, OVERALL

ABSTRACT

The career prospects for pharmacy professionals in Georgia are influenced by a range of factors that shape their professional growth and opportunities within the healthcare sector. This study explores the key elements that impact the occupational development of pharmacists, focusing on educational pathways, regulatory frameworks, technological advancements, and evolving healthcare models. By analyzing trends in the job market, shifts in patient care, and the integration of pharmacists into interdisciplinary healthcare teams, the study provides a comprehensive overview of the challenges and opportunities faced by pharmacy professionals in Georgia. The research highlights the increasing demand for specialized pharmaceutical services, as well as the need for continuous professional development to keep pace with changes in healthcare practices and technologies. Additionally, the study examines how workforce shortages and the expansion of pharmacists' roles in patient care contribute to shaping career trajectories in the field. This paper offers insights into strategies that can support the professional growth of pharmacists, including enhanced training programs, policy adjustments, and workforce planning. The findings emphasize the importance of fostering a dynamic and adaptable pharmacy workforce to meet future healthcare needs in Georgia. This study explores the academic discourse surrounding the career trajectories of pharmacy professionals, with a focus on identifying and evaluating the key factors that influence occupational development for pharmacists in Georgia. Through a comprehensive analysis of vocational perspectives, the research highlights the challenges and opportunities that shape the professional growth of pharmacists in this region. Insights gathered from surveys, interviews, and literature reviews reveal critical elements such as educational advancements, regulatory frameworks, workplace dynamics, and societal perceptions that impact career progression. The study also assesses the role of continuing education, technological integration, and healthcare policies in fostering a conducive environment for professional development. By providing a holistic evaluation of these factors, this research aims to offer actionable recommendations for enhancing the career outlook of pharmacy professionals in Georgia. Ultimately, the findings underscore the importance of addressing these influences to ensure the sustained growth and adaptability of pharmacists in an evolving healthcare landscape. The career outlook for pharmacy professionals is shaped by a dynamic interplay of factors that influence their occupational growth and professional development. This study examines the key elements affecting the career prospects of pharmacists in Georgia, analyzing both local and global trends in the pharmacy sector. It delves into the academic discourse surrounding the evolving roles of pharmacists, with a particular focus on how education, healthcare policy, technological advancements, and shifts in patient care models impact their career trajectories. Through a comprehensive review of literature and stakeholder perspectives, the study assesses critical factors such as job market demands, professional competencies, and regulatory changes that are essential in defining the future of pharmacy practice. Moreover, it highlights the challenges and opportunities faced by pharmacists, addressing issues such as workforce shortages, the integration of pharmacists into interdisciplinary healthcare teams, and the expanding scope of pharmaceutical services. The paper also provides insights

into the strategies required to enhance career development opportunities for pharmacists in Georgia, including advancements in training programs, continued professional development, and the need for adaptive workforce planning. Ultimately, the findings contribute to a better understanding of the critical factors shaping pharmacists' careers and offer recommendations for stakeholders to foster a robust, adaptable, and sustainable pharmacy profession.

Keywords: Pharmacists', vocational, perspectives, evaluation, factors, influence, occupational, development, Georgia.

INTRODUCTION

The main goal of the study was to analyze the pharmacists' vocational perspectives impressions and evaluations of key issue of factors having influence on pharmacists' occupational development in Georgia, in general. The study was a quantitative investigation and analysis of pharmacists' vocational perspectives impressions and evaluations of key issue of factors having influence on pharmacists' occupational development in Georgia, in general by using questionnaires. Were conducted a survey study. The in-depth interview method of the respondents was used in the study. The approved questionnaires were used (Respondents were randomly selected): Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. Were used methods of systematic, sociological (surveying, questioning), comparative, mathematical-statistical, graphical analysis. The data were processed and analyzed with the SPSS program. Were conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p< 0.05$ as significant for all analyses. The research implementation required the following sub studies: The scientific talks of pharmacists' vocational perspectives impressions and evaluation of key issue of factors having influence on pharmacists' occupational development in Georgia, in general. According the study results found: Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines. Being a health care professional means being part of a team that is focused on one goal- helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient The were found and estimated factors having influence on pharmacists' professional development, these factors were: Interesting and valuable (informative) work; The favorable (prosperous) psychological climate within the collective in the colleagues' team; The possibility of career growth (development); The possibility of professional education or training; The social importance of the profession; Independence in work.

Pharmacists should see themselves as the main health care providers who can use their clinical experience in various public institutions. Pharmacists will always be an important health care provider based on their availability to patients through community pharmacy setting. This specific role of provider should never be reduced, as it serves the critical needs of patients (eg, dispensing and counseling for drug experience in nonprescription drugs, compounding, vaccinations, and the use of medication administration or monitoring devices) that not addressed by other health care providers [1-2].

However, this does not exclude pharmacists serving as suppliers of innovative alternative settings, such as outpatient clinics located in pharmacies and other retail outlets; in independent practice with a focus on medication management therapy, medication reconciliation, drug counseling or Pharmacogenomic; institution or organization, where they are responsible for the integration and promotion of patient care through the many other health care providers to facilitate continuity of care community; or organizations that coordinate research to improve practice through pharmacy practice based research networks [3-4]. Pharmacy providers should look for opportunities to engage in professional activities

between patient care, when and where they occur or as they develop in communities. For example, alternative practices may change to concentrate on providing pharmacy and health services for adults and retirement communities, given the growing number of them as Georgian population continues to age.

Pharmacy graduates who serve in the health services of Georgia, as these pharmacists to develop innovative practice settings, they should be drivers for expansion within the pharmacy practice in community, state and national levels. Pharmacy educators must ensure that graduates have the necessary knowledge, skills, attitudes/values, and practice experience, as well as confidence, drive, and entrepreneur spirit to be a driving force for change in order to facilitate these and other advances in the scope and type of community pharmacy practice [5-6]. Hospitals and other institutions and facilities, such as outpatient clinics, drug-dependency treatment facilities, poison control centers, drug information centers, and long-term care facilities, may be operated by the government or privately.

While many of the pharmacist's activities in such facilities may be similar to those performed by community pharmacists, they differ in a number of ways. Additionally, the hospital, clinic or institutional pharmacist has more possibility to interact closely with the prescriber and, therefore, to promote the rational prescribing and use of drugs in larger hospital and institutional pharmacies, is usually one of several pharmacists, and thus has a greater opportunity to interact with others, to specialize and to gain greater expertise, having access to medical records, is in a position to effect the option of drugs and dosage regimens, to monitor patient compliance and therapeutic response to drugs, and to recognize and report adverse drug reactions; can more easily than the community pharmacist assess and monitor patterns of drug usage and thus recommend changes where necessary serves as a member of policy-making committees, including those concerned with medicine choice, the use of antibiotics, and hospital infections and thereby actions of the preparation and composition of an essential-drug list or formulary is in a better position to educate other health professionals about the rational use of drugs, more easily participates in studies to determine the beneficial or adverse effects of drugs, and is involved in the analysis of drugs in body fluids, can control clinical manufacture and acquisition of drugs to ensure the supply of high-quality products, takes part in the planning and implementation of clinical trials [7-8].

Patient safety is a priority for all professionals - pharmacists - who care about the health. Patient safety is defined as the prevention of harm to patients, including by errors. For centuries, pharmacists were guardians / safeguards against "poisons" of substances that can cause harm to society. Now more than ever, pharmacist's responsibility is receiving safely the medication to the patient [9-10].

Protecting the people is the primary goal of pharmacy boards. On a broad scale, this mission requires a pharmacist to attend university for a specific number of years and to pass the state competency examination. Boards also set the parameters for what happens if a law or regulation is violated, what penalties result, and what infractions can cause if a pharmacist lose his or her license [11-12].

Pharmacy is one of the most regulated professions in the western countries and pharmacist profession is one of the most ethically challenging position. In EU countries state boards regulate, administer and influence every phase of pharmacy practice, including the demands and licensing testing for pharmacist. In western countries each state board is staffed up of pharmacists who come from every practice area — hospitals, clinic, chains, independent pharmacies, pharmaceutical factory, industrial pharmacy — as well as at least one consumer

(non pharmacist) representative. In most states, pharmacy board members are appointed by the government [13-14].

The health care brigade composes of the patient and all the health care professional specialists who have liability for patient care. This health care brigade demands to be well determined, and cooperation needs to be actively sought. Pharmacists have considerable character and role to play in this brigade. Pharmacists must demand to acclimatize their skills, knowledge, information and attitudes to this innovated role, which consolidates all traditional pharmaceutical sciences with hospital/clinical aspects of the patient care, clinical/hospital skills, management, administration and communication skills, active cooperation with medical brigade and solving of drug-related issues. If they are to be recognized as full members of the health care brigade, pharmacists will demand to adopt the essential attitudes required by health professional specialists laboring in this space: visibility, liability, duty, responsibility, accessibility in a working practice targeted at the general population, commitment to confidentiality and patient orientation. Pharmacists will demand to be competent, qualified, knowing and possess all that vision, opinion and a voice to fully integrate themselves into the health care brigade [15-16].

So, Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines. Being a health care professional means being part of a team that is focused on one goal- helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. This is a big job one that pharmacists cannot do alone. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient. The were found and estimated factors having influence on pharmacists' professional development, these factors were: Interesting and valuable (informative) work; The favorable (prosperous) psychological climate within the collective in the colleagues' team; The possibility of career growth (development); The possibility of professional education or training; The social importance of the profession; Independence in work.

Goal

The main aim of the study was to analyze the pharmacists' vocational perspectives impressions and evaluations of key issue of factors having influence on pharmacists' occupational development in Georgia, in general.

Methodology

Research objectives are materials of sociological research: the study was quantitative investigation by using survey (Questionnaire). The study was quantitative investigation by using survey (Questionnaire). The in-depth interview method of the respondents was used in the study. The approved questionnaires were used (Respondents were randomly selected. Questionnaire for pharmacist specialist, 810 pharmacist specialists participated in the study. We used methods of systematic, sociological (surveying, questioning), comparative, segmentation, mathematical-statistical, graphical analysis. The data was processed and analyzed with the SPSS program. Results and discussion: Questions and answers are given in the tables. On each question are attached diagrams or table. Questionnaire and diagrams

are numbered. Study of the data was processed and analyzed with the SPSS program. We conducted descriptive statistics and regression analyses to detect an association between variables. Statistical analysis was done in SPSS version 11.0. A Chi-square test was applied to estimate the statistical significance and differences. We defined $p < 0.05$ as significant for all analyses. The study's ethical items. In order to provide the study's ethical character each participant of it was informed about the study's goal and suggested of willingness of the work to be done. So, the respondents' written or oral compliance was got on that issue. All the studies were carried out by the selected organizations administrations' previous compliance. Were used Informed consent form for each respondent to participate in an anonymous survey. During the whole period of research, the participants incognita was also provided. For the international rules and criteria' conformity this human subject comprising given study was discussed and confirmed on the Bioethics Committee sessions of the YSMU. In order to meet the objectives, set in the research we also used the results obtained through analysis of available official information, studies and opinions about pharmacists, as well as the methods of quantitative studies. The research implementation required the following sub studies: The pharmacists' vocational perspectives impressions and evaluations of key issue of factors having influence on pharmacists' occupational development in Georgia, in general.

RESULTS AND DISCUSSION:

The career outlook for pharmacy professionals in Georgia is influenced by several critical factors that shape their roles, responsibilities, and opportunities within the healthcare system. As the scope of pharmacy practice evolves, there is an increasing demand for pharmacists to assume broader roles in patient care, particularly in areas like medication therapy management, disease prevention, and patient counseling. This shift is driven by the expanding recognition of pharmacists as integral members of interdisciplinary healthcare teams, capable of contributing to improved patient outcomes.

Educational pathways and continuous professional development play a significant role in shaping pharmacists' careers. As the healthcare landscape becomes more complex, the need for pharmacists to stay updated on the latest advancements in drug therapy, technology, and regulatory changes is crucial. The incorporation of new technologies such as automated dispensing systems, telepharmacy, and electronic health records requires pharmacists to develop specialized knowledge and skills. Therefore, investing in advanced training and certification programs is essential to ensuring that pharmacists remain well-prepared to meet the demands of modern healthcare.

However, while there are ample opportunities for growth, several challenges hinder the development of pharmacy professionals in Georgia. A critical issue is the shortage of pharmacists, which has placed additional strain on existing professionals and can impact their job satisfaction and career advancement. Furthermore, the current healthcare system's reliance on traditional roles for pharmacists often limits their ability to expand into more diverse areas of patient care. Overcoming these barriers requires not only changes in workforce planning but also a redefinition of the pharmacist's role in healthcare delivery.

The integration of pharmacists into primary care teams and their involvement in direct patient care represents a promising avenue for enhancing their professional standing and career prospects. Expanding pharmacists' responsibilities in managing chronic conditions, conducting health screenings, and providing immunizations offers opportunities for further occupational growth while simultaneously addressing healthcare gaps in Georgia.

Additionally, creating collaborative practice agreements and improving reimbursement structures for these expanded services will encourage pharmacists to take on these enhanced roles.

The career development of pharmacy professionals in Georgia hinges on addressing these critical factors—educational advancement, workforce shortages, role expansion, and policy reforms. By fostering an environment that encourages continuous learning, broadens the scope of pharmacy practice, and enhances workforce planning, Georgia can cultivate a more dynamic and sustainable pharmacy profession. Such measures will not only improve career prospects for pharmacists but also contribute to the overall improvement of healthcare delivery in the state.

In western countries are actively working clinician pharmacist, pharmacist and family doctor system, it plays an important role in pharmaceutical care. In western countries and in many developing countries pharmacist professions a regulated sector in health, as well as family medicine. Pharmacist, as well as the family doctor, needs higher education, further Diploma, and continuing pharmaceutical education, Pharmacist's license and periodic accreditation. in pharmacy, on pharmacists position works only higher pharmaceutical education specialists, Who graduated by the state recognized and accredited universities, and colleges. In Georgia pharmacist further diploma , continuing pharmaceutical education, pharmacist licensing and accreditation regulatory legislative base is not perfect. Today, the pharmacist profession in Georgia is impaired, pharmacist profession is deleted from health adjustable medical fields, Therefore degree in pharmacy or higher education in pharmacy losing profession opinion and values. In Georgia not conducted pharmacists certification, re-certification, accreditation and licensing state programs. Therefore profession pharmacist specialty becomes given position by the pharmacy owner, and not only from the university awarded qualification. Because of the above reasons in Georgia in drugstores for pharmacist position is no longer necessary higher pharmaceutical education, in drugstore any person has the right to work as a pharmacist position, any educated person or a person without medical or pharmaceutical education may be given a "position" Pharmacist "according pharmacy owner desired, pharmacy profession granting needs 4-5 year study at medical and other universities.In Georgia drugstore pharmacist interpreted as the only drug-dealer-seller. Pharmacist as regulated medical specialists ignored in Georgian Health-care System. That is why higher pharmaceutical education system should be moved to a new model direction, which will be more focused on pharmacotherapy, pharmaceutical care, and clinical pharmacy. Therefore, in future pharmacist profession in Georgian health care system should become most important link. In the state health policy, it is necessary to develope pharmacist profession's concepts and common principles. pharmacist profession should become regulated health care job, look like family doctor. In Georgia should be developed and implemented pharmacists registration, licensing, and accreditation new standards accordance with international pharmaceutical programs. Also qualified pharmacist in Georgia should have the right to work as pharmacist in other European Countries. Georgian pharmacist Certificate should have recognition in western countries, and Georgia should create pharmacist registration standard which is exist in Great Britain and other Western countries [17-20].

On the question to what extent, you have realized your professional capabilities, skills and habits? Pharmacists' 18.4% answer -to the full extent, pharmacists' 46.3% answer -partially, more than 50% of own potential, pharmacists' 24.7% answer- partially, less than 50% of own potential, pharmacists' 10.6% answer-cannot say. See Table-1.

Table 1. To what extent respondents have realized professional capabilities, skills and habits.

To what extent you have realized your professional capabilities, skills and habits?					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 To the full extent	149	18.4	18.4	18.4
	2 Partially, more than 50% of own potential	375	46.3	46.3	64.7
	3 Partially, less than 50% of own potential	200	24.7	24.7	89.4
	4 Can not say	86	10.6	10.6	100.0
	Total	810	100.0	100.0	

Source – study results

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor). Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work. On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work-pharmacists' 2.6% evaluate by 1 point, pharmacists' 4.9% evaluate by 2 points, pharmacists' 14.7% evaluate by 3 points, pharmacists' 42% evaluate by 4 points, pharmacists' 35.8% evaluate by 5 points. See Table-2.

Table 2. Interesting and valuable (informative) work of respondents', having influence on professional development, evaluated under 5-points scale (system).

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	21	2.6	2.6	2.6
	2	40	4.9	4.9	7.5
	3	119	14.7	14.7	22.2
	4	340	42.0	42.0	64.2
	5	290	35.8	35.8	100.0
	Total	810	100.0	100.0	

Source – study results

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The favorable (prosperous) psychological climate within the collective in the colleagues' team. On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The favorable (prosperous) psychological climate within the collective in the colleague's team. -pharmacists' 3.1% evaluate by 1 point, pharmacists' 4.2% evaluate by 2 points, pharmacists' 17.7% evaluate by 3 points, pharmacists' 35.6% evaluate by 4 points, pharmacists' 39.5% evaluate by 5 points. See Illustration-1.

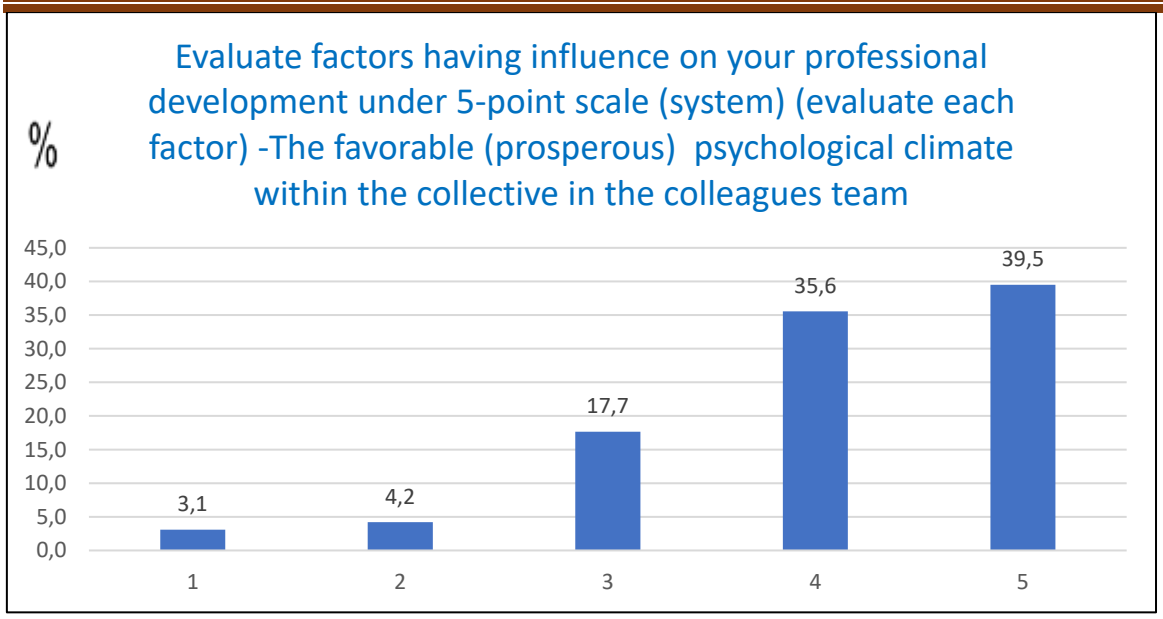


Illustration 1. The favorable (prosperous) psychological climate within the collective in the colleague's team of respondent's, having influence on professional development, evaluated under 5-points scale (system).
Source – study results.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development). On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development)- pharmacists' 5.1% evaluate by 1 point, pharmacists' 5.2% evaluate by 2 points, pharmacists 17.2% evaluate by 3 points, pharmacists' 39.6% evaluate by 4 points, pharmacists' 33% evaluate by 5 points. See Table-3.

Table 3. The possibility of career growth (development) of respondents', having influence on professional development, evaluated under 5-points scale (system).

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development)					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	41	5.1	5.1	5.1
	2	42	5.2	5.2	10.2
	3	139	17.2	17.2	27.4
	4	321	39.6	39.6	67.0
	5	267	33.0	33.0	100.0
	Total	810	100.0	100.0	

Source – study results

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "The possibility of professional education or training". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The possibility of professional education or training-pharmacists '2.3 % evaluate by 1 point, pharmacists' 3.7% evaluate by 2 points, pharmacists' 15.3% evaluate by 3 points, pharmacists' 33.8% evaluate by 4 points, pharmacists' 44.8% evaluate by 5 points. See Illustration-2.

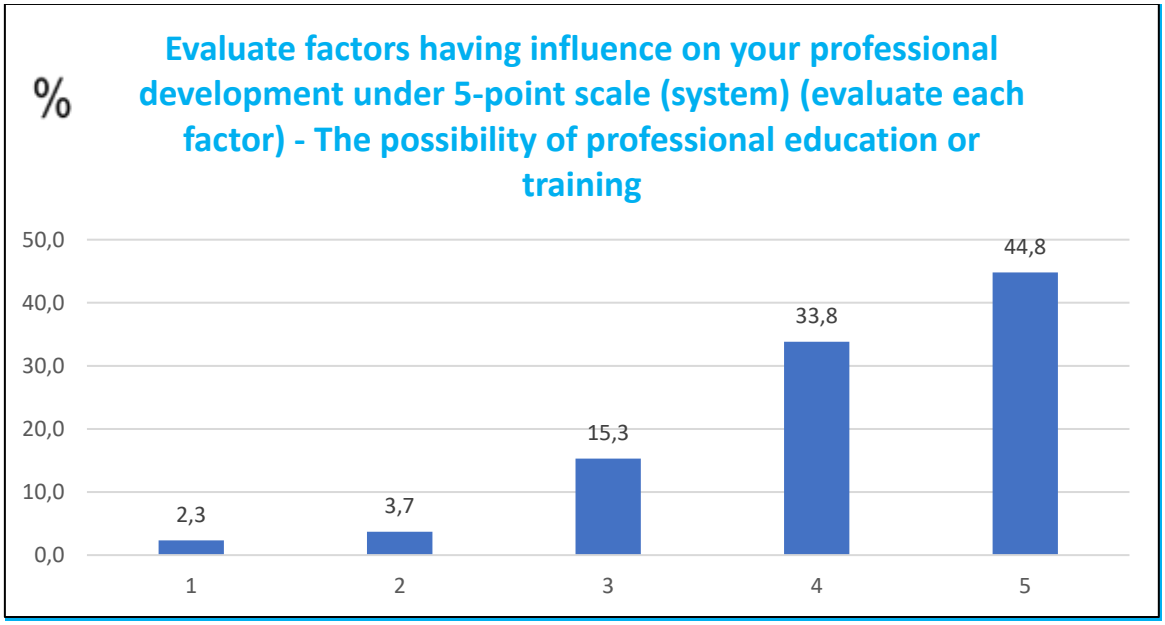


Illustration 2. The possibility of professional education or training of respondents', having influence on professional development, evaluated under 5-points scale (system). Source – study results.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "The social importance of the profession". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The social importance of the profession-pharmacists' 3.5% evaluate by 1 point, pharmacists' 3.8% evaluate by 2 points, pharmacists' 14% evaluate by 3 points, pharmacists' 36% evaluate by 4 points, pharmacists' 42.7% evaluate by 5 points. See Table-4.

Table 4. The social importance of the profession of respondents, having influence on professional development, evaluated under 5-points scale (system).

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The social importance of the profession					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	28	3.5	3.5	3.5
	2	31	3.8	3.8	7.3
	3	113	14.0	14.0	21.2
	4	292	36.0	36.0	57.3
	5	346	42.7	42.7	100.0
	Total	810	100.0	100.0	

Source – study results

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) – "Independence in work". On the question-Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - Independence in work-pharmacists' 3.8% evaluate by 1 point, pharmacists' 4.1% evaluate by 2 points, pharmacists' 14.6% evaluate by 3 points, pharmacists 34.9% evaluate by 4 points, pharmacists' 42.6% evaluate by 5 points. See Illustration-3

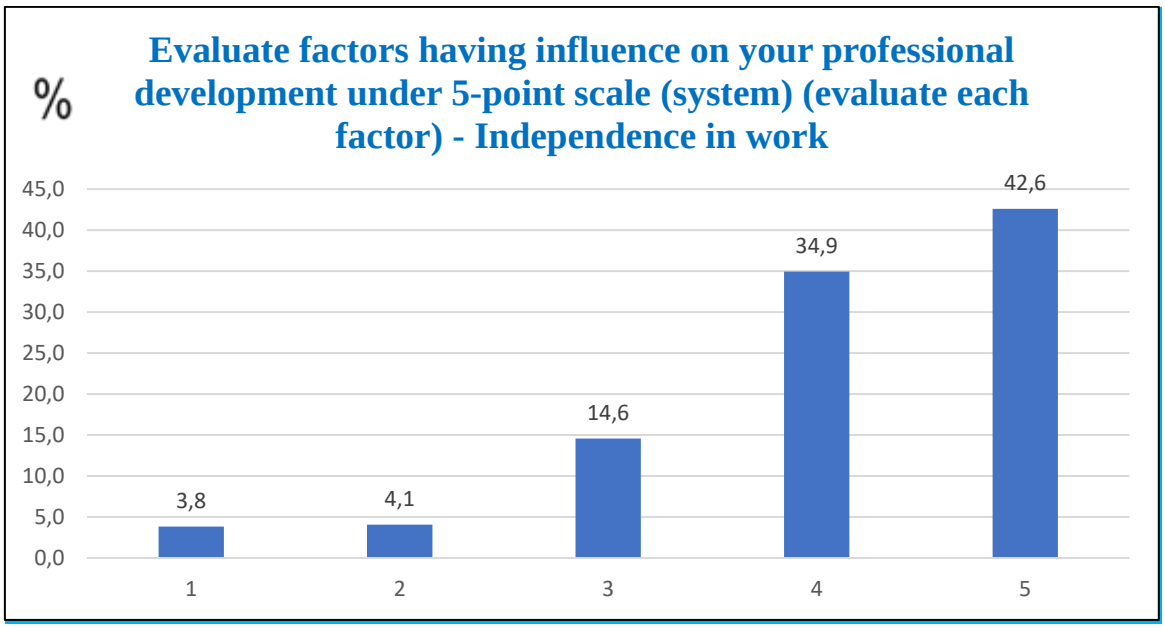


Illustration 3. Independence in work of respondents', having influence on professional development, evaluated under 5-points scale (system).
Source – study results.

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor). Report on the question- Evaluate factors having influence

on your professional development under 5-points scale (system) (evaluate each factor). See-Table-5.

Table 5. Report of factors having influenced of respondents' professional development evaluated under 5-points scale (system).

Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor)			
Report	Mean	Median	Std. Deviation
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -Interesting and valuable (informative) work	4.03	4.00	0.967
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The favorable (prosperous) psychological climate within the collective in the colleagues' team	4.04	4.00	1.008
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) -The possibility of career growth (development)	3.90	4.00	1.075
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The possibility of professional education or training	4.15	4.00	0.969
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - The social importance of the profession	4.11	4.00	1.010
Evaluate factors having influence on your professional development under 5-points scale (system) (evaluate each factor) - Independence in work	4.08	4.00	1.036

Source – study results

In your opinion, at what level it is possible to cease education? On the question -In your opinion, at what level it is possible to cease education? Pharmacists' 4.3% answer -after getting specialist diploma (degree), pharmacists' 11.2% answer- after getting the specialist certificate, pharmacists' 84.4% answer -education should not be ceased. See Table-6.

Table 6. Respondents' opinion, at what level possible to cease education.

In your opinion, at what level it is possible to cease education?					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 After getting specialist diploma (degree)	35	4.3	4.3	4.3
	2 After getting the specialist certificate	91	11.2	11.2	15.6
	3 Education should not be ceased	684	84.4	84.4	100.0
	Total	810	100.0	100.0	

Source – study results

On the question-have you used knowledge in the practice, obtained from professional publications? Pharmacists' 51.4 % answer yes, pharmacists' 40.7% answer –partially, pharmacists' 7.9% answer-no. See Illustration-4.

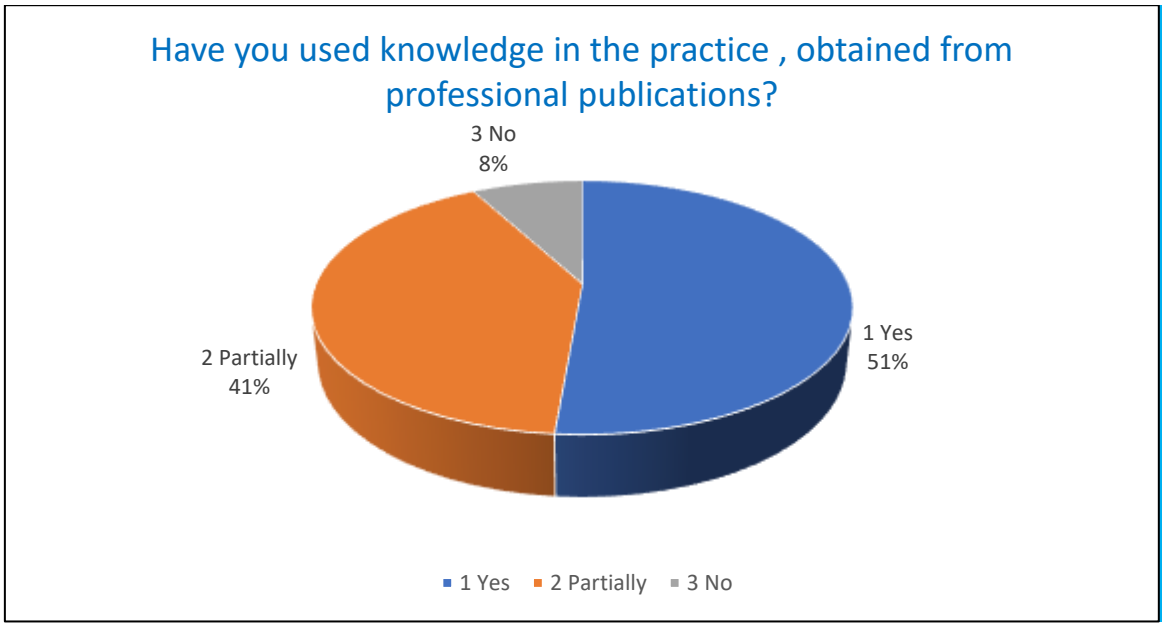


Illustration 19. Opinion of respondents having used knowledge in the practice, obtained from professional publications.
Source – study results.

What issues (questions) of pharmaceutical activity are the most essential (relevant) for you? (You can specify several answers). On the question-What issues (questions) of pharmaceutical activity are the most essential (relevant) for you? Pharmacists' 64% answer new drugs (medications), about drugs generic, chemical and brand names, pharmacists' 59% answer psychology of communication (relations) with customers , pharmacists' 66.8% answer issues of pharmacotherapy of certain diseases, pharmacists' 68.9% answer the safety , effectiveness and quality of the drugs (medications), pharmacists' 70.6% answer pharmacology, pharmacodynamics and pharmacokinetics issues, pharmacists' 44.9% answer the normative legal regulation of pharmaceutical activity, pharmacists' 29.8 % answer drug technology issues, pharmacists' 13.6 % answer pharmacognosy, pharmacists' 19% answer pharmaceutical organization and economics and pharmaceutical business, pharmacists' 34.7% answer pharmacy management and pharmaceutical marketing , pharmacists' 11.1% answer pharmacochemistry, pharmacists' 11.9% answer toxicology, pharmacists' 33% answer clinical pharmacy , pharmacists' 60.1% answer pharmaceutical care, pharmacists' 9.5% answer pharmaceutical analysis, pharmacists' 6.2 % answer toxicological chemistry, pharmacists' 10.6% answer pharmaceutical technologies, pharmacists' 11.7% answer nutrition, pharmacists' 22% answer pharmaceutical cosmetics and perfume, pharmacists' 18% answer social pharmacy and public health, pharmacists' 17.3% answer computer technology and pharmaceutical information, pharmacists' 16.3% answer phytotherapy, pharmacists' 22.6% answer routes of drug administration, pharmacists' 19.5% answer drug forms and drug design, pharmacists' 24.2% answer drugs toxic effects, pharmacists' 29.3% answer rules of drug administration, pharmacists' 15.3%

answer cost-effectiveness and cost-benefits of drugs, pharmacists' 32% answer terms and conditions of storage of drug (Conditions and shelf-life). See Table-7.

Table 7. Mostly essential pharmaceutical activity issues for respondents.

What issues (questions) of pharmaceutical activity are the most essential (relevant) for you? (You can specify several answers).		
	Count	Column N %
1 New drugs (medications), about drugs generic, chemical and brand names	518	64.0%
2 Psychology of communication (relations) with customers	478	59.0%
3 Issues of pharmacotherapy of certain diseases	541	66.8%
4 The safety, effectiveness and quality of the drugs (medications)	558	68.9%
5 Pharmacology, pharmacodynamics and Pharmacokinetics issues	572	70.6%
6 The normative legal regulation of pharmaceutical activity	364	44.9%
7 Drug Technology issues	241	29.8%
8 Pharmacognosy	110	13.6%
9 Pharmaceutical organization and economics and pharmaceutical business	154	19.0%
10 Pharmacy Management and pharmaceutical Marketing	281	34.7%
11 Pharmachemistry	90	11.1%
12 Toxicology	96	11.9%
13 Clinical Pharmacy	267	33.0%
14 Pharmaceutical care	487	60.1%
15 Pharmaceutical Analysis	77	9.5%
16 Toxicological Chemistry	50	6.2%
17 Pharmaceutical Technologies	86	10.6%
18 Nutrition	95	11.7%
19 Pharmaceutical cosmetics and perfume	178	22.0%
20 Social Pharmacy and Public Health	146	18.0%
21 Computer Technology and Pharmaceutical Information	140	17.3%
22 Phytotherapy	132	16.3%
23 About routes of drug administration	183	22.6%
24 Drug forms and drug design	158	19.5%
25 About drugs toxic effects	196	24.2%
26 About rules of drug administration	237	29.3%
27 About cost-effectiveness and cost-benefits of drugs	124	15.3%
28 About terms and conditions of storage of drug (Conditions and shelf-life)	259	32.0%
29 Other	0	0.0%

Source – study results

What is your attitude to qualification upgrading (improvement) study courses? On the question-What is your attitude to qualification upgrading (improvement) study courses? Pharmacists' 55.6% answer I learn with great pleasure, pharmacists' 38.6 % answer learning process rise interest to me, pharmacists' 5.8% answer -I have indifferent attitude toward learning. See Table-8.

Table 8. Attitude of respondents to qualification upgrading (improvement) study courses.

What is your attitude to qualification upgrading (improvement) study courses?					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 I learn with great pleasure	450	55.6	55.6	55.6
	2 Learning process rise interest to me	313	38.6	38.6	94.2
	3 I have indifferent attitude toward learning	47	5.8	5.8	100.0
	Total	810	100.0	100.0	

Source – study results

Pharmacists have a lot of public health functions that can benefit from the unique experience of pharmacists, which may include pharmacotherapy, pharmaceutical care, and pharmacy assistance. In addition to dispensing medicines, pharmacists have proved to be an accessible resource for information on health and medicines. The centralized position of the pharmacist in the society and clinical competence are invaluable. It is important to review and integrate public health practices into pharmacological training and pharmaceutical care. Encouraging cross-training will also increase the resources and help meet the needs of the workforce in the fields of pharmacy and public health. The Georgian Pharmacists Association has strongly supported the role of the pharmacist in public health. Through Trans disciplinary approaches, it is assumed that the pharmacist's contribution to public health, health care, health education, disease prevention and health promotion, public health promotion and the quality of health will help in achieving optimal public health outcomes [21-25].

As pharmacists proceed to become more clinically-oriented health care professionals, with increased responsibilities, liability and accountabilities for pharmaceutical care clear pathways for workforce development, coupled with professional recognition and credentialing of practitioners, is an important consideration. This represents a clear opportunity for transnational collaboration and further opportunities for transnational recognition of advanced capabilities for the pharmacy workforce. An obviously display and assurance of competence and facilities that is well-proportioned with progressive and expert practice is an obviously message to fostered public that pharmacists own this competence; occupational recognition, credentialing and quality assured specialism are part of this to show of competence, skills and capability. There is in the interest of patients, health systems and pharmacist profession that were develop a common and shared understanding of what we mean by specialization and by innovative practice. This is a key driver for future workforce perfection. [26-28]

The rational use of drugs remains the exception rather than the rule. For those people who do take medicines, more than half of all prescriptions are incorrect and more than half of the people involved fail to get them correctly. In additive, there is growing concern at the

increase in the global spread of antimicrobial resistance, a major public health challenge. The global trend is for pharmacy to continue to become a more clinical, patient-facing profession, with enhanced responsibilities and accountabilities for pharmaceutical care in clinical environments; hence, clear pathways for workforce development, coupled with professional acknowledgment and credentialing of practitioners, becomes an important consideration. There is a clear opportunity for transnational collaboration and further opportunities for transnational recognition of advanced skills, capabilities for the pharmacy workforce management [29-32].

Responsible use of medicines implies that health-system stakeholder activities and capabilities are aligned to ensure that patients receive the right medicines at the right time, use them appropriately, and benefit from them. Bringing the right drugs to the patients who need them demands the engagement of all actors, including state, governments, and a vision on how to integrate society, public, people and private interests and to mobilize resources. While appropriate drug therapy is safer and more cost-effective than other treatment alternatives, there is no doubt that the personal and economic consequences of inappropriate drug therapy are enormous. It is important for public and people to be guaranteed that spending on pharmaceuticals represents good value for money. In view of their extensive academic background and their traditional role in preparing and providing medicines and informing patients about their use, pharmacists are well positioned to expect responsibility for the management of drug therapy. [33-36].

Pharmacists, as well noted as druggists, who are health care team professionals, they working in pharmacy (drug-story), the field of health sciences focusing on safe and effective using drugs. The pharmacist is a part of the health care team directly engaged with patient care services. The pharmacists hold university degree level training and education to consider the pharmacological mechanisms and actions of drugs, pharmacology, pharmacotherapy, toxicology,drug uses, therapeutic roles, side effects of drugs, possible drug interactions, and checking parameters [3]. This is engaged to Botany, biology, anatomy, chemistry, physiology, histology, Biophysics and pathophysiology. Pharmacists interpret and communicate this particularized information to patients, physicians, doctors and other health care producers [37-39].

Being a health care professional means being part of a team that is focused on one goal: helping the patient achieve better health. Pharmacists are a part of this health care team, and their duty is to help the patients make the best use of their medication. This is a big job one that pharmacists cannot do alone. Thus, within their profession, pharmacists have developed other categories of pharmacy workers to help get the work done more efficiently and allow pharmacists to be more focused on the patient [40-42].

Common pharmacies have been providing health care for many years, via giving consultation, advice, providing and delivering medicine when needed, or referring patients to other health care professionals. This report, however, reflects and represent the embedding of a formalized approach whereby pharmacies are covering for these services, and where self-care through pharmacists is measured as an integral part of the health system [43-45].

Pharmacists are health professionals who are dispensing prescription drugs to patients, also provide information about the medicines ordered by doctors. They explain the doctors' instructions to patients so that, people can safely and effectively use these medications. Another big issue is ensuring that drugs are used reasonably and rationally. This demands that patients get drugs assign to their clinical/hospital necessity, in doses that meet their own

individual needs for the sufficient period of time, and at the lowest cost to them and their public [46-49].

A pharmacist is a personality who is professionally competent and qualified to prepare and dispense medicine. The Pharmacist dispense drugs, check patient's health, and make sure that drugs do not interact in a harmful route. Pharmacist are drug experts eventually interested about their patients' wellness and health. Public health service interventions, higher level pharmaceutical care, rational pharmacotherapy and effective medicines supply chain management are main components of an accessible, sustainable, affordable and equitable health care system which ensures the efficacy, safety and quality of drugs. It is clear that pharmacy has a great role to play in the health sector reform process [50-53]. To do it so, although, the role of the pharmacist needs to be redefined and reoriented. Pharmacists have the capability and possibility to enhance therapeutic results and patients' quality of life within accessible resources, and must position themselves at the forefront of the health care system. The movement towards pharmaceutical care is a critical factor in this matter. While efforts to communicate the proper information to patients are as significant as providing the medicine itself. Pharmacists also have a vital contribution to make to patient care through managing pharmacotherapy and concurrent non-prescription or alternative therapies [54-56].

The analysis of key factors influencing the career prospects of pharmacy professionals in Georgia revealed several important trends and outcomes.

1. **Evolving Role of Pharmacists**: One of the most notable findings is the growing recognition of pharmacists as integral members of healthcare teams. Pharmacists are increasingly being involved in direct patient care, medication management, and disease prevention. The expansion of their responsibilities, including managing chronic conditions, conducting health screenings, and providing immunizations, is offering significant career growth opportunities and improving their job satisfaction.

2. **Educational Advancements**: The study found that continuous education and professional development are essential to keeping pharmacy professionals abreast of the latest developments in healthcare. With the integration of new technologies, such as telepharmacy and electronic health records, pharmacists in Georgia are increasingly pursuing advanced certifications and specialized training. This trend demonstrates a strong commitment to maintaining high standards of practice and meeting the growing demands of the healthcare sector.

3. **Workforce Shortages**: A critical issue identified in the results is the ongoing shortage of pharmacists in Georgia. This shortage has placed considerable pressure on the existing workforce, resulting in high workloads and potential burnout. However, the shortage also creates opportunities for job security and professional growth, as employers seek to fill positions in various healthcare settings.

4. **Impact of Regulatory and Policy Changes**: Regulatory and policy changes in Georgia are also shaping pharmacists' career opportunities. The state has made strides in expanding the role of pharmacists through collaborative practice agreements and adjustments in reimbursement policies, which have allowed pharmacists to take on more responsibilities in patient care. These changes are expected to continue to positively influence career development by expanding pharmacists' scope of practice and ensuring fair compensation for their expanded roles.

5. **Technological Integration**: The adoption of new technologies in healthcare, such as automated dispensing systems and telemedicine, has significantly altered the landscape for pharmacy professionals. Pharmacists are increasingly required to develop technological competencies to stay competitive in the job market. The integration of these technologies has opened new opportunities for pharmacy professionals to work in innovative settings, such as telepharmacy and digital health platforms, which are expected to grow in importance in the coming years.

In conclusion, the results highlight a positive trend toward the expansion of pharmacists' roles in healthcare, driven by increasing responsibilities, evolving education, and advancements in technology. However, the challenges posed by workforce shortages and the need for further policy reforms remain central to shaping the future career prospects for pharmacy professionals in Georgia.

CONCLUSION:

The career prospects of pharmacy professionals in Georgia are shaped by a complex array of factors, ranging from evolving healthcare needs to advancements in technology and changes in the regulatory environment. As the role of pharmacists continues to expand within healthcare teams, their contributions to patient care are becoming increasingly recognized, offering new opportunities for professional growth. However, challenges such as workforce shortages, the need for continued education, and the integration of pharmacists into diverse healthcare settings require focused attention to ensure the sustainability of the profession. To foster the long-term development of pharmacists, it is crucial to implement strategies that support continuous learning, enhance career opportunities, and adapt to the changing landscape of healthcare. Strengthening educational programs, updating policies, and providing resources for professional development will be key in equipping pharmacists with the necessary tools to succeed. Furthermore, addressing workforce shortages and optimizing the use of pharmacists in patient care will ensure that the profession thrives in Georgia. By understanding and addressing the factors that influence career development, stakeholders can help build a resilient pharmacy workforce capable of meeting the evolving healthcare demands in Georgia. Ultimately, fostering a dynamic and well-equipped pharmacy profession will enhance the overall healthcare system and contribute to improved patient outcomes in the region.

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THE KEY ISSUE FEATURES OF WEARABLE-DEVICE-IDENTIFIED RAPID HEART RHYTHM – INNOVATIVE TECH ADVANCEMENTS SUPPORTING MEDICAL CARE (A CASE REPORT)

ABSTRACT

The integration of wearable technology into healthcare has revolutionized the detection and management of rapid heart rhythms, offering unprecedented opportunities for early intervention and improved patient outcomes. This study explores the critical aspects of wearable-device-identified rapid heart rhythms, emphasizing the role of innovative

technological advancements in enhancing clinical practice. By leveraging continuous monitoring capabilities, these devices provide real-time data, enabling timely diagnosis and personalized treatment strategies. The research highlights the accuracy, reliability, and accessibility of wearable technologies, while also addressing challenges such as data interpretation, patient adherence, and integration into existing healthcare systems. Furthermore, the study discusses future directions for wearable technology, including the development of advanced algorithms, improved sensor precision, and expanded applications in preventive cardiology. The findings underscore the transformative potential of wearable devices in supporting medical care, ultimately contributing to more efficient, patient-centered healthcare solutions. In modern era different types of electronic devices, such as smartwatches, have become very popular for the monitoring of health, especially for people with heart conditions. Arrhythmia symptoms are frequent complaints in patients with heart problems, often require a repeated electrocardiogram (ECG) and Holter monitoring. Data regarding the clinical utility of wearable technologies are limited in that population. We hypothesize, that an Apple Watch can capture life threatening arrhythmias in cases, when it has not been detected with Holter monitor. In this case report we present the heart electrical recordings of a 40 years old male patient with previous history of acute myocardial infarction (MI), who submitted recordings obtained from his Apple Watch during moments, when he had feeling of palpitations and sense of near feinting. Past history was remarkable with coronary stent implantation due to ST segment elevation acute anterior myocardial infarction (STEMI). It was delayed admission to the hospital with total akinesis of the left anterior descending artery (LAD) zone and deceased ejection fraction (EF) 35%. Implantable cardioverter defibrillator (ICD) was recommended, but the patient refused. The Apple Watch captured rhythm abnormalities that matched patient's complaints. Smartwatch detected ventricular tachycardia (VT) and finally patient underwent successful implantation of ICD. This case demonstrates, that use of smartwatches can be helpful and enable clinicians to identify abnormalities that many traditional at-home monitoring devices do not detect. Thus, wearable devices, such as the Apple Watch, could be used to help identify heart rhythm disorders in patients with high susceptibility having arrhythmias.

Keywords: Cardiac arrhythmia; Smartwatch; Ventricular tachycardia.

Introduction:

The rapid evolution of wearable technology has ushered in a new era in healthcare, particularly in the field of cardiology. Among its most promising applications is the detection and monitoring of rapid heart rhythms, a condition that, if left unaddressed, can lead to severe complications such as stroke, heart failure, or even sudden cardiac arrest. Wearable devices, such as smartwatches and fitness trackers, have emerged as powerful tools for continuous, non-invasive monitoring, enabling the early identification of arrhythmias like ventricular tachycardia. These innovations bridge the gap between traditional clinical settings and real-world patient experiences, providing clinicians with actionable insights derived from real-time data.

The integration of wearable technology into medical practice represents a significant advancement, offering the potential to transform how cardiovascular conditions are diagnosed, managed, and prevented. By empowering patients to take an active role in their health and providing healthcare professionals with a wealth of data

In recent years, wearable technology has revolutionized how we monitor health, providing unprecedented opportunities for early detection of critical medical conditions. Among these innovations, smartwatches have emerged as invaluable tools for cardiovascular health, with their ability to detect arrhythmias such as ventricular tachycardia (VT) standing out as a remarkable breakthrough. This capability is reshaping clinical practice, bridging the gap between consumer technology and advanced healthcare [15-16].

Ventricular tachycardia is a life-threatening arrhythmia originating in the heart's ventricles. It is characterized by an abnormally fast heart rate that can compromise cardiac output, leading to symptoms like dizziness, palpitations, syncope, or even cardiac arrest. Early detection is crucial, as untreated VT can escalate to ventricular fibrillation, a condition that requires immediate medical intervention [17-19].

Traditional detection methods, such as Holter monitors and implantable cardiac devices, are effective but often limited by accessibility, patient compliance, and cost. This is where smartwatches equipped with advanced sensors and algorithms offer a promising alternative.

VT and ventricular fibrillation (VF) are leading causes of sudden cardiac death (SCD) in patients with heart failure with reduced ejection fraction (HFrEF) [20-22].

Smartwatches are a widespread technology in this world and represent an innovation among most wearable devices. Modern smartwatches have developed in such a way that they can combine various functions, including making an ECG recording.

Smartwatches have mainly been studied to detect and monitor atrial arrhythmias, especially atrial fibrillation (AFB) [1-2] while there is a limited data in literature on detection of life-threatening ventricular arrhythmias [3,4,5]. We have no definite recommendations on use of new smartwatches for monitoring these arrythmias.

The Role of Smartwatches in VT Detection

Modern smartwatches are equipped with photoplethysmography (PPG) sensors and electrocardiogram (ECG) capabilities that enable continuous monitoring of heart rhythms. These devices utilize machine learning algorithms to analyze patterns and detect

irregularities indicative of arrhythmias. Several key features make them effective in VT detection:

1. **Continuous Monitoring**: Unlike traditional devices that are used intermittently, smartwatches provide 24/7 monitoring, increasing the likelihood of capturing transient arrhythmias.
2. **ECG Functionality**: Many smartwatches allow users to record single-lead ECGs on demand. These recordings can detect VT and other arrhythmias with clinically relevant accuracy.
3. **Real-Time Alerts**: Smartwatches can notify users when abnormal rhythms are detected, prompting timely medical attention.
4. **Data Sharing**: Most smartwatches integrate with health apps, enabling seamless sharing of data with healthcare providers for further evaluation.
   The integration of smartwatch technology into clinical practice has far-reaching implications:

1. **Early Diagnosis**: Early detection of VT can prevent adverse outcomes by facilitating timely intervention.
2. **Accessibility**: Smartwatches make arrhythmia detection more accessible to a broader population, including those in remote areas.
3. **Patient Engagement**: The use of consumer-friendly devices empowers patients to take an active role in their health management.
4. **Cost-Effectiveness**: Compared to traditional cardiac monitoring solutions, smartwatches offer a more affordable and scalable option.

As technology advances, smartwatches are likely to become even more sophisticated, with multi-lead ECG capabilities, improved algorithms, and integration with artificial intelligence for predictive analytics. Collaborative efforts between tech companies and healthcare providers will be pivotal in realizing the full potential of these devices in cardiology [23-27].

Our article is the one of the few published case reports of smartwatch-detected VT. Ease of use makes smartwatches a promising modern technology in the service of clinical practice for identifying ventricular arrhythmias and potentially improving patient outcomes [28-29].

Advancements in wearable technology have significantly influenced healthcare, particularly in the management of cardiovascular diseases. Smartwatches, initially designed for general fitness tracking, now feature sophisticated health-monitoring capabilities, such as heart rate tracking, photoplethysmography (PPG), and single-lead electrocardiogram (ECG) functionalities. These features have gained popularity among individuals with known cardiac conditions, offering continuous monitoring and immediate feedback [30-31].

Arrhythmias, including ventricular tachycardia (VT), are common in patients with heart disease and pose significant risks if undetected or untreated. Standard diagnostic tools like Holter monitors and implantable cardiac devices are effective but are often limited by availability, patient compliance, and cost. Wearable devices, such as the Apple Watch, provide a patient-friendly alternative that bridges the gap between clinical monitoring and daily health management [32-33].

Despite the potential of wearable devices, data on their utility in detecting life-threatening arrhythmias in high-risk populations remain limited. This highlights the need for further exploration of their role in clinical practice. This case report examines how a smartwatch

detected VT in a patient with a history of myocardial infarction and reduced ejection fraction, leading to timely and effective intervention [34-35].

The integration of wearable technology into clinical practice is redefining how arrhythmias, including life-threatening conditions like ventricular tachycardia (VT), are detected and managed. This case report exemplifies the potential of smartwatches, particularly the Apple Watch, as diagnostic tools in cardiac care. The patient's ability to capture VT episodes during symptomatic events provided crucial diagnostic data that traditional Holter monitoring failed to identify. This capability demonstrates the smartwatch's value as a patient-centric monitoring tool and highlights its broader implications for cardiovascular medicine [36-37].

Smartwatches equipped with electrocardiogram (ECG) capabilities enable real-time monitoring of cardiac activity. In this case, the Apple Watch identified VT during episodes of palpitations and near-syncope, aligning with the patient's symptoms and leading to the timely implantation of an implantable cardioverter defibrillator (ICD). These devices empower patients to document their symptoms and provide healthcare professionals with actionable data, bridging gaps in traditional cardiac diagnostics [38-40].

Unlike Holter monitors, which are used for a limited duration and require clinical oversight, smartwatches offer continuous, non-invasive monitoring and can be worn indefinitely. The convenience, accessibility, and affordability of these devices make them particularly beneficial for patients with high arrhythmic risk, such as those with reduced ejection fraction or prior myocardial infarction. This case demonstrates how wearable devices can complement conventional methods, offering additional insights when standard tools fall short [41-43].

This case underscores the transformative potential of wearable devices in arrhythmia detection. As technology evolves, smartwatches could be equipped with advanced features such as multi-lead ECG capabilities, real-time arrhythmia alerts, and automated reporting to healthcare providers. Moreover, their use could expand beyond arrhythmia detection to include other aspects of cardiac health, such as ischemia monitoring and heart failure management [45-46].

Case report:

We present a case of 40 years-of-age Caucasian male patient who had signs of an arrhythmia documented by an Apple Watch. He already had a formal arrhythmia diagnosis not yet conformed on other ambulatory cardiac monitoring studies, findings of Holter monitoring were nonconclusive, which did not detect arrhythmias matched his clinical symptoms.

Remarkable moments from the patient's past and family history: otherwise healthy person with stressful profession, nonsmoker, non-diabetic, with mild insulin resistance, physically active, mildly overweight, mildly elevated blood pressure, no complaints, coronary artery decease (CAD) genetically presented (his father and uncle suffered from MI in their 40-45 years). At first planed cardiologic checkup: normal ECG, normal echocardiography, normal exercise stress test, blood test reviled high level of low-density lipoprotein (LDL) 220 mg/dl; Statin for dyslipidemia and perindopril for hypertension ware prescribed, healthy life style, hypolipidemic diet and moderate physical activity had recommended.

Few weeks after, the patient was admitted to our hospital with new onset severe chest pain. Acute anterior STEMI due to total occlusion of proximal LAD had angiographically

confirmed. Admission was delayed 16-18 hours from the onset of the pain, patient was successfully treated by percutaneous coronary intervention, one drug eluting stent had impanated in LAD followed with medical therapy. Case was complicated with early effusive pericarditis, moderate mitral regurgitation, bilateral pleural effusion, heart failure. The left ventricular ejection fraction (EF) decreased to 32% due to total akinesia of the LAD zone. After recovery the patient was discharged with full guideline directed medical treatment (GDMT) of HFrEF, ICD implantation was strongly recommended to prevent SCD. The patient followed all recomndations, but refesed to implant the divice. As of his three-six-month evaluation, he remained well, but due to reduced EF 35% ICD implantation was still recommended. The patient refused again. After a period, he developed signs of an arrhythmia, ambulatory Holter monitoring revealed supraventricular and monomorphic ventricular extrasystoles, which have been managed with short course of amiodaron, unfortunately it caused subclinical hyperthyroidism and therefor was discontinued. Periodically patient felt as though his heart rhythm was abnormal and he had feeling of irregular heartbeat-palpitations and sense of near feinting. VT was considered. Repeated ambulatory Holter monitoring did not reveal any arrythmia. The patient refused to have the device. After Holter monitoring failed to capture a symptomatic event, the patient with his cardiologist decided to purchase a smartwatch for home monitoring. He recorded his ECG-s with Apple Watch. In few days he developed chest discomfort associated with palpitations and lightheadedness. He was on a routine job at his office, when these symptoms started abruptly and persisted for approximately several seconds (from 20 to 40). Recurrence of his symptoms resulted in a recording of a wide complex tachycardia suggestive and labeled by the device algorithm as potential “VT”. The patient sent recordings to his doctor. It turned out, that his Apple Watch recorded a wide complex tachycardia concerning for VT (Figure1) and a representative example of sinus rhythm (Figure 2).



Figure 1: Ventricular tachycardia

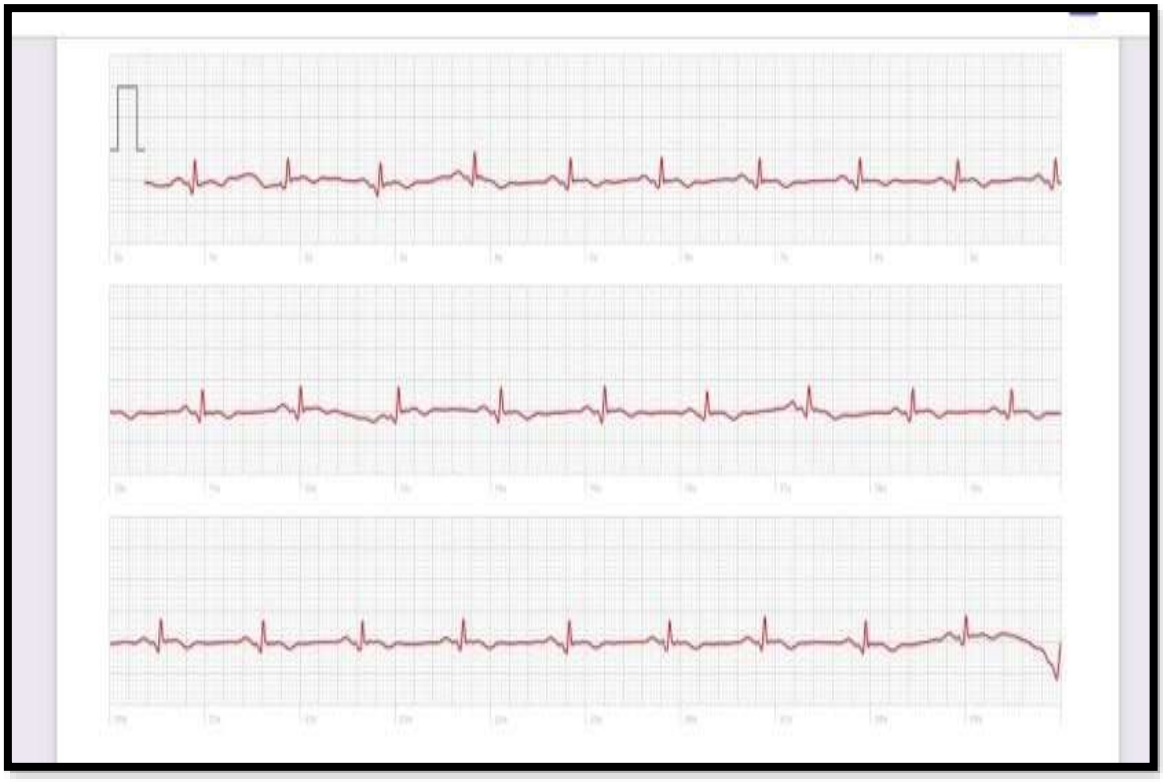


Figure 2: Normal sinus rhythm

Figure**1:** Apple Watch recording of symptomatic VT. Apple Watch recording demonstrating a regular, wide complex tachycardia-VT; The patient reported symptoms of chest discomfort associated with palpitations and lightheadedness.

Figure **2:** Apple Watch recording in normal sinus rhythm without symptoms.

Finally, the patient agreed and shortly after this incident underwent successful implantation of ICD.

Discussion:

The integration of smart watch technology into clinical practice represents a paradigm shift in cardiac monitoring and patient care. This case exemplifies the unique advantages and challenges associated with these devices, particularly in the detection of life-threatening arrhythmias like ventricular tachycardia (VT).

Key Strengths

1. **Early Detection of Critical Events**: The Apple Watch successfully identified VT, which traditional methods, such as Holter monitoring, might have missed due to intermittent usage or logistical challenges. This highlights the smartwatch's ability to provide continuous, non-invasive monitoring.
2. **Patient Empowerment**: The patient-driven nature of the monitoring process allowed the individual to capture and document symptomatic events as they occurred. This patient-initiated approach fosters engagement and enhances the reliability of diagnostic data.

3. **Clinical Correlation**: The smartwatch recordings directly aligned with the patient's reported symptoms, demonstrating their potential clinical relevance. This correlation between subjective complaints and objective data strengthens the case for their integration into routine practice.
4. **Cost and Accessibility**: Compared to traditional monitoring tools, smartwatches offer a more affordable, accessible solution for patients, particularly those in resource-limited settings or individuals reluctant to use invasive options.

Challenges and Limitations

1. **Accuracy and Reliability**: While the Apple Watch detected VT in this case, concerns about false positives and negatives persist. Variability in algorithm sensitivity and specificity across different devices must be addressed to ensure reliable clinical utility.
2. **Regulatory and Legal Considerations**: As consumer devices transition into medical-grade tools, stringent regulatory oversight is essential to validate their use in clinical practice. Clear guidelines on their application are necessary to establish trust among healthcare providers and patients.
3. **Integration into Healthcare Systems**: Seamless integration of wearable data into electronic health records (EHR) and clinical workflows remains a logistical challenge. Addressing this issue would maximize their impact in healthcare settings.
4. **Data Privacy and Security**: The collection and transmission of sensitive health data by smartwatches raise concerns about privacy and cybersecurity. Ensuring robust safeguards will be crucial in building confidence in these devices.

Implications for Clinical Practice

This case underscores the potential of wearable technology to complement traditional monitoring methods, particularly in high-risk cardiac patients. While challenges exist, the successful detection of VT and subsequent intervention in this case demonstrate the tangible benefits of smartwatch integration into clinical care. By addressing existing limitations and enhancing the technology, smartwatches could become indispensable tools for arrhythmia detection and broader cardiovascular health management [47-49].

The case of a 40-year-old male with a history of acute myocardial infarction (MI) and reduced ejection fraction highlights the transformative potential of smartwatch technology in detecting life-threatening arrhythmias. Despite previous recommendations for an implantable cardioverter defibrillator (ICD), the patient declined the procedure. Using his Apple Watch, the patient captured electrical heart recordings during episodes of palpitations and near-fainting sensations. These recordings revealed ventricular tachycardia, aligning with the patient's clinical symptoms and prompting successful ICD implantation [50-52].

This case underscores several critical points:

1. **Enhanced Detection Capability**: The Apple Watch successfully identified VT, a life-threatening condition that may have been missed by traditional Holter monitoring. This demonstrates the added value of wearable devices in capturing transient arrhythmias that occur sporadically.

2. **Patient-Initiated Monitoring**: Wearable devices empower patients to actively participate in their health monitoring. By recording symptoms as they occur, patients provide clinicians with valuable diagnostic data, bridging gaps in conventional monitoring.
3. **Clinical Utility in High-Risk Populations**: Patients with significant cardiac history, like the one in this case, can benefit immensely from smartwatch technology. These devices offer a non-invasive, accessible, and real-time monitoring solution for high-risk individuals.
4. **Integration into Standard Care**: The successful outcome in this case highlights the potential for smartwatches to complement existing diagnostic tools, particularly in cases where conventional methods fail or are declined by patients.

Although in recent years the popularity of smartphones has been increasing in terms of health monitoring, especially in arrhythmia monitoring, data regarding the use of wearable technologies in clinical practice are limited. Most studies include detection of AFB with smart- watches [6,7,8], there is less information about the detection of other arrhythmias [9,10,11].

Our case illustrates the potential benefits of this technology. This particular case turned out to be crucial in getting the right decision for the patient. However, caution and additional studies are needed to implement modern technologies in the cardiology service. With the Apple Watch, episodes of atrial fibrillation can be detected with the same success, which will allow us to think about prescribing adequate anticoagulation and protecting the patient from stroke[8]. Wearable devices have been well-studied in adults to recognize atrial fibrillation, however there is less information available on their effectiveness in monitoring of other rhythm disorders, especially life threatening arrythmias, such as VT [3,4,5].

Our case was interesting in that, despite maximal GDMT, the systolic function of left ventricle EF did not exceed 35%, the expected risks of SCD were explained to the patient many times and ICD implantation was strongly recommended, but it was difficult for a patient to make a correct decision, he dined to have a device [53-55].

By the time a 12-lead surface ECG was performed, it was a normal sinus rhythm with T-wave inversions in leads V1–V4 due to past anterior MI. Later the patient developed intermittent palpitations, feeling of an irregular heartbeat, rapid palpitations associated with near syncope. Holter monitoring was performed several times, not a single VT episode was observed. The patient was young and abstained from implantation for almost one year after acute episode, in the meantime he had acquired an Apple Watch and was sending normal cardiograms to his cardiologist. However, the recommendation for the ICD remained in force, he doubted the implantation until the end. Faintly decisive ECG was taken with a smartwatch and a VT episode was recorded (the watch makes a record in the form of a pdf file and the patient easily sends it to your mobile phone). According to this, implantation of ICD had performed successfully.

This case highlights that use of Apple Watche can enable clinicians to identify abnormalities that many traditional at-home monitoring devices do not detect. Thus, wearable devices, such as the Apple Watch, could be used to help identify heart rhythm disorders especially in cardiologic patients with high susceptibility having various arrhythmias.

Smartphones and connected devices allow patients to monitor their health condition in a different way. In our case a patient had complaints of palpitations and near faintness. Standard studies were unremarkable. However, an ECG recorded through his Apple Watch

showed VT episode. This case underlines the importance of proactively requesting such information from patients. Controlled clinical studies are needed to confirm this practice.

It seems that this will greatly help the users to identify and monitor different types of arrhythmias in order to diagnose and treat them in time. According to most of scientific papers AFB is frequently detected type of arrythmias, which is often detected using the Apple Watch. Therefore, most of the studies are related to AFB detection [6,7,8], less to other arrhythmias (supraventricular tachycardia (SVT), VT, heart block, atrial flutter etc.) [9,10]. Levent Pay et al. showed in a review, that cardiac arrhythmias other than atrial fibrillation are also frequently detected using smartwatches and smartwatches offer important potential beyond traditional arrhythmia detection methods in clinical practice [11].

Aydin Zahedivash et al. reviewed the heart electrical 145 recordings in a group of children who provided recordings obtained from their Apple Watches at times when they felt their heart rhythm was abnormal. The Apple Watches captured rhythm abnormalities in 28 % of patients: 88% SVT, 7% VT, 2.5 % heart block, that matched the diagnoses obtained using heart monitors used clinically [12].

Most of published articles are case reports or case series [3,4,5,13], few cohort studies detecting various arrhythmias another then AFB and several reviews in this field [10,11,14]. We believe that, further studies may contribute to the development of protocols for the appropriate use of smart devices to detect different arrythmias, especially life-threatening types, allowing the patients timely receive appropriate medical care, as well as the monitoring and assessment of effectivenes already existing antiarrhythmic therapy.

The advent of smartwatch-detected ventricular tachycardia marks a new era in cardiovascular care. By combining continuous monitoring, user-friendly interfaces, and real-time analytics, these devices offer an effective and accessible tool for arrhythmia detection. While challenges remain, ongoing advancements in wearable technology hold the promise of transforming clinical practice and improving outcomes for patients with cardiac arrhythmias.

This case report highlights the transformative role of wearable technology, specifically the Apple Watch, in detecting life-threatening arrhythmias such as ventricular tachycardia (VT). A 40-year-old male with a history of acute myocardial infarction and significantly reduced ejection fraction utilized his smartwatch to record heart rhythms during episodes of palpitations and near-fainting. The smartwatch recordings revealed VT, a finding consistent with his symptoms, ultimately leading to the successful implantation of an implantable cardioverter defibrillator (ICD).

This case underscores the clinical potential of smartwatches as complementary tools for arrhythmia detection, especially in patients who are unable or unwilling to undergo conventional monitoring methods. By providing continuous monitoring, patient-initiated recordings, and real-time alerts, smartwatches enable early detection and timely interventions. Despite challenges such as algorithm accuracy and data security, wearable technology holds great promise in improving the management of arrhythmias and advancing personalized cardiac care.

This case report demonstrates the profound potential of smartwatch technology, specifically the Apple Watch, in detecting and facilitating timely intervention for life-threatening arrhythmias such as ventricular tachycardia (VT). By providing continuous, non-invasive

monitoring and patient-driven data collection, smartwatches bridge critical gaps in traditional cardiac diagnostics, offering a novel solution for individuals with significant cardiac risk factors. The ability to capture transient and symptomatic arrhythmias in real time, as illustrated in this case, underscores their value as a complementary tool in modern cardiology.

Despite their advantages, challenges such as accuracy variability, data security, and integration into healthcare systems remain. Addressing these issues will be essential to fully realize the potential of wearable technology in clinical practice.

Considerations:

Clinical Adoption and Integration: Healthcare systems should explore incorporating smartwatch technology into routine monitoring for high-risk cardiac patients. Integrating wearable data into electronic health records (EHRs) could enhance diagnostic accuracy and improve patient outcomes.

Regulatory Oversight and Standards: Regulatory bodies should establish clear guidelines and standards for wearable devices to ensure they meet medical-grade accuracy and reliability requirements.

Public Awareness and Education: Patients and healthcare providers must be educated on the appropriate use and limitations of smartwatch technology. Empowering patients to understand their role in health monitoring will maximize the effectiveness of these devices.

Future Research: Further studies are needed to validate the clinical efficacy of smartwatches in detecting arrhythmias, particularly in larger, diverse populations. Research should also focus on optimizing algorithms to minimize false positives and negatives.

Collaboration and Innovation: Partnerships between technology companies, healthcare providers, and regulatory authorities will be vital in advancing wearable technology. Collaborative efforts can ensure the development of more accurate, secure, and integrated systems for widespread use.

By addressing these recommendations, smartwatches and other wearable devices can play an increasingly critical role in cardiovascular care, providing both patients and clinicians with reliable, real-time tools to manage and mitigate the risks of arrhythmias effectively.

Conclusions:

Different cardiac arrhythmias in addition to atrial fibrillation are also often detected by smart- watches. We demonstrate that the Apple Watch can record life threatening arrhythmia events, such is VT, not identified on traditionally used ambulatory monitors. Smartwatches, in addition to traditional methods, have significant potential in arrhythmia detection. Therefore, modern technology can be used in service of clinical practice. Considering all the above mentioned, we believe that there is a need to conduct trials in this direction, taking into account smartwatches as additional diagnostic tool of arrythmia detection and monitoring.

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COMPARATIVE QUALITATIVE PHYTOCHEMICAL CONTENTS AND ANTIMICROBIAL ACTIVITIES OF METHANOL EXTRACT OF CALOTROPIS PROCERA FLOWER AND LATEX

ABSTRACT

Microbial infections are common disease among many ages and sexes. The most pathetic circumstances about their management is their resistance to the available drugs; which necessitate alternative therapy. Both *C. procera* flower and latex have been widely used locally in Nigeria to tackle microbial skin infections without any antimicrobial comparisons. Therefore, this study investigated the phytochemical constituents and in vitro activities of methanol extract of *C. procera* flower (MECPF) and its latex (CPL) against *E. coli*, *Pseudomonas aeruginosa and Staphylococcus aureus* using standard methods. Maximum inhibitory concentration of both MECPF and CPL were carried out on each bacterium at 20 mg/ml, 40 mg/ml and 60 mg/ml using standard methods. The MECPF and CPL revealed the presence of phenol, flavonoids, anthraquinone, steroids and terpenoids, while glycoside and tannins are only present in CPL. None of the concentration (20 mg/ml, 40mg/ml and 60 mg/ml) of CPL is however active against *E. coli*, while only 40 mg/ml and 60 mg/ml of MECPF are active against the same organism. The maximum concentration (20 mg/ml) of CPL shows higher zone of inhibition when compared with 60 mg/ml of MECPF on *pseudomonas aeruginos*a. Contradictorily, maximum concentration (20 mg/ml) of CPL shows higher zone of inhibition on staphylococcus aureus compared to the maximum concentration (60 mg/ml) of MECPF. Therefore, CPL possesses higher antimicrobial activities on *pseudomonas aeruginosa and Staphylococcus aureus* but lower antimicrobial activities against E. coli when compared with MECPF.

Keywords: *Calotropis procera*, Microbial infections, *Pseudomonas aeruginos*a, Phytochemicals.

INTRODUCTION

Many modern antibiotics drugs have been used to battle infectious diseases after the discovery of the first drug ‘’penicillin’’ in the year 1928 by Sir Alexander Fleming (Bello et al, 2020; Alshiekheid, 2023). However, overuse and indiscriminate uses of antibiotics in human and veterinary medicine have led to dramatically increased resistance by the microbes (Bello et al, 2020). Bacterial infections have become issue of major concern due to the evolution of bacterial resistance over the years (Ahmed et al., 2024). There is a concerning rise in the number of deaths linked to bacterial infections as a result of bacteria developing resistant to antibiotics (Zhang et al., 2024).

The antibiotic resistance among Nigerians are more compounded probably due to inadequate medical services (Bello et al., 2020). Additionally, it has been projected that, by 2050, nearly 10 million annual death will be as a result of antibiotic resistance (Church and McKillip, 2021). In order to curtail this menace, novel and alternative treatment options need to be sought. Therefore, natural sources like medicinal plants could be explored as affordable antimicrobial agents.

Plants have been used as a medicinal source since primitive times. The traditional and folk medicines utilize plant, animals and their products for the treatment of various transmittable illnesses (Asefa et al., 2025). Furthermore, numerous studies have confirm the potential use of plant and animals materials for novel drug discovery and development (Asefa et al., 2025).

Calotropis procera is commonly called Sodom apple, dead sea apple, swallowwort, milkweed (English), kisher (Arabic), pomme de sodome (French), bomubomu (Yoruba), and tumfafiya (Hausa), is a wild-growing plant that belongs to the family *Asclepiadaceae*. It is widely distributed in the tropical and subtropical regions of Africa and Asia (Bello et al., 2020). Conventionally, *C. procera* is used to treat fever, rheumatism, pain, asthma, bronchitis, ulcer, indigestion, cold, eczema, measles, diarrhea, abscesses, and jaundice. elephantiasis, cough among others (Sigh et al., 2024).

Hence, the aim of this study was to determine the phytochemical contents and the antimicrobial effect of the methanol extract and latex of *Calotropis procera*.



Plate 1 : *Calotropis procera*

MATERIALS AND METHODS

MATERIALS

Collection and Identification of the Plant Material

The *Calotropis procera* flower and latex was collected within the school environment in Federal University of Technology, Minna Gidan kwano Campus, Bosso Local Government, Niger State, Nigeria on 4th of April, 2024. The plant was identified at the Department of Plant Biology, Federal University of Technology, Minna by Dr. Daudu O. A. Y. Voucher number FUT/PLB/ASC/004 was allotted to the plant and the sample was deposited at the herbarium of the Department of Plant Biology, Federal University of Technology, Minna, Nigeria.

Experimental Organisms

The *E. coli*, *staphylococcus aureus and Pseudomonas aeruginosa* used were obtained from Microbiology section of Centre of Genetic Engineering Federal University of Technology, Minna. The bacteria were cultured in agar plates in a temperature of about 37°c (body temperature) under aerobic condition in a sterile environment to prevent contamination.

Methods

Samples preparation

The flowers were removed from the stalk and washed thoroughly to remove unwanted materials. Thereafter, the flowers were spread under the shade at 30℃. The dried samples were later pulverized using electric blender and later transferred into air tight plastic container before being refrigerated at 2℃ for further use.

Furthermore, the latex sample was collected from the whole plant in a clean conical flask afterwhich the sample was lyophilized using freeze dryer. The dried sample was later transferred into a air tight glass container before being refrigerated at 2℃ for further use.

Extraction of *C. procera* Flower

Extraction of *C. procera* performed by soaking 250 g powder of *C. procera* flower in 500 mL of absolute methanol in 1 Liter volumetric flask. The mixture was left for 72 hours with constant vortexing. Subsequently, the liquid extract was separated with Whatman filter paper (No 1). Finally, the methanol fraction of the extract was obtained by evaporating methanol solvent using rotary evaporator, then with water bath at 40℃. Thereafter, the resulting molten solution was lyophilized using freeze dryer

Phytochemical Screening

Qualitative and quantitative tests were carried out on the powdered sample of the dried flower and latex sample using standard procedures described by (Sofowara, 1993),

Qualitative Phytochemical Screening of *C. procera*

Test for Flavonoids

A portion of powdered plant in each case was heated with 10 ml of ethyl acetate in a test tube over a steam bath for 3 min. The mixture was filtered and 4 ml of the filtrate was shaken

with 1 ml of dilute ammonia solution. Yellow coloration was observed thus indicating the presence of flavonoids.

Test for Tannins

0.5g of the dried powdered sample was boiled in 20ml distilled water in a test tube and filtered. 0.1% ferric chloride ($FeCl_3$) solution was added to the filtered. The appearance of brownish green or a blue-black colouration indicate the presence of tannins in the test sample

Test for Saponins

2.0g of the powdered sample was boiled in 20ml of distilled water in a test tube in boiling water bath and filtered. 10 ml of the filtrate was mixed with 5 ml of distilled water and was shaken vigorously to the formation of stable persistent froth. The frothing was mixed with drop of olive oil and shaken vigorously for the formation of emulsion thus a characteristic of saponins

Test for Alkaloid

0.5 of extract was stirred with $5cm^3$ of 1% aqueous HCI on a steam bath, few drops of picric acid solution was added to $2cm^3$ of the extract. The formation of a reddish-brown precipitate was taken as a preliminary evidence for the presence of alkaloids.

Test for steroids

0.5g of ethanolic extract fraction of each plant was mixed with 2 ml of acetic anhydride followed by 2 ml of sulphuric acid. The colour changed from violet to blue or green in some samples indicated the presence of steroids.

Test for Cardiac glycosides (Keller-Killani test)

5ml of each plant extract was mixed with 2ml of glacial acetic acid containing one drop of ferric chloride (Fecl3) solution, followed by the addition of 1ml concentrated sulphuric acid. Brown ring formed at the interface indicates deoxy sugar characteristics of cardenloides. A violet ring may appear beneath the brown ring, while in the acetic acid, layer; a greenish ring may also form just gradually throughout the thin layer.

Test for Anthraquinones (Borntrager's test)

0.5g of plant extract was shaken with 5ml chloroform, the chloroform layer was filtered and 0.5cm3 of 10% ammonia was added to the filtrate. The mixture was shaken thoroughly, the formation of a pink/violet or red, yellow colour in the ammonical phase indicates the presence of anthraquinones.

Test for Reducing Sugar (Benedict test)

0.5g of the plant extract was mixed thoroughly with 3cm3 distil water and filtered, 3 drops of the filtrate were added to 3cm3 Benedict reagents and placed in a boiling water bath for 5mins. The formation of a brick red precipitate indicates reducing sugar.

Collection of standard cultures

The standard cultures of bacteria under study were collected from different samples. After obtaining the culture, the test organisms were streaked on nutrient agar plates and incubated

at 37^0C for 24 hours before gram staining was performed on the isolated colony.
The organism thus obtained were tested for their purity and confirmed by their morphological, cultural and biochemical characteristics.

Preparation of Media and **Standard Culture Inoculum**

The media used in the study were prepared according to the manufacturer's recommendation. Thereafter, two to three similar appearance colonies from nutrient agar plate were touched with the inoculating loop aseptically. It was then transferred to a tube containing 2 ml of sterile nutrient broth.

Screening and Evaluation of Antimicrobial (antibacterial) Activities

Agar well diffusion method was used in this study for screening and evaluation of antibacterial activity of *C. Procera* flower and latex extract. The antimicrobial activity test has carried out as described by Rajamohan et al. (2014). Briefly, agar was prepared and autoclaved at 15 lbs pressure for 20 minutes and cooled to 45˚C. The cooled media have poured on to a sterile petri plates and allowed for solidification. The plates with the media have seeded with the respective microbial suspension using sterile swab. The plant extracts have prepared at different dose individually placed in each petri plates, discs and placed control and standard (Gentamycin 10 µg/ml) discs. The plates have incubated at 37˚C for 24 hrs. After incubation period, the zone of inhibition surrounding the discs has measured using a transparent ruler and the diameter recorded in mm.

Statistical Analysis

The results of this study were presented as mean ± standard deviation of three replicates using excel package. The experimental data were tested for homogeneity of variance and then subjected to one-way analysis of variance (ANOVA) and the difference between the samples mean were tested by Tukey post-hoc test using SPSS software version 23. A $p \leq 0.05$ was considered statistically significant.

RESULTS

Qualitative Phytochemical Analysis of methanol extract of *C. Procera* flower and latex.

Table 1 show the phytochemical constituents of methanol extract of *C. procera* flower and its latex. Methanol extract of *C. procera* flower indicates the presence of tannins, phenol, flavonoids, terpenoids, glycosides and steroids and the absence of saponins and alkaloids. The latex shows the presence of phenols, flavonoids, terpenoids, alkaloids, steroids, phlobatanins and anthraquinone and the absence of tannins and glycosides

Table 1: Qualitative Phytochemical Analysis of methanol extract of *C. Procera* flower and latex.

Phytochemicals	MECPF	CPL
Tannins	++	-
Phenols	+++	++
Flavonoids	+++	++
Terpenoids	+	+
Glycosides	+	-
Saponins	-	+++
Alkaloids	-	+++
Steroids	+	+++
Phlobatannins	+	+
Anthraquinones	+	+++

+ = Present, ++ = Moderately Present. +++ = Highly present

MECPF: Methanol extract of *C. procera* flower, CPL: *C. procera* latex

Antimicrobial Activities of Methanol Extract of *C. procera* Flower and Latex

Table 2 show antimicrobial activities of methanol extract of C. *procera* flower and latex. None of the concentration (20 mg/ml, 40mg/ml and 60 mg/ml) of CPL is however active against *E. coli*, while only 40 mg/ml and 60 mg/ml of MECPF are active against the same organism. The maximum concentration (20 mg/ml) of CPL shows higher zone of inhibition when compared with 60 mg/ml of MECPF on *pseudomonas aeruginos*a. Contradictorily, maximum concentration (20 mg/ml) of CPL shows higher zone of inhibition on staphylococcus aureus compared to the maximum concentration (60 mg/ml) of MECPF

Table 2: Antimicrobial Activities of Methanol Extract of *C. procera* flower and latex

GROUP	*E. Coli*	*Pseudomonas aeruginosa*	*Staphylococcus aureus*
CFE 20mg/ml	0.00^{a}	17.00 ± 1.00^{b}	11.33 ± 0.589^{a}
CFE 40mg/ml	13.00 ± 1.00^{c}	21.33 ± 2.08^{c}	14.00 ± 1.00^{a}
CFE 60mg/ml	21.00 ± 1.00^{d}	34.67 ± 1.15^{d}	18.00 ± 1.00^{b}
CPL 20mg/ml	0.00 ± 1.00^{d}	33.00 ± 1.00^{a}	33.00 ± 1.00^{c}
CPL 40mg/ml	0.00 ± 0.00^{a}	33.00 ± 1.00^{d}	22.67 ± 1.70^{b}
CPL 60mg/ml	0.00 ± 0.00^{a}	34.33 ± 1.15^{d}	33.00 ± 1.00^{a}
Standard	28.00 ± 26.4^{b}	26.33 ± 4.04^{a}	26.33 ± 3.51^{a}

MECPF: Methanol extract of *C. procera* flower, CPL: *C. procera* latex

DISCUSSION

E. coli is a prominent cause of enteritis and urinary tract infection and only MECPF produced reasonable antibiotic activities on this organism. This might be due to the presence of glycoside and high quantities of tannins, flavonoids and phenols when compared to CPL. Tannins, flavonoids, glycoside and phenols are good sources of antimicrobial agents (Kováč, et al., 2022). The contrast results as observed in the activity of CPL against *Pseudomonas aeruginosa* and *Staphylococcus aureus* especially at high concentration specifically for P. aeruginosa and generally for *Staphylococcus aureus* can be inferred from the presence of strong secondary metabolites presence in the CPL. Metabolites like alkaloids, saponins, steroids are strong antimicrobial agents aside from flavonoids, terpenoids and phenols that also contained in CPL (Kováč, et al., 2022). Similar activities of several parts of *C. procera* have also been reported to produced antimicrobial activities on several microbes and fungi due the presence of these aforementioned parameters (Sigh et al., 2024)

However, various mechanisms through which MECPF and CPL exhibit their antimicrobial activities are not known, but various report show that the medicinal plant could interact with microbes membrane and causes its disruption, damaging of microbes DNA, deactivate their metabolic enzymes among others.

From this study we can conclude that CPL possesses higher antimicrobial activities on *pseudomonas aeruginosa and Staphylococcus aureus* but lower antimicrobial activities against E. coli when compared with MECPF due to its minimum concentration that exhibit maximum effects.

Hence, CPL could be exploited further by isolating the specific active compound(s) the is responsible for the antimicrobial activities.

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THE NATIONS WHICH BELONG TO SHAHDAGH GROUP OF LANGUAGES

ABSTRACT

The protection of ethnic-cultural diversity by the state, which forms the basis of the worldview and activities of peoples, and plays a positive role in their lives, is a phenomenon that is overall positive in nature and directly related to the fundamental principles of social justice, tolerance, and a democratic legal society. The preservation of ethnic-cultural diversity is a part of the regulation policy implemented by the state. Proper regulation of these diversities should take into account the interests of both the state and the ethnic and religious minorities. If ethnic-cultural diversity is not properly regulated, serious problems will arise in various areas of society's development. Therefore, for any multicultural state, proper regulation should have significant practical importance.

Keywords: state, multiculturalism, ethnic-cultural diversity, national minorities

ŞAHDAĞ DİL QRUPUNA AİD XALQLAR

Açar sözlər: dövlət, multikulturalizm, etnik-mədəni müxtəliflik, milli azlıqlar

Giriş:

Xalqların etnik-mədəni dəyərlərini, mədəniyyətlərini, onların dünyagörüşü və fəaliyyətlərinin əsasını təşkil edən, həyatında müsbət rol oynayan və öz mahiyyətinə görə ümumilikdə müsbət fenomen olan etnik-mədəni müxtəliflikləri dövlət tərəfindən qorunması demokratik hüquqi cəmiyyətin sosial ədalət, tolerantlıq kimi mühüm prinsiplərdən irəli gəlir. Etnik-mədəni müxtəliflikləri qorunması dövlət tərəfindən həyata keçirilən tənzimlənmə siyasətinin tərkib hissəsidir. Bu müxtəliflikləri düzgün tənzimlənməsi həm dövlətin, həm də etnik və dini azlıqların maraqlarını nəzərə almalıdır. Etnik-mədəni müxtəlifliyi düzgün tənzimlənmədikdə cəmiyyətin inkişafının müxtəlif sahələrində ciddi problemlər yaranar və bu səbəbdən hər bir çoxmədəniyyətli dövlət üçün düzgün tənzimlənmə böyük praktik əhəmiyyət kəsb etməlidir.

Azərbaycan qədim tarixə, zəngin mədəni irsə malik olan bir ölkədir. Azərbaycan həmçinin dünyanın multikulturalizm mərkəzlərindən biridir. Yüzillər boyu ən müxtəlif millətlərin və dinlərin təmsilçiləri bu məmləkətdə dinc, yanaşı, mehriban yaşayıb, bir-birinin həyat tərzinə, inancına hörmətlə yanaşıb, xeyir-şərində iştirak edib, yaxın qohum olub, qaynayıb-qarışıblar. Taleyin hökmü və yaxud uzaq keçmişdən siyasi təzyiqlər, təbii fəlakətlər, hansısa digər səbəblərdən vətənlərini tərk etmək məcburiyyətindən ölkəmizə təşrif gətirib uzun müddət burada məskunlaşan insanlar özlərini burada heç bir zaman yad hiss etməyiblər. Bu gün respublikamızın ayrı-ayrı regionlarında Azərbaycanlılardan başqa bir sıra azsaylı xalqlar və milli azlıqların məskunlaşması ilə etnik rəngarəngliyin tam mənzərəsi canlanmaqdadır. Əhalinin etnik tərkibi baxımından maraq doğuran ərazilərdən biri də respublikamızın şimal-şərqində yerləşən Quba, Qusar və Xaçmaz rayonlarıdır. Azərbaycanlılarla bərabər ləzgilər, tatlar, yəhudilər və Şahdağın ətəklərində yerləşdiyinə görə etnoqrafiya elmində "Şahdağ etnik qrupları" və ya "Şahdağ xalqları"adları ilə məşhur olan xınalıqlılar, qrızlılar, buduqlular, haputlular, ceklilər, əliklilərin yaşadıqları bu rayonlarda muxtəlifdilli xalqların birgə yaşayış tərzi qarşılıqlı inkişaf prosesi ilə səciyyələnir. Bu proses təkcə maddi, iqtisadi və mədəni əlaqələr çərçivəsində qalmır, həm də bu xalqların varlığının başlıca əlaməti sayılan dillərinə də aiddir.

Azərbaycanda yaşayan hər bir xalq öz etnik xüsusiyyətini saxlamaqla bərabər, digər xalqların və etnik qrupların həyat tərzində, məişətində, adət və ənənəsində, mədəniyyətindəki bir çox mütərəqqi amilləri əxz edərək, onları qarşılıqlı surətdə inkişaf etdirmişdir. Ümumi birgəyaşayış qaydalarına əməl olunan zamanlarda bu xalqlar bir-birinə daha da yaxınlaşmış, lakin öz dillərini, etnoqrafik xüsusiyyətlərini qoruyub saxlamışlar. Şahdağ xalqlarının etnik mənşəyi ilə bağlı aparılan araşdırmalar bu etnosların Azərbaycanın qədim dövləti olan Qafqaz Albaniyasında məskunlaşan, Azərbaycanın, həmçinin Qafqazın qədim və orta əsr mədəniyyətinin əsas yaradıcılarından sayılan alban tayfalarından olduqlarını söyləməyə əsas verir. Azərbaycan tarixində özünəməxsus izləri olan xınalıqlılar, qrızlılar, buduqlular müstəqil etnik qruplar kimi öz kəndlərinin adı ilə tanınsalar da, bu etnosların etnik özünüadlandırmasında qədim *hər, qat* kimi Qafqaz Albaniyasına məxsus etnonimlər özünü büruzə verir.

Şahdağ xalqları və ya Şahdağ milli etnik qrupuna daxil olan etnoslar Quba rayonunun Buduq, Cek, Əlik, Haput, Qrız, Xınalıq və Yergüc kəndlərinin adlarına müvafiq olaraq buduqlular, ceklilər, əliklilər, haputlular,

qrızlılar, xınalıqlılar, yergüclülər adlanır. Say etibarilə az olsalar da, bu kəndlərin hərəsinin əhalisi ayrı-ayrılıqda bir etnik qrupdur. Təxmini hesablamalara görə, xınalıqlıların sayı 2,2 min, buduqların sayı 15 min, qrızların sayı isə 4,4 min nəfərdir. Hələ XIX əsrin 40-cı illərində buduqların və qrızların bir hissəsi Azərbaycanın düzən rayonlarına köçərək oba tipli yaşayış məskənləri salmışlar. Bu xalqların əsas məşğuliyyəti qoyunçuluqdur.

Şahdağ etnik qrupları tarixən formalaşmış qədim maddi mədəniyyətə malikdir. Onların kəndləri öz formaları və quruluşlarına görə keçmiş patriarxal icma münasibətlərini özündə əks etdirən yaşayış məskənləridir. Belə ki, hər bir kənd indi də məhəllələrə bölünür. Keçmişdə hər bir məhəllədə ayrı-ayrı nəsillər yaşayırdı. Məhəllə bəzən inzibati vahid rolunu oynayırdı. Hər məhəllənin ağsaqqalı, qəbiristanlığı və piri var idi. Məhəllələrin bəziləri orada vaxtilə məskən salmış ulu nəsillərin adları ilə adlanırdı. Xınalıq, Qrız, Haput kəndləri abidələrlə zəngindir. Onlardan Xınalıqdakı Pir Cumərt, Cümə məscidi, Atəşgah, Haputdakı Cümə məscidi, Babadilim piri və s. qeyd etmək olar.

Azərbaycan dili Şahdağ xalqları üçün də hər zaman ümumi ünsiyyət vasitəsi olmuşdur. Hələ XVIII əsrdə alman mənşəli coğrafiyaşünas və etnoqraf Yohan Qerber Şahdağ xalqları arasında ikidilliliyin olduğunu qeyd etmiş, onların, xüsusilə buduqluların və əliklilərin Azərbaycan dilindən istifadə etdiklərini bildirmişdir. Azərbaycan xalqının etnososial birliyinə daxil olan bu etnoslar bütövlükdə Azərbaycan etnomədəni mühitində formalaşaraq bölünməz Azərbaycan xalqının etnik tarixində əvəzsiz yer tutmuşlar.

Şahdağlılar ta qədim dövrlərdən azərbaycanlılarla təmasda olan, qaynayıb-qarışan ikidilli xalqlardır. Azərbaycan dili həmin azsaylı xalqların həyatında aparıcı rol oynayır. Ona görə də Y.D. Deşeriyevin "İki dilin qarşılıqlı təsirində bir dilin başqa dilə təsir dərəcəsi, həmçinin onlardan hər birinin ictimai vəzifələri, cəmiyyətin həyatında onların rolu ilə müəyyənləşdirilir" fikri tamamilə yerinə düşür. Şahdağ dillərində külli miqdarda Azərbaycan dilindən alınmış sözlərin işlənməsi onunla izah olunur ki, bu dillərdə danışan xalqlar uzun müddət eyni ərazidə və mehriban qonşuluq münasibətlərində olmuşlar. Şahdağlılar, eləcə də Dağıstanın digər xalqları arasında Azərbaycan dili geniş yayılmış, anlaşıqlı bir dil olmuşdur.

Şahdağ etnik qrupunun nümayəndələrinin yaşayış tərzi, toy və yas mərasimləri Azərbaycanın digər əhalisinin həyat ərzindən köklü şəkildə fərqlənmir. Lakin Şahdağ xalqlarını xarakterizə edən əsas cəhətlərdən biri onların ailə və məişət həyatı ilə bağlı adət-ənənələridir. Şahdağlıların ailə tərkibi çoxuşaqlılığı ilə səciyyələnir. Vaxtı ilə burada böyük ailələr mövcud olub. 40-50 nəfərdən ibarət ailəyə ata başçılıq edib, ata olmayanda isə böyük oğul bu vəzifəni icra edib. Ümumiyyətlə, patriarxal münasibətlər üzərində qurulan ailədə kişi hakim mövqeyə malik olub, ailənin bütün təsərrüfatının, keçinəcəyinin təmin edilməsinə özü rəhbərlik edir. Qadınlara məxsus işlər ya ananın özü tərəfindən, ya da onun rəhbərliyi altında icra edilir. Bu ailələrdə tarixən böyüyə hörmət, ehtiram mövcuddur. Şahdağlı ailələr öz möhkəmliyi ilə də seçilir. Şahdağlılar həmişə Azərbaycanın siyasi, ictimai və elmi həyatında fəalı iştirak ediblər. Şahdağ etnik qrupundan görkəmli alimlər, tədqiqatçılar, tarixçilər yetişib.

Bu gün Azərbaycanda formalaşan yeni, demokratik cəmiyyət müstəqil dövlət quruculuğunda fəal iştirak edir. Hər bir kəsin milli kimliyi onun bu gün özünü azərbaycanlı kimi hiss etməyinə mane olmur. Hər bir kəs öz ana dilində danışa, yaza bilər və özünün digər vacib olan mədəni ehtiyaclarını ödəyə bilər. Konstitusiyamızın "Milli mənsubiyyət hüququ" adlı 44-cü maddəsində göstərilir: "Hər kəsin milli mənsubiyyətini qoruyub saxlamaq hüququ vardır. Heç kəs milli mənsubiyyətini dəyişdirməyə məcbur edilə

bilməz”. Azərbaycanda yaşayan müxtəlif xalqların və etnik qrupların nümayəndələrini bu gün müstəqil Azərbaycanın hər bir sahəsində – siyasətdə, iqtisadiyyatda, təhsildə, idmanda, mənəvi həyatda, bir sözlə, bütün sahələrdə görmək mümkündür.

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THE GUT–BLOOD PRESSURE CONNECTION: MICROBIOTA'S ROLE IN HYPERTENSION AND DRUG RESPONSE

ABSTRACT

Background: Although hypertension is the most significant modifiable risk factor for cardiovascular disease and related mortality, the underlying mechanisms of essential hypertension are still not fully elucidated. Recent studies suggest that the gut microbiota may play a key role in blood pressure regulation and the individual response to antihypertensive therapies. This review aims to assess the impact of gut microbiota on the development of hypertension and the efficacy of antihypertensive therapies based on recent literature.

Methods: This study is a literature review based on human and animal studies published between 2017 and 2024.. The databases PubMed, Scopus and Web of Science were queried using a predefined set of keywords related to gut microbiota and hypertension. Selected studies were assessed for relevance to pathophysiological mechanisms and pharmacological outcomes.

Results: The gut microbiota and its metabolites—short-chain fatty acids (SCFAs), lipopolysaccharides (LPS), and trimethylamine N-oxide (TMAO)—exert significant pathophysiological effects on the cardiovascular system. In individuals with hypertension, a reduction in microbial diversity has been observed, particularly involving a decline in SCFA-producing bacterial populations. SCFAs such as acetate, propionate, and butyrate act through GPR41 and GPR43 receptors to promote vasodilation and suppress inflammatory responses. In contrast, TMAO, a microbial-derived metabolite, has been associated with endothelial dysfunction, vascular inflammation, and atherosclerotic processes. Moreover, both experimental and clinical studies have demonstrated that probiotic and prebiotic interventions exert blood pressure-lowering effects. Additionally, the gut microbiota may influence the metabolism and bioavailability of certain antihypertensive agents, thereby modulating individual treatment responses.

Conclusion:
The gut microbiota has emerged as a pivotal factor in the pathogenesis of hypertension and the modulation of individual responses to antihypertensive therapies. Ongoing advancements in this area hold significant promise for the development of personalized therapeutic strategies and the identification of novel microbiome-targeted interventions.

Keywords: gut microbiota, hypertension, antihypertensive drugs

BAĞIRSAK–KAN BASINCI BAĞLANTISI: MİKROBİYOTANIN HİPERTANSİYON VE İLAÇ YANITI ÜZERİNDEKİ ROLÜ

ÖZET

Amaç: Hipertansiyon, kardiyovasküler hastalıklar ve bunlara bağlı ölümler açısından en önemli risk faktörü olmasına rağmen, esansiyel hipertansiyonun altta yatan mekanizmaları hâlâ tam olarak aydınlatılamamıştır. Son yıllarda yapılan çalışmalar, barsak mikrobiyotasının kan basıncının düzenlenmesinde ve antihipertansif tedavilere bireysel yanıtta önemli bir rol oynayabileceğini göstermektedir. Bu derlemenin amacı, güncel literatür ışığında barsak mikrobiyotasının hipertansiyonun gelişimi ve antihipertansif ilaçların etkinliği üzerindeki etkisini değerlendirmektir.

Yöntemler: Bu çalışma, 2017–2024 yılları arasında yayımlanmış insan ve hayvan araştırmalarına dayalı bir literatür derlemesidir. PubMed, Scopus ve Web of Science veri tabanlarında, barsak mikrobiyotası ve hipertansiyonla ilişkili anahtar kelimeler kullanılarak sistematik bir tarama yapıldı. Seçilen çalışmalar; patofizyolojik mekanizmalar ve farmakolojik sonuçlar açısından değerlendirildi.

Bulgular: Barsak mikrobiyotası ve onun metabolitleri—kısa zincirli yağ asitleri (SCFA), lipopolisakkaritler (LPS) ve trimetilamin-N-oksit (TMAO)—kardiyovasküler sistem üzerinde belirgin fizyopatolojik etkilere sahiptir. Hipertansif bireylerde intestinal mikrobiyal çeşitliliğin azaldığı ve özellikle SCFA üreten bakterilerin oranının anlamlı ölçüde düştüğü gösterilmiştir. Asetat, propiyonat ve bütirat gibi SCFA'lar, GPR41 ve GPR43 reseptörleri üzerinden etki ederek vazodilatasyonu desteklemekte ve inflamatuar yanıtları baskılamaktadır. Buna karşılık, mikrobiyota kaynaklı bir metabolit olan TMAO'nun, endotel disfonksiyonu, vasküler inflamasyon ve aterosklerotik süreçlerle ilişkili olduğu bildirilmektedir. Ayrıca, probiyotik ve prebiyotik müdahalelerin hem deneysel modellerde hem de klinik çalışmalarda kan basıncını düşürücü etkiler oluşturduğu saptanmıştır. Bunun yanı sıra, barsak mikrobiyotası bazı antihipertansif ajanların metabolizması ve biyoyararlanımı üzerinde etkili olarak, tedaviye verilen bireysel yanıtları değiştirebilmektedir..

Sonuç: Barsak mikrobiyotası, hipertansiyonun patogenezinde ve antihipertansif tedavilere verilen bireysel yanıtta önemli bir belirleyici olarak öne çıkmaktadır. Bu alandaki bilimsel ilerlemeler, kişiye özel tedavi stratejilerinin geliştirilmesine ve mikrobiyotayı hedef alan yeni tedavi yaklaşımlarının ortaya çıkmasına olanak sağlayabilir.

Anahtar Kelimeler: barsak mikrobiyotası, hipertansiyon, antihipertansif ilaçlar

Giriş

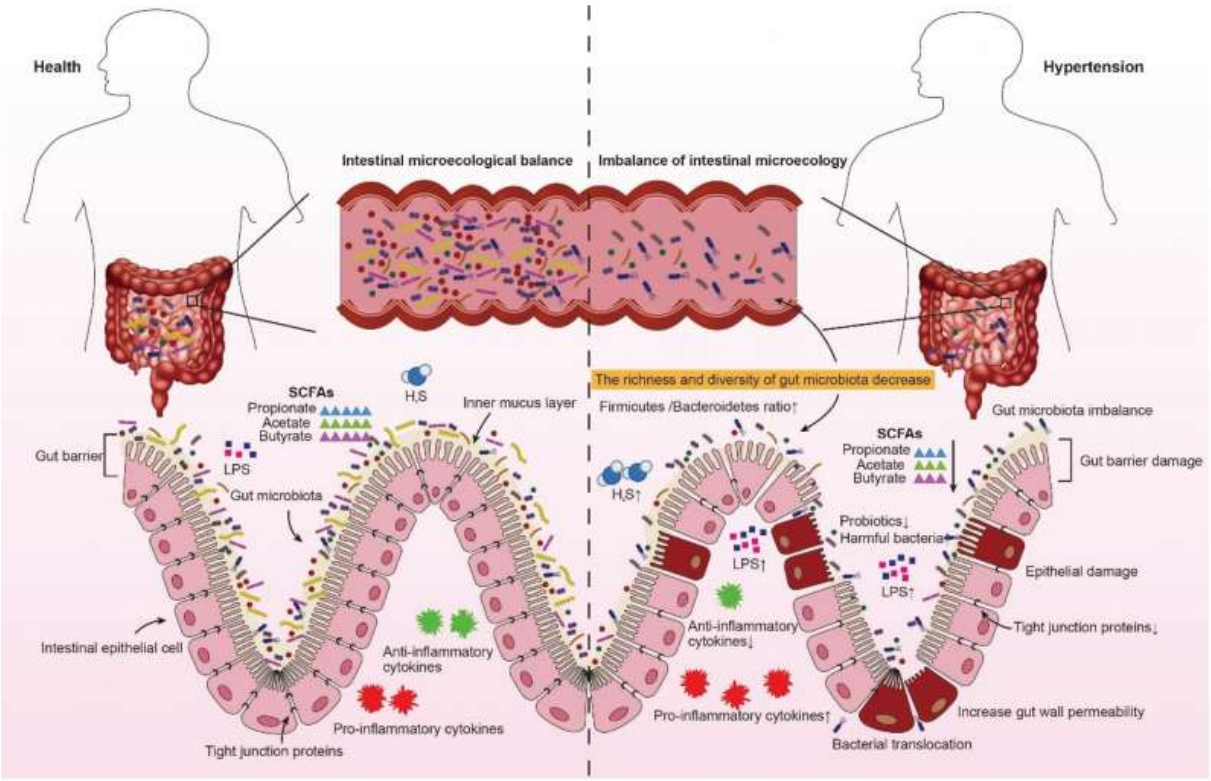
Hipertansiyon, yalnızca küresel düzeyde önemli bir halk sağlığı sorunu olmakla kalmayıp, aynı zamanda kardiyovasküler hastalıkların en temel risk faktörlerinden biri olup topluma önemli bir ekonomik yük getirmektedir. Genel anlamda hipertansiyon, genetik ve çevresel etkenlerin birleşimiyle ortaya çıkan multifaktöriyel bir hastalık olarak tanımlanmaktadır.[1] Hipertansiyonun klasik patogenezinde; sempatik sinir sistemi hiperaktivitesi, renin-anjiyotensin-aldosteron sistemi (RAAS) aktivasyonu, vasküler endotel disfonksiyonu, insülin direnci ve nörohümoral faktörlerin disregülasyonu gibi mekanizmalar yer almaktadır.[2,3] Hipertansiyona yönelik önceki araştırmaların büyük bir bölümü; periferik vasküler yeniden yapılanma ve santral sinir sistemi düzeyinde regülasyon mekanizmalarına odaklanmışken, çevresel faktörler, özellikle vücudun içsel ekosisteminin önemli bir parçası olan bağırsak mikrobiyotası, bu alanda yeterince araştırılmamıştır.[4]

İnsan bağırsaklarında çok sayıda mikroorganizma bulunmakta olup, bu mikroorganizmalar konak sağlığının korunması ve düzenlenmesinde temel roller üstlenmektedir.[5] Mikrobiyota kolonizasyonu doğumla birlikte başlamakta ve yaşam süresi boyunca çeşitli faktörlerin etkisiyle sürekli olarak yeniden şekillenmektedir; bu durum, bireyler arasında belirgin mikrobiyal çeşitlilik ve heterojenliğe yol açmaktadır. Doğum şekli (vajinal ya da sezaryen) ve beslenme yöntemi (anne sütü ya da formül mama) gibi erken yaşam dönemine ait etkenler, yenidoğan dönemindeki bağırsak mikrobiyotasının bileşimini belirleyen temel faktörler arasında yer almaktadır.[6] Son yıllarda yapılan çok sayıda çalışma, bağırsak mikrobiyotasındaki bozulmanın (disbiyozis), hipertansiyonun ortaya çıkışı ve ilerleyişinde önemli bir rol oynayabileceğini göstermiştir.[4] Öte yandan, hipertansiyonun da mikrobiyal yapı ve kompozisyonda anlamlı değişikliklere neden olabileceği bildirilmiştir.[7] Bununla birlikte, hipertansiyon ile disbiyoz arasındaki ilişkiyi ortaya koyan çok sayıda çalışma mevcut olsa da, hipertansiyona bağlı olarak gelişen disbiyozisin altında yatan mekanizmalar henüz tam olarak aydınlatılamamıştır.[8]

Bağırsak mikrobiyotasının bolluğu, çeşitliliği ve homojenliği, mikrobiyal kompozisyonun değerlendirilmesinde temel parametreler olarak kabul edilir. 2005 yılında Eckburg ve arkadaşları, metagenomik analiz yöntemleri kullanarak insan bağırsak mikrobiyotasını Firmicutes, Bacteroidetes, Proteobacteria, Actinobacteria, Verrucomicrobia ve Fusobacteria olmak üzere altı ana filuma ayırmıştır.[9] Bu gruplar arasında Firmicutes ve Bacteroidetes, baskın bakteriyel toplulukları oluşturmaktadır. Firmicutes/Bacteroidetes (F/B) oranı, mikrobiyal kompozisyondaki dengenin bozulduğunu gösteren bir biyobelirteç olarak değerlendirilmektedir.

Disbiyozis, hipertansiyonun patogenezi ve ilerlemesiyle yakından ilişkilidir; ayrıca bağırsak mikrobiyotası tarafından üretilen metabolitler, kan basıncının düzenlenmesinde önemli rol oynamaktadır. Bu bağlamda, Mell ve arkadaşları, ilk kez Dahl tuz duyarlı (salt-sensitive) ve tuz dirençli (salt-resistant) sıçanların çekum mikrobiyal bileşimleri arasında belirgin farklılıklar olduğunu ortaya koymuştur. Aynı yıl, Yang ve arkadaşları, normotansif WKY sıçanlarıyla karşılaştırıldığında, spontan hipertansif sıçanlarda (SHR) mikrobiyal çeşitlilik, bolluk ve homojenlik düzeylerinin anlamlı şekilde azaldığını; F/B oranının arttığını ve özellikle asetat ve bütirat üreten bakterilerin azaldığını raporlamıştır. Bu bulgular, kronik anjiyotensin II infüzyonuna maruz bırakılan hayvan modellerinde de doğrulanmıştır.[5] Tüm bu veriler, hayvan modelleri temelinde hipertansiyonun, bağırsak mikrobiyotasındaki yapısal bozulmalarla ilişkili olduğunu ve bu değişikliklerin yeni farmakolojik hedeflerin belirlenmesi açısından önemli bir potansiyel taşıdığını göstermektedir.

Bağırsak mikrobiyotasının, hipertansiyonun oluşumu ve ilerleyişinde çok yönlü mekanizmalar aracılığıyla rol oynadığına dair artan sayıda kanıt bulunmaktadır. Bu süreçte özellikle bağırsak bariyer fonksiyonu, mikrobiyal kompozisyonun yapısal özellikleri ve mikrobiyota kaynaklı metabolitler, patogenezde etkili olan başlıca bileşenler olarak öne çıkmaktadır. Bağırsak mikrobiyotası ile hipertansiyon arasındaki ilişki, bu karmaşık etkileşimleri yansıtacak şekilde Şekil 1'de şematik olarak sunulmuştur.



Şekil 1. Sağlıklı bireylerde bağırsak mikrobiyotası, homeostazın sürdürüldüğü dinamik bir denge içerisindedir; bu denge, mikrobiyal çeşitliliğin korunmasını ve bağırsak bariyerinin fizyolojik bütünlüğünü destekler. Hipertansiyon gelişiminde ise mikrobiyal kompozisyonda belirgin bir bozulma (disbiyozis) ve buna bağlı olarak bağırsak bariyer fonksiyonlarında zayıflama gözlenmektedir. Bu durum; zararlı bakteri popülasyonlarının, hidrojen sülfür ve lipopolisakkarit (LPS) düzeylerinin artışı, faydalı bakteriler ile kısa zincirli yağ asitlerinin azalması, sıkı bağlantı proteinlerinin (tight junctions) ekspresyonunda azalma ve bağırsak geçirgenliğinde artış ile karakterizedir [7].

I. Mikrobiyota Kaynaklı Metabolitler Ve Hipertansiyon

Bağırsak mikrobiyotası, konak organizma ile çok yönlü etkileşimler kuran çeşitli bakteriyel metabolitler üretir. Bu metabolitler arasında trimetilamin-N-oksit (TMAO), kısa zincirli yağ asitleri (SCFAs), kortikosteron, hidrojen sülfür (H_2S), kolin, safra asitleri (BAs), indol sülfat ve lipopolisakkarit (LPS) gibi moleküller yer almaktadır. Mikrobiyota kaynaklı bu metabolitler yalnızca bağırsak sağlığını değil, aynı zamanda bağışıklık sistemi, vasküler yapı ve kardiyak fonksiyonlar gibi uzak organ sistemlerini de etkileyebilmektedir (10). Bu

metabolitler arasında özellikle SCFAs, TMAO, safra asitleri, H_2S ve LPS, hipertansiyonun gelişimi ile yakından ilişkilidir. Bazı metabolitlerin, kan basıncı düzenlenmesi, renal sodyum homeostazı ve ateroskleroz patogenezi ile ilişkili olduğu gösterilmiştir. Mikrobiyota tarafından üretilen metabolitler, etkilerine göre sınıflandırıldığında, faydalı bileşikler arasında kısa zincirli yağ asitleri ve vitaminler yer almakta; buna karşılık zararlı etkiler gösteren bileşikler arasında ise trimetilamin-N-oksit (TMAO), lipopolisakkarit (LPS), üremik toksinler ve ikincil safra asitleri bulunmaktadır [8].

Kısa Zincirli Yağ Asitleri (SCFAs)

İnsan bağırsak mikrobiyotasının temel işlevlerinden biri, kalın bağırsakta sindirilemeyen diyet liflerinin fermantasyonudur. Bu süreç sonucunda başlıca asetat, propiyonat ve bütirat olmak üzere kısa zincirli yağ asitleri (SCFAs) üretilir (9). SCFA'lar gastrointestinal sistemde ya absorbe edilir ya da dışkı yoluyla atılır. SCFA'ların, özellikle antiinflamatuar ve vazodilatör özellikleri aracılığıyla kan basıncı (KB) düzenlenmesinde önemli bir rol oynayabileceği bildirilmektedir. Üç ana SCFA olan asetat, propiyonat ve bütirat, toplam SCFA havuzunun yaklaşık %80'ini oluşturur. Her ne kadar etki alanları başlıca gastrointestinal sistemle sınırlı olsa da, bu moleküller intestinal bariyeri geçerek portal dolaşımla sistemik sirkülasyona katılabilmektedir (7). Ancak karaciğer metabolizması nedeniyle, fizyolojik koşullar altında periferik kanda SCFA düzeyleri genellikle mikromolar – düşük milimolar aralığında kalmakta olup, dolaşımda en baskın SCFA asetattır (10). Fare modellerinde, SCFAs, başta GPR41, GPR43, GPR109A, Olfr558 ve Olfr78 olmak üzere G-protein bağlı reseptörleri (GPCR) aracılığıyla biyolojik sinyal yollarını aktive ederek çeşitli fizyolojik yanıtları tetikleyebilir (7). Bu reseptörlerden Olfr78, özellikle böbrekteki jukstaglomerüler aparatta eksprese olur ve SCFA'lara yanıt olarak renin sekresyonunu düzenler. Olfr78 gen mutasyonu taşıyan farelerde, bazal kan basıncı ve plazma renin düzeyleri, vahşi tip farelere kıyasla belirgin şekilde düşüktür. Buna karşılık, akut SCFA uygulamasının anestezili farelerde KB'yi düşürdüğü ve bu etkinin esas olarak GPR41 aracılığıyla gerçekleştiği bildirilmiştir. Bu bağlamda, Olfr78'in hipertansif, GPR41'in ise hipotansif etkili olduğu düşünülmekte ve bu iki reseptör, SCFA düzeylerindeki değişimlere karşı kan basıncını fizyolojik sınırlar içinde dengelemede tamamlayıcı rol oynamaktadır. Yapılan çalışmalar, spontan hipertansif sıçanlarda SCFA üretiminin azaldığını göstermektedir. Ek olarak, yüksek tuz içeren diyetle beslenen Dahl tuz duyarlı sıçanlarda, normal tuz diyetiyle beslenenlere kıyasla dışkıdaki asetat, propiyonat ve izobütirat düzeylerinin arttığı; ancak bütirat düzeyinde anlamlı bir artışın gözlenmediği bildirilmiştir [9].

Robles-Vera ve arkadaşlarının çalışmasında, SCFA'lardan bütirat ve asetatın, prohipertansif bir ajan olan anjiyotensin II (Ang II) ile indüklenen endotel disfonksiyonunu geri çevirdiği gösterilmiştir. Bu moleküller, aort halkalarında endotele bağlı vazodilatasyonu (NO üretimi) yeniden sağlamış ve NADPH oksidaz ile mitokondri kaynaklı hücre içi ROS üretimini azaltmıştır. Ayrıca, GPR41 ve GPR43 antagonistleri, Ang II'ye bağlı endotel disfonksiyonunda bütiratın faydalı etkilerini bloke ederken, asetatın etkileri bu blokajdan etkilenmemiştir. Bir klinik çalışmada, meyve ve sebze tüketiminin (doğal SCFA kaynakları) kan basıncını düşürebileceği ve kardiyovasküler mortalite insidansı ile ters yönde ilişkili olduğu bildirilmiştir [11,12]. Bununla birlikte, SCFA'ların hipertansiyon üzerindeki etkilerini açıklığa kavuşturmak ve mekanizmalarını detaylandırmak amacıyla daha fazla kontrollü klinik ve deneysel çalışmaya ihtiyaç vardır.

Trimetilamin-N-oksit (TMAO)

Trimetilamin-N-oksit (TMAO), bağırsak mikrobiyotası kaynaklı bir metabolit olup, aterojenik ve trombojenik özellikler göstermektedir. Dolaşımdaki TMAO düzeyleri ile kardiyovasküler hastalık riski arasında pozitif bir korelasyon bulunduğu gösterilmiştir. 6.176 hipertansif bireyin dahil edildiği bir meta-analiz, TMAO düzeylerinin hipertansiyon riskiyle doz-bağımlı olarak ilişkili olduğunu ortaya koymuştur. Buna göre, TMAO konsantrasyonunda her 5 µmol/L'lik artış, hipertansiyon görülme riskini %9 oranında artırmaktadır . TMAO'nun vücutta üretimi, başlıca diyetle alınan besinler, bağırsak mikrobiyotasının bileşimi ve aktivitesi ile karaciğerde bulunan flavin mono oksijenaz (FMO) enzimleri tarafından düzenlenmektedir; eliminasyonu ise böbrekler aracılığıyla gerçekleştirilir. TMAO'nun öncül maddesi olan trimetilamin (TMA), fosfatidilkolin, betain ve karnitin gibi TMA grubu içeren bileşiklerden sentezlenir; bu bileşikler özellikle kırmızı et, kümes hayvanları, karaciğer, yumurta ve süt ürünlerinde yaygın olarak bulunur. Bu bileşiklerin metabolizması büyük ölçüde bağırsak mikrobiyotası tarafından salgılanan enzimler aracılığıyla gerçekleştirilir. Bağırsak lümeninde oluşan TMA, portal ven yoluyla karaciğere taşınır ve burada FMO1 ve FMO3 enzimleri tarafından TMAO'ya oksitlenir. Bu nedenle, beslenme tercihleri, mikrobiyota kompozisyonu ve fonksiyonu ile karaciğer FMO aktivitesi, TMAO üretimini belirleyen temel faktörlerdir.TMAO'nun hipertansiyon üzerindeki etkilerine yönelik deneysel çalışmalar, bu metabolitin anjiyotensin II (Ang II) ile indüklenen vazokonstriktif yanıta katkı sağladığını ve Ang II'nin hipertansif etkisini uzattığını ortaya koymuştur. TMAO tedavisinin, afferent arterler ve vasküler düz kas hücrelerinde, Ang II ile uyarılan hücre içi kalsiyum (Ca^{2+}) salınımını artırdığı, bu etkinin PERK/ROS/CaMKII/plc-β3 sinyal aksı üzerinden gerçekleştiği ve sonuç olarak Ang II'ye bağlı vazokonstriksiyonu güçlendirdiği gösterilmiştir. Bununla birlikte, Tomasz ve arkadaşlarının çalışmasında, düşük dozda uygulanan TMAO'nun, hipertansif sıçanlarda diyastolik disfonksiyonu ve kardiyak fibrozisi azalttığı, dolayısıyla kardiyovasküler sistem üzerinde koruyucu etkiler gösterebileceği öne sürülmüştür.Tüm bu bulgular ışığında, TMAO'nun hipertansiyon üzerinde doğrudan bir etkisi olduğuna dair henüz kesin ve yeterli kanıt bulunmamaktadır. Ancak, TMAO'nun hipertansiyonun patogenezine katkıda bulunabileceği, hastalığın ilerleyişini hızlandırabileceği ve ilgili komplikasyonlarla ilişkili olabileceği düşünülmektedir[13].

Üremik toksinler,

Böbrek fonksiyon bozukluğu durumlarında vücutta biriken ve konak üzerinde zararlı etkiler gösteren metabolitlerdir. Bu toksinlerin bir kısmı kolonik mikrobiyota tarafından protein fermentasyonu sonucu oluştuğundan, bağırsak mikrobiyotasının durumu, plazmadaki üremik toksin düzeylerini etkileyebilir. p-Kresil sülfat ve indoksil sülfat, mikrobiyota kökenli başlıca üremik toksinlerdir ve oksidatif stres, fibrozis ve inflamatuar yanıtların indüklenmesi gibi çok yönlü zararlı etkiler gösterirler. Diyetle alınan tirozin ve triptofanın kolonik fermantasyonu sonucunda sırasıyla p-kresol ve indol oluşur; bu bileşikler daha sonra p-kresil sülfat ve indoksil sülfata metabolize edilir. Bu üremik toksinler doğrudan hipertansiyona neden olmasalar da, sahip oldukları vasküler toksisite nedeniyle vasküler kalsifikasyon, ateroskleroz ve arteriyel sertlik artışı gibi kardiyovasküler risk faktörlerini teşvik ederler [8].

II. Bağırsak Bariyer Fonksiyonu ve Kan Basıncının Düzenlenmesi

Bağırsak bariyeri, konak ile dış çevre arasındaki etkileşimde kritik bir savunma hattı oluşturur. Fizyolojik koşullarda, bu bariyerin bütünlüğü korunduğunda intestinal geçirgenlik

düşüktür; bu da patojen mikroorganizmaların, enteroendotoksinlerin ve diğer zararlı bileşiklerin sistemik dolaşıma geçişini etkili bir biçimde sınırlandırır. Sonuç olarak, organ düzeyinde akut ve kronik inflamasyonun azalması sağlanır ve buna bağlı olarak vasküler inflamasyon hafifler, kan basıncı düzeyi korunabilir. Ancak, bağırsak mikrobiyotasındaki dengenin bozulması (disbiyozis), bağırsak bariyeri fonksiyonunun zayıflamasına ve intestinal geçirgenliğin artmasına neden olur. Bu durum, patojenik bakteriler ile lipopolisakkaritlerin (LPS) sistemik dolaşıma geçişini kolaylaştırarak yaygın bir inflamatuar yanıtı tetikler. Bu süreç, endotelyal disfonksiyon ve vasküler sertlik gibi değişikliklere yol açarak hipertansiyonun gelişimine veya mevcut hipertansiyonun şiddetlenmesine katkıda bulunabilir. Ek olarak, bağırsak bariyeri bütünlüğünün bozulması, probiyotik türlerin kolonizasyonunu da olumsuz etkileyerek mikrobiyota dengesinin daha da bozulmasına neden olur. Bu durum, patojenik bakterilerin çoğalması ve LPS düzeylerinde artış ile sonuçlanır. Bu zararlı moleküller, mezenteriyal dolaşım üzerinden sistemik kan akımına geçerek, enflamasyon aracılığıyla kan basıncını daha da yükseltebilir [7].

III. Bağırsak Mikrobiyota Yapısı ve Kan Basıncının Düzenlenmesi

Bağırsak mikrobiyotası, kan basıncının stabilitesinin korunmasında önemli bir rol oynar ve mikrobiyota yapısındaki değişiklikler, hipertansiyonun ortaya çıkışıyla yakından ilişkilidir (46). Mevcut çalışmalar, hipertansif bireylerde mikrobiyota yapısının bozulduğunu ve özellikle Proteobakteri gibi zararlı bakteri gruplarının sayısının anlamlı düzeyde arttığını göstermiştir. Bu bakteriler, intestinal inflamasyon ve immün bozukluklarla yakından ilişkilidir.

Disbiyozisin hipertansiyon gelişimine katkı sağlayan mekanizmaları çok basamaklıdır:

1. Probiyotik türlerde azalma ve patojenik bakterilerde artış, bağırsak ortamında inflamatuar yanıtları tetikler. Bu süreç, bağırsak mukozasında yer alan sıkı bağlantı proteinleri (zonula okkludin-1 [ZO-1], okkludin vb.) ekspresyonunun bozulmasına yol açarak intestinal geçirgenliği artırır ve böylece bağırsak bariyer fonksiyonu zayıflar.

2. İnce bağırsakta patojenik bakteri yükü ve enterotoksin düzeyleri yükseldiğinde, bu maddeler mezenteriyal damarlar aracılığıyla sistemik dolaşıma geçerek kronik inflamasyonu başlatır, endotel hasarına neden olur ve vazodilatör faktörlerin azalması, vazokonstriktör mediatörlerin artması gibi değişikliklerle sonuçlanır.

3. Bu patofizyolojik süreçler, periferik vasküler direncin artmasına yol açar ve bu durum, kan basıncının yükselmesine neden olur.

4. Ek olarak, bağırsak mikrobiyotası, konak bağışıklık sistemini ve inflamatuar yanıtları modüle ederek, dolaylı yoldan kan basıncı regülasyonunu etkileyebilir [7].

IV. Mikrobiyota - Antihipertansif İlaç Etkileşimi

Bağırsak mikrobiyomu, karaciğerde bulunanlara benzer şekilde çok sayıda katalitik enzim sınıfını barındırması nedeniyle, ilaç-bakteri etkileşimleri açısından önemli bir biyolojik ortam sunar. Mikrobiyota, konakçıya ait ilaç metabolizmasından sorumlu enzimlerin (örneğin sitokrom P450 izoenzimleri) ekspresyonunu etkileyebileceği gibi, bazı antihipertansif ajanların doğrudan mikrobiyal biyotransformasyonuna da aracılık edebilir Bu durum, antihipertansif ilaçların biyoyararlanımını, plazma konsantrasyonlarını ve dolayısıyla tedavi etkinliğini belirgin şekilde değiştirebilir. Antibiyotikler veya probiyotik uygulamalarıyla mikrobiyotanın modifikasyonu, bu etkiyi daha da artırabilir.

Nitekim, Lactobacillus casei gibi bazı probiyotik bakteri türlerinin, bağırsak mukozasında CYP3A4 enzim aktivitesini etkileyerek ilaç metabolizmasını değiştirebileceği düşünülmektedir. CYP3A4 ile metabolize edilen nifedipin adlı kalsiyum kanal antagonisti, L. casei ile önceden tedavi edilen sıçanların bağırsaklarına uygulandığında, plazmadaki maksimum konsantrasyonu kontrol grubuna göre %40 daha yüksek bulunmuştur. Bu sonuç, probiyotiklerin bağırsak mukozasındaki ilaç metabolizması üzerinde anlamlı bir etki oluşturabileceğini göstermektedir. İlginç bir şekilde, dirençli hipertansiyon vakası olan bir hastada yoğun antibiyotik tedavisi sonrası kan basıncı kontrolünde belirgin iyileşme sağlandığı bildirilmiştir . Ancak bu tür mikrobiyota aracılı ilaç–ilaç etkileşimlerinin klinik önemi, hâlen yeterince anlaşılmamış ve çoğu zaman göz ardı edilmektedir. Buna ek olarak, antihipertansif ilaçların da bağırsak mikrobiyota kompozisyonunu değiştirme kapasitesine sahip olduğu bilinmektedir. Mikrobiyotada meydana gelen bu değişimler, ilacın terapötik etkinliğini artırabilir ya da azaltabilir. Örneğin, losartan ve kandesartan gibi anjiyotensin II tip 1 reseptör antagonistlerinin, mikrobiyota kompozisyonunu düzenleyerek kan basıncı düşürücü etkilerine katkı sağladığı gösterilmiştir. Ancak, mikrobiyotanın antihipertansif ilaçların farmakokinetiği üzerindeki etkisine ilişkin doğrudan kanıtlar hâlâ sınırlıdır [8].

Ayrıca dirençli hipertansiyon, standart antihipertansif tedavilere yeterli yanıt vermeyen ve bu nedenle kronik kardiyovasküler komplikasyonlar açısından yüksek risk taşıyan bir hasta alt grubunu temsil eder. Güncel bulgular, bağırsak mikrobiyotasının antihipertansif ilaçların metabolizmasında rol oynayabileceğini ve bu yolla dirençli hipertansiyonun patofizyolojisine katkı sağlayabileceğini ortaya koymaktadır. Ancak, bu sürece ilişkin moleküler mekanizmalar henüz tam olarak aydınlatılamamıştır. Bu nedenle, bağırsak mikrobiyotasını dikkate alan yeni tedavi stratejilerinin geliştirilmesi, dirençli hipertansiyon yönetiminde, daha etkili ve kişiselleştirilmiş klinik yaklaşımların önünü açabilir.

Sonuç

Bağırsak mikrobiyotası ve onun metabolitleri, hipertansiyonun başlangıcı ve progresyonuyla yakından ilişkili fizyopatolojik süreçlerde önemli rol oynamaktadır. Son yıllarda yapılan çalışmalar, bağırsak mikrobiyotasının kan basıncı regülasyonunda etkili olabilecek çok sayıda mikrobiyota aracılı mekanizmayı ortaya koymuştur. Bu bulgular, mikrobiyota–konak etkileşimlerinin, yalnızca hipertansiyonun patogenezine ışık tutmakla kalmayıp, aynı zamanda yeni tedavi hedeflerinin belirlenmesine de olanak sağladığını göstermektedir.

Bu doğrultuda, bağırsak mikrobiyotasının modülasyonu yoluyla hipertansiyonun yönetilmesi, mevcut tedavi yaklaşımlarının sınırlılıklarını aşabilecek, yenilikçi ve tamamlayıcı bir strateji olarak değerlendirilmektedir. Özellikle, yüksek lif içeren diyetler, probiyotik ve prebiyotik takviyeleri, dışkı mikrobiyota transplantasyonu (FMT) ve bitkisel/fitoterapötik ürünler gibi mikrobiyotaya yönelik müdahalelerin, konvansiyonel antihipertansif ilaçlarla birlikte kullanılması, optimal kan basıncı kontrolü sağlanmasına katkı sunabilecek bütüncül bir yaklaşım olarak öne çıkmaktadır.

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VASCULAR PROTECTIVE MECHANISMS OF SGLT-2 INHIBITORS: BEYOND GLUCOSE LOWERING

ABSTRACT

Objective: Sodium-glucose cotransporter-2 (SGLT2) inhibitors, initially developed for glycemic control in type 2 diabetes mellitus (T2DM), have shown unexpected cardiovascular and renal protective effects in large-scale clinical trials. These benefits extend beyond glucose regulation, prompting investigations into their roles in vascular biology. In this review, the protective effects of SGLT2 inhibitors on the vascular system at the cellular and molecular levels are discussed in the context of endothelial function, vascular tone, atherosclerosis, vascular remodeling, inflammation, oxidative stress, and autophagy.

Methods: In this review, literature published between 2015 and 2023 was searched using PubMed and Scopus databases. Leading randomized controlled trials, such as EMPA-REG OUTCOME, CANVAS, DAPA-HF and DAPA-CKD, and recent meta-analyses were evaluated.

Results: SGLT2 inhibitors have been shown to exert consistent antihypertensive effects across both clinical and preclinical models. Although improvements in endothelial function and arterial stiffness have been reported, clinical data remain heterogeneous. In experimental studies, SGLT2 inhibitors have demonstrated attenuation of atherosclerotic plaque development, inhibition of neointimal hyperplasia, and protective effects against abdominal aortic aneurysm and pulmonary hypertension. At the molecular level, these vascular benefits are attributed to the suppression of oxidative stress, downregulation of key inflammatory pathways such as NF-κB and NLRP3 inflammasome signaling, enhancement of nitric oxide bioavailability, and inhibition of vascular smooth muscle cell proliferation. Moreover, modulation of autophagic activity and cellular senescence has been implicated in the preservation of vascular integrity.

Conclusion: SGLT2 inhibitors exert significant protective effects on the cardiovascular and renal systems through multiple mechanisms that influence vascular biology beyond glycemic control. However, multidisciplinary studies conducted by both basic and clinical sciences are needed to fully elucidate and optimize their clinical potential.

Keywords: SGLT2 inhibitors, vascular biology, endothelial function, atherosclerosis, oxidative stress, inflammation, cardiovascular protection

SGLT-2 İNHİBİTÖRLERİNİN VASKÜLER KORUYUCU MEKANİZMALARI: GLUKOZ DÜŞÜRÜCÜ ETKİNİN ÖTESİNDE

ÖZET

Amaç: Başlangıçta tip 2 diyabet mellitus (T2DM) tedavisinde glisemik kontrol amacıyla geliştirilen sodyum-glukoz kotransporter-2 (SGLT2) inhibitörleri, geniş ölçekli klinik çalışmalarda beklenmedik kardiyovasküler ve renal koruyucu etkiler göstermiştir. Bu etkilerin glukoz regülasyonunun ötesine geçmesi, SGLT2 inhibitörlerinin damar biyolojisindeki rollerinin araştırılmasına neden olmuştur. Bu derlemede, SGLT2 inhibitörlerinin damar sistemi üzerindeki hücresel ve moleküler düzeydeki koruyucu etkileri; endotelyal fonksiyon, damar tonusu, ateroskleroz ve vasküler remodeling, inflamasyon, oksidatif stres ve otofaji bağlamında ele alınmaktadır.

Yöntem: Bu derlemede, 2015–2023 yılları arasında yayımlanan literatür, PubMed ve Scopus veritabanları kullanılarak taranmıştır. EMPA-REG OUTCOME, CANVAS, DAPA-HF ve DAPA-CKD gibi önde gelen randomize kontrollü çalışmalar ile güncel meta-analizler değerlendirilmiştir.

Bulgular: SGLT2 inhibitörlerinin, hem klinik hem de preklinik modellerde tutarlı bir şekilde kan basıncını düşürücü etkiler gösterdiği bildirilmektedir. Endotelyal fonksiyon ve arteriyel sertlikte iyileşmeler gözlemlenmiş olmakla birlikte, klinik veriler zaman zaman heterojenlik göstermektedir. Deneysel çalışmalarda, SGLT2 inhibitörlerinin aterosklerotik plak oluşumunu azalttığı, neointimal hiperplaziyi inhibe ettiği ve abdominal aort anevrizması ile pulmoner hipertansiyona karşı koruyucu etkiler sağladığı ortaya konmuştur. Moleküler düzeyde bu vasküler yararlar; oksidatif stresin baskılanması, NF-κB ve NLRP3 inflamatuar yolaklarının downregülasyonu, nitrik oksit biyoyararlanımının artırılması ve damar düz kas hücrelerinin proliferasyonunun inhibisyonu ile ilişkilendirilmektedir. Ayrıca, otofajik aktivitenin ve hücresel yaşlanmanın düzenlenmesi, vasküler bütünlüğün korunmasına katkı sağlamaktadır.

Sonuç: SGLT2 inhibitörleri, glisemik kontrolün ötesinde, vasküler biyolojiyi etkileyen çoklu mekanizmalar aracılığıyla kardiyovasküler ve renal sistem üzerinde belirgin koruyucu etkiler göstermektedirler. Ancak SGLT2 inhibitörlerinin klinik potansiyelini tam olarak ortaya koyabilmek için temel ve klinik bilimlerce yürütülecek multidisipliner çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: SGLT2 inhibitörleri, damar biyolojisi, endotelyal fonksiyon, ateroskleroz, oksidatif stres, inflamasyon, kardiyovasküler koruma

Giriş

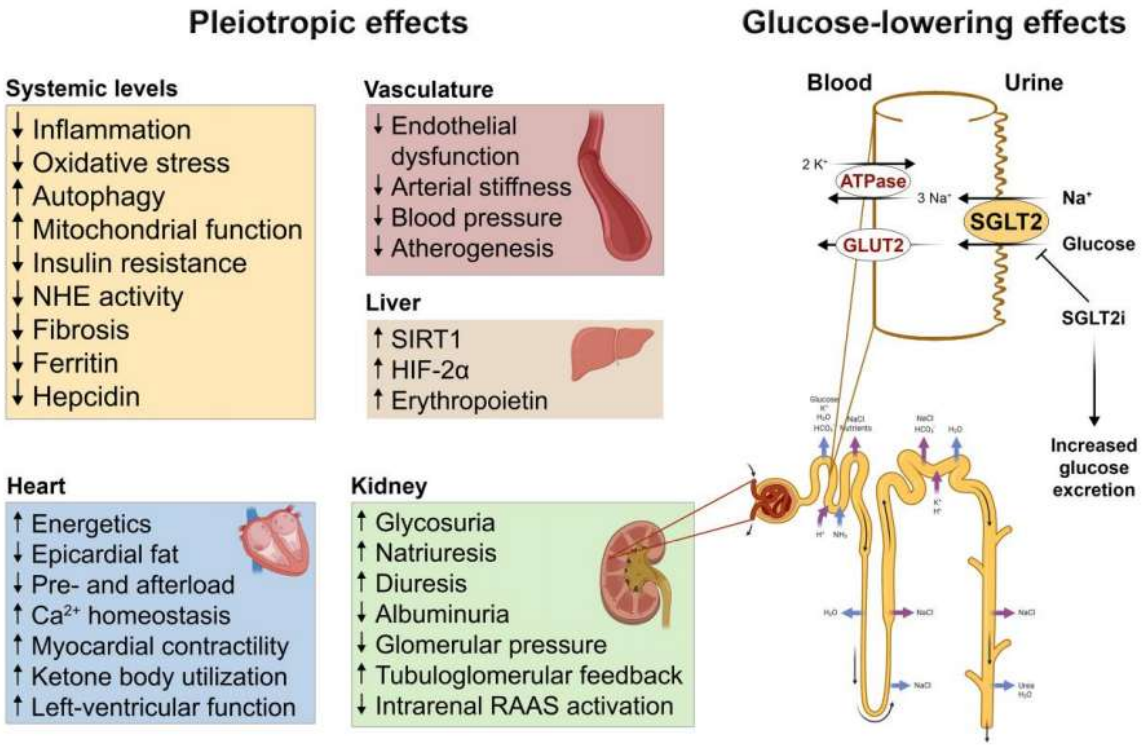
Sodyum-glukoz ko-taşıyıcı 2 (SGLT2) inhibitörleri, diğer adıyla gliflozinler, kan glukoz düzeyini düşürmek amacıyla böbreklerin proksimal kıvrımlı tübüllerinde glukoz reabsorpsiyonunu seçici olarak engelleyerek etki gösteren oral antidiabetik ilaçlardır [1]. Bu nedenle, SGLT-2 inhibitörleri insülin veya β-hücre fonksiyonlarından bağımsız olarak, doğrudan böbrekleri hedef alarak etki gösterir. Normal koşullarda, böbrekler günde yaklaşık 180 gram glukozu süzer. Bu glukozun neredeyse tamamı, sodyum-glukoz taşıyıcıları (SGLT'ler) aracılığıyla reabsorbe edilir. SGLT'ler, hücrelerin bazolateral yüzeyinde bulunan sodyum/potasyum ATPaz pompalarının oluşturduğu sodyum gradyanını kullanarak sodyum ve glukozu hücre içine taşır. Renal glukoz reabsorpsiyonunun yaklaşık %10'u SGLT-1 aracılığıyla, yaklaşık %90'ı ise erken proksimal tübülde yer alan SGLT-2 aracılığıyla gerçekleşir [2]. Ancak diyabetik hastalarda olduğu gibi, serum glukoz düzeyleri 200 mg/dL'nin üzerine çıktığında, bir miktar glukoz idrarla da atılmaktadır. Özellikle tip 2 diyabetli bireylerde, böbrek tübüler glukoz reabsorpsiyonu artmıştır[3]. Bu artış, SGLT-2 taşıyıcılarının ekspresyonundaki artışa bağlanmaktadır. Hipergliseminin, SGLT-2 taşıyıcılarının ekspresyonunu artırdığı gösterilmiştir. Taşıyıcı sayısındaki bu artış, glukozun daha fazla geri emilmesine yol açar. Bununla birlikte, artmış reabsorpsiyona rağmen tedavi edilmeyen hiperglisemi, serum glukoz düzeylerinin böbrek eşik değerinin üzerine çıkmasına neden olur ve bu da glukozüri ile sonuçlanır [4].

Tıbbî araştırmalar tarihinde, farmakolojik ajanların öngörülemeyen etkileri, kimi zaman yeni endikasyonların tanımlanmasına, kimi zaman ise mevcut ilaç sınıflarının klinik kullanımdan çıkarılmasına yol açmıştır. Sodyum-glukoz ko-taşıyıcı 2 (SGLT2) inhibitörleri, başlangıçta yalnızca tip 2 diyabet tedavisine yönelik olarak geliştirilmişken, son yıllarda kardiyovasküler sistem üzerindeki öngörülmeyen fakat klinik açıdan anlamlı yararları ile dikkat çekmiş ve bu özellikleri sayesinde diyabetik olmayan bireylerde de terapötik bir seçenek olarak değerlendirilmeye başlanmıştır. Kardiyovasküler sonuçlara ilişkin elde edilen güçlü kanıtlar doğrultusunda, SGLT2 inhibitörleri günümüzde kalp yetersizliği tedavi algoritmalarına giderek artan şekilde dâhil edilmekte ve glisemik duruma bakılmaksızın, kalp yetersizliği olan hastalarda hastane yatışlarının azaltılması ve ventriküler yeniden yapılanmanın desteklenmesi amacıyla kullanılmaktadır [5].

Sodyum-glukoz ko-taşıyıcı 2 (SGLT2) inhibitörlerinin kardiyovasküler sonuçlar ve kronik böbrek hastalığı (KBH) progresyonu üzerindeki etkilerini değerlendirmek amacıyla çeşitli randomize kontrollü klinik çalışmalar gerçekleştirilmiştir. Bu çalışmalar, SGLT2 inhibitörlerinin yalnızca glisemik kontrolü iyileştirmekle sınırlı kalmayıp; aynı zamanda majör advers kardiyovasküler olayları (MACE; kardiyovasküler ve tüm nedenlere bağlı mortalite, fatal veya nonfatal miyokard enfarktüsü ya da inme) ve kalp yetersizliği nedeniyle hastaneye yatış oranlarını anlamlı düzeyde azalttığını, ayrıca KBH'li hastalarda klinik prognozu iyileştirdiğini ortaya koymuştur. Elde edilen bu kardiyovasküler ve renal faydalar, hem diyabetik hem de diyabetik olmayan hasta popülasyonlarında tutarlı biçimde doğrulanmıştır. Tip 2 diyabetli bireylerde yürütülen Empagliflozin Cardiovascular Outcome Event Trial (EMPA-REG OUTCOME) çalışmasında, empagliflozinin MACE insidansını anlamlı düzeyde azalttığı gösterilmiştir [6]. Söz konusu çalışmanın post-hoc analizleri, empagliflozinin makroalbüminüri progresyonunu yavaşlattığını, serum kreatinin düzeyinde iki kat artışı önlediğini, renal replasman tedavisi ihtiyacını azalttığını ve böbrek hastalığına bağlı mortalite riskini düşürdüğünü ortaya koymuştur. Benzer biçimde, Canagliflozin Cardiovascular Assessment Study (CANVAS) ve DECLARE-TIMI 58 çalışmalarında,

sırasıyla canagliflozin ve dapagliflozinin renal sonuçlar açısından koruyucu etkiler sağladığı rapor edilmiştir [1].

Bu derleme, SGLT2 inhibitörlerinin kardiyovasküler faydalarına ilişkin mevcut kanıtları incelemekte olup, özellikle vasküler etkileri ve olası etki mekanizmaları üzerinde durmaktadır.



Şekil 1. Gliflozinlerin sistemik, vasküler, kardiyak ve renal düzeylerdeki rolüne ilişkin mekanistik bulgular. Preklinik kanıtlar, gliflozinlerin böbrek, kalp ve damar patolojilerini taklit eden preklinik modellerde potansiyel yararlı etkiler gösterebileceğini ortaya koymaktadır. Glukoz düşürücü etkilerinden bağımsız olarak çeşitli mekanizmaları içeren SGLT2 inhibisyonu; inflamatuar sinyal yollarını baskılamakta, oksidatif stresi azaltmakta, otofajik akışı iyileştirmekte ve mitokondriyal fonksiyonu artırmaktadır. Bu etkiler aracılığıyla kardiyorenal ve vasküler düzeyde terapötik yarar sağlamaktadır. **Kısaltmalar:** SGLT2, sodyum-glukoz taşıyıcı 2; NHE, sodyum/hidrojen değiştirici [7].

SGLT-2 İnhibitörlerinin vasküler Etkileri

Diyabetik ve diyabetik olmayan hastalarda yürütülen klinik çalışmalar, SGLT2 inhibitörlerinin umut verici etkilerini destekleyen giderek artan kanıtlar sunmaktadır. Ancak bu etkilerin altında yatan **moleküler mekanizmalar** henüz tam olarak aydınlatılamamıştır. Yakın dönemde yapılan **in vitro** ve **ex vivo** çalışmalar, bu vasküler etkileri aracılık edebilecek çok sayıda **hücresel süreç** ve **moleküler yolak** tanımlamış olup, bu mekanizmaların büyük olasılıkla **glisemik kontrolden bağımsız** işlev gördüğü düşünülmektedir. Bazı etkiler doğrudan böbrek tübüllerindeki SGLT2 üzerinden gerçekleşirken, gliflozinlerin bu yolaktan **bağımsız** etkiler de gösterdiği bilinmektedir. Bu

durumu destekleyen bir çalışmada, empagliflozinin **renal SGLT2 ekspresyonu olmayan farelerde** dahi kardiyoprotektif etkiler gösterdiği rapor edilmiştir. Mevcut çalışmalar, SGLT2 inhibitörlerinin **kan basıncı, endotelyal fonksiyon, ateroskleroz, restenoz ve abdominal aort anevrizması (AAA)** gibi kardiyovasküler parametreler üzerinde çoklu mekanizmalar aracılığıyla **olumlu etkiler** gösterdiğini ortaya koymuştur. Bu yararlı etkiler, SGLT2 inhibitörlerinin **inflamasyon, oksidatif stres, damar tonusu, hücre proliferasyonu ve migrasyonu, otofaji ve hücresel yaşlanma** gibi süreçleri düzenlemedeki rollerine bağlı olabilir (Şekil 1).

Kan Basıncı

Hipertansiyon, tip 2 diyabet mellitus (T2DM) ile sık görülen bir komorbiditedir; hipertansiyonun kontrol altına alınması, kardiyovasküler ölümleri ve hastalık progresyonunu önlemektedir. Kan basıncını düşürme etkisi, SGLT2 inhibitörlerinin bildirilen ilk kardiyovasküler etkileri arasında yer almaktadır. Yapılan deysel ve klinik çalışmalarda SGLT-2 inhibitörlerinin kan basıncı üzerindeki etkileri değerlendirilmiştir. Kan basıncı düşürücü etkilerin altında yatan mekanizmalar hâlen araştırılmaktadır. Bu etkiler; diüretik etki, arteriyel sertliğin azalması, endotel fonksiyonunun düzeltilmesi, sempatik sinir sisteminin baskılanması ve metabolik yeniden programlama gibi mekanizmalarla ilişkili olabilir [8-11].

Endotelyal Fonksiyon

Endotelyal hücreler (EC'ler), damar bütünlüğünün korunmasında hayati roller üstlenir. Bu işlevler arasında damar tonusunun, geçirgenliğin, inflamatuar yanıtların ve trombotik süreçlerin düzenlenmesi yer alır [12,13]. Kapsamlı deneysel kanıtlar, SGLT2 inhibitörlerinin glukoz düşürücü etkilerinden bağımsız olarak vasküloprotektif etkiler oluşturduğunu ortaya koymaktadır (Şekil 1). Gliflozinlerin endotelyal fonksiyon üzerindeki olumlu etkileri aşağıdaki mekanizmalarla ilişkilidir:

i) Nitrik oksit (NO) biyoyararlanımının artırılması,

ii) Oksidatif stresin azaltılması,

iii) Mikrovasküler disfonksiyonun giderilmesi,

iv) Mitokondriyal fonksiyonun korunması,

v) İnflamasyonun baskılanması,

vi) Enerji homeostazisinin yeniden sağlanması.

Bu mekanizmalar birbirleriyle sıkı bir şekilde bağlantılıdır ve bu nedenle hangisinin klinik fayda açısından daha belirleyici olduğu şu aşamada net olarak ortaya konulamamıştır. Ancak mitokondriyal fonksiyon ve hücresel enerji dengesi üzerindeki düzenleyici etkilerin, gliflozinlerin kardiyovasküler faydalarının oluşmasında özellikle önemli rol oynadığı düşünülmektedir [14].

Arteriyel Sertlik

Damar duvarının rijitliğinde artış anlamına gelen arteriyel sertlik, vasküler disfonksiyonun ve yaşlanmanın önemli bir göstergesidir. Hipertansiyon ve ateroskleroz ile yakından ilişkilidir. Arteriyel sertliği değerlendirmede kullanılan **nabız dalga hızı (pulse wave**

velocity – PWV) ve **artış indeksi (augmentation index – AIx)** gibi parametreler, kardiyovasküler hastalıkların (KVH) klinik sonuçları ve diyabete bağlı kardiyovasküler komplikasyonlar açısından prognostik değere sahiptir. Lin ve arkadaşları, empagliflozinin koroner arter duvar kalınlaşmasını ve perikoroner fibrozisi iyileştirdiğini gözlemlemişlerdir. Aroor ve çalışma arkadaşları ise, empagliflozinin sistemik ve renal arteriyel sertliği azalttığını bildirmiştir. Yapılan klinik çalışmalarda; Dapagliflozin, kanagliflozin ve tofogliflozin gibi SGLT2 inhibitörlerinin arteriyel sertliği azalttığı bildirilmiştir. Ancak yakın zamanda gerçekleştirilen çok merkezli keşif niteliğindeki LUSCAR çalışmasında, luseogliflozin tedavisi sırasında kan basıncı ve metabolik parametreler üzerinde etkiler gözlenmiş olmasına rağmen, arteriyel sertlikte anlamlı bir değişiklik saptanmamıştır [8].

Ateroskleroz

Ateroskleroz, diyabetin en önemli komplikasyonlarından biridir ve sıklıkla **miyokard enfarktüsü (MI)** ile **inme** gibi olaylara yol açar; bu durumlar diyabetik hastalarda morbidite ve mortalitenin en büyük kısmını oluşturur. Büyük ölçekli klinik sonlanım çalışmaları, antidiabetik tedavilerin —özellikle SGLT2 inhibitörlerinin— ateroskleroza bağlı fatal ve nonfatal olayları azalttığını göstermiştir. Hayvan modellerinden elde edilen bulgular, SGLT2 inhibitörlerinin ateroskleroza karşı koruyucu etkiler gösterebileceğini ortaya koymuştur. Empagliflozin, yüksek yağlı diyet (HFD) veya Western diyeti ile beslenen ApoE−/− farelerde aortik aterosklerotik lezyonları anlamlı şekilde azaltmıştır [15-16]. Hiperkolesterolemik ve diyabetik fare modellerinde, empagliflozin plak gerilemesini desteklemiş; inflamatuar hücre infiltrasyonunu ve lipid birikimini azaltırken, kolajen içeriğini artırarak lezyon stabilitesi üzerinde olumlu etkiler göstermiştir[17]. Benzer şekilde, kanagliflozin, ipragliflozin ve dapagliflozin de yüksek yağlı diyetle beslenen veya streptozotosin (STZ) ile diyabetik hale getirilmiş ApoE−/− farelerde ateroskleroz progresyonunu baskılamıştır [18].

Aort Anevrizması

Diyabet ile aort anevrizması arasında ters yönlü bir ilişki olduğuna dair kanıtların ortaya konması, SGLT2 inhibitörlerinin aort anevrizmaları üzerindeki potansiyel etkilerini önemli bir araştırma alanı haline getirmiştir [19]. Yakın tarihli bir preklinik çalışmada, **empagliflozinin**, anjiyotensin II ile infüze edilen **ApoE−/−** farelerde **abdominal aort anevrizması (AAA)** gelişimini anlamlı şekilde engellediği gösterilmiştir. Söz konusu koruyucu etkinin **doza bağımlı** olduğu ve **kan şekeri ile kan basıncı üzerindeki etkilerden bağımsız** olarak gerçekleştiği rapor edilmiştir. Bu bulgular, empagliflozinin etkisinin, glisemik ve hemodinamik değişikliklerden ziyade, **lezyon bölgesindeki makrofaj infiltrasyonunu ve neovaskülarizasyonu baskılamasıyla** ilişkili olabileceğini düşündürmektedir [20].

Antiinflamatuar Etki

SGLT2 inhibitörleri, belirgin **antiinflamatuvar özellikler** göstermektedir. Gerçekten de gliflozin tedavisi, çeşitli kardiyometabolik hastalık modellerinde **nükleer faktör kappa B (NF-κB)** transkripsiyon faktörünün aktivasyonunu azaltmış; bununla birlikte **monosit kemotaktik protein-1 (MCP-1)**, **TNF-α**, **interlökin-6 (IL-6)** ve **yüksek duyarlılıklı C-reaktif protein (hsCRP)** düzeylerinde azalma sağlamıştır. Ayrıca SGLT2 inhibitörleri, **NLRP3 inflamatuvar kompleksinin aktivasyonunu**, **ICAM-1**, **VCAM-1**, **P-selektin** ve **E-selektin** ekspresyonunu baskılamış; bu yolla **inflamatuvar hücrelerin damar duvarına göçünü ve aktivasyonunu** azaltmıştır (Şekil 1). Bu mekanizmalar sayesinde **endotelyal**

bütünlük ve **damar bariyer fonksiyonu** desteklenmektedir. Her ne kadar küçük ölçekli bir pilot çalışma umut verici sonuçlar ortaya koymuş olsa da, daha önceki çalışmalarda gliflozinlerin arteriyel trombüs oluşumu üzerinde nötr etki gösterdiği bildirilmiştir; bu bulgu, büyük ölçekli klinik çalışmaların sonuçlarıyla da uyumludur [7].

Antioksidan etki

Çeşitli **SGLT2 inhibitörlerinin** sistemik **oksidatif strese karşı etkili olduğu** gösterilmiştir. Bu ajanlar, diyabetik kemirgenlerde **böbrek, aort, kalp, kas, yağ dokusu, beyin, kan ve idrar** gibi birçok dokuda **oksidatif türlerin düzeyini azaltırken**, aynı zamanda **antioksidan gen ekspresyonunu artırmıştır**.

Hücre Proliferasyonu ve Migrasyonunun Önlenmesi

Ateroskleroz ve diyabete bağlı vasküler komplikasyonların gelişiminde, endotelyal hücreler (EC'ler) ve damar düz kas hücrelerinin (SMC'ler) **kontrolsüz proliferasyonu (çoğalması)** ve **migrasyonu (göçü)** temel patofizyolojik süreçler arasında yer alır. Bu hücresel olaylar; damar duvarında **neointima oluşumu**, **plak gelişimi** ve **damar tıkanıklığına** zemin hazırlar.SGLT2 inhibitörlerinin, çeşitli deneysel modellerde **hücre proliferasyonu ve migrasyonunu baskıladığı** gösterilmiştir. Bu etkiler, özellikle **anti-inflamatuvar**, **antioksidan**, ve **enerji metabolizmasını düzenleyici** özellikleriyle ilişkilendirilmekte ve damar bütünlüğünün korunmasında potansiyel katkılar sağlamaktadır.

Hücresel Yaşlanma

Vasküler yaşlanma (senesens), **hiperglisemi** gibi metabolik risk faktörleriyle hızlanabilir ve bu durum **ateroskleroz** ve **diyabet** dahil olmak üzere kardiyometabolik hastalıkların hem insanlarda hem de hayvan modellerinde belgelenmiştir [147, 148]. Bununla birlikte, **SGLT2 inhibitörlerinin yaşlanma karşıtı (anti-senesens) etkilerinin altında yatan moleküler mekanizmalar** henüz tam olarak aydınlatılamamıştır.

Otofaji

SGLT2 inhibitörleri, kardiyomiyopati ve nefropatinin gelişimi ve ilerleyişi üzerinde belirgin bir koruyucu etki paterni oluşturur. Bu etkiler; **oksidatif ve endoplazmik retikulum stresinin azalması**, **mitokondriyal sağlığın yeniden tesis edilmesi** ve **mitokondriyal biyogenezisin artışı**, **proinflamatuvar ve profibrotik yolakların baskılanması**, ayrıca **hücresel ve organ düzeyinde bütünlük ile canlılığın korunması** gibi mekanizmalarla karakterizedir.Mevcut bilimsel kanıtlar, bu belirgin fayda deseninin, **SGLT2 inhibitörlerinin otofajik akışı artırarak hücresel temizlik (cellular housekeeping) süreçlerini desteklemesi** yoluyla açıklanabileceğini göstermektedir. Bu durum; **AMPK (adenozin monofosfat ile aktive olan protein kinaz)**, **SIRT1**, **SIRT3**, **SIRT6** ve **PGC1-α (peroksizom proliferatör-aktive edici reseptör-γ koaktivator 1-α)** gibi metabolik düzenleyicilerin ekspresyon ve aktivitelerinde artış, **mTOR (mammalian target of rapamycin)** aktivasyonunda ise azalma ile kendini gösterir. Dikkat çekici olarak, **SGLT2 inhibitörlerinin otofajik akışı artırma etkisi**, SGLT2 ekspresyonu bulunmayan veya çevresel glukoz/keton değişimine maruz bırakılmayan **izole hücre ve dokularda dahi gözlemlenmiştir**. Bu durum, söz konusu ilaçların, doğrudan **hücre içi sinyal yollarına bağlanabilme** özelliğiyle ilişkili olabilir [21].

Sonuç

Sodyum-glukoz ko-taşıyıcı 2 (SGLT2) inhibitörleri, başlangıçta glisemik kontrol amacıyla geliştirilmiş olsa da, son yıllarda yürütülen geniş kapsamlı klinik çalışmalar bu ajanların kardiyovasküler ve renal sonuçlar üzerinde belirgin faydalar sağladığını ortaya koymuştur. T2DM hastalarında, SGLT2 inhibitörleri kardiyovasküler mortaliteyi ve kalp yetersizliğine bağlı hastaneye yatışları azaltmakta; ejeksiyon fraksiyonu azalmış ya da korunmuş kalp yetersizliği olan bireylerde prognozu iyileştirmektedir. Diyabet varlığına bakılmaksızın, böbrek odaklı çalışmalarda da böbrek yetmezliği insidansını düşürdüğü gösterilmiştir. SGLT2 inhibitörlerinin kardiyorenal faydalarının altında yatan temel mekanizmaları daha iyi anlayabilmek, **glisemik olmayan etkileri** ve **güvenlilik profilleri** ile ilgili daha ileri araştırmalara ihtiyaç duyulmaktadır.

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EXAMINATION OF THE EFFECT OF PERSONNEL PRACTICES ON COSTS IN MEDICAL WASTE MANAGEMENT

ABSTRACT

Problem of the Study: The medical waste problem of our world, which is rapidly developing technologically and medically every day, is increasing in parallel. The resources used for the disposal of medical waste, which is one of the important wastes, are limited and costly. In particular, poorly managed wastes threaten the environment and human health and pose an economic problem for countries. For this reason, in line with the regulations, the practices of waste personnel involved in the separation, transportation, storage and disposal of waste at the source significantly affect the cost of waste.

Purpose of the Study: With this study, it is aimed to benefit the national economy by examining the efficiency and effectiveness of personnel practices in medical waste applications in terms of conscious use of waste equipment, consumables and correct waste separation in order to protect the environment and human health.

Method: Within the scope of Medical Waste Regulation, the relevant Regulation, Waste Regulation, annual waste data of the Ministry of Environment, Urbanization and Climate Change of the Republic of Turkey, secondary data sources were analyzed.

Findings: As a result of the rapid advancement of industry and technology in our developing world, the type of wastes and disposal methods are also changing. Medical waste disposal methods are costly processes. It is seen that the resources used for waste disposal in developing economies are very limited. In accordance with Medical Waste management, segregation at source, proper transportation and temporary storage are very important. However, in order to produce less waste, to contribute to the national economy, to create a healthier environment, it is important to raise awareness and create positive consciousness in people responsible for medical waste, in terms of sustainability and development of resources.

Conclusions: Medical waste management, which causes a great pressure on the environment, cannot be solved with a single approach. In order for Medical Waste Management to be successful and sustainable, it is important to ensure the applicability of the regulations determined in stages, to carry out studies to reduce the amount of waste, to have sufficient medical waste equipment and waste personnel in hospitals, and to organize training programs to raise awareness of medical waste personnel. This will contribute to the national economy by reducing the cost of waste.

Keywords: Medical waste, regulation, qualified waste personnel

TIBBİ ATIK YÖNETİMİNDE, GÖREVLİ PERSONEL UYGULAMALARININ MALİYETE ETKİSİNİN İNCELENMESİ

ÖZET

Çalışmanın Problemi: Her geçen gün teknolojik ve tıbbi açılardan hızla gelişmekte olan dünyamızın tıbbi atık sorunu da buna paralel olarak artmaktadır. Önemli atıklardan olan tıbbi atıkların yok edilmesi için kullanılan kaynaklar sınırlı ve maliyetlidir. Özellikle iyi yönetilmeyen atıklar çevre ve insan sağlığını tehdit etmekle beraber, ülkeler açısından ekonomik olarak sorun teşkil etmektedir. Bu nedenle yönetmelikler doğrultusunda, atığı kaynağında ayrıştıran, taşıyan, depolayan ve bertaraf etme işlemlerinde görev alan atık personelinin uygulamaları atık maliyetini önemli ölçüde etkilemektedir.

Çalışmanın Amacı: Bu çalışma ile çevre ve insan sağlığını korumak amacına yönelik olarak, atık ekipmanı, sarf malzemelerinin bilinçli kullanımı ve doğru atık ayrıştırması açısından tıbbi atık uygulamalarında görevli personel uygulamalarının verimlilik ve etkinliğinin incelenerek ülke ekonomisine fayda sağlanması amaçlanmaktadır.

Metod: Tıbbi Atık Yönetmeliği kapsamında ilgili Yönetmelik, Atık Yönetmeliği, T.C. Çevre, Şehircilik ve İklim Değişikliği Bakanlığı yıllık atık verileri, ikincil veri kaynakları incelenmiştir.

Bulgular: Gelişen dünyamızda endüstrinin ve teknolojinin hızla ilerlemesi sonucunda atıkların türü ve yok edilme yöntemleri de değişmektedir. Tıbbi atık bertaraf yöntemleri maliyetli işlemlerdir. Gelişen ekonomilerde atıkların yok edilmesi için kullanılmakta olanın kaynakların oldukça sınırlı olduğu görülmektedir. Tıbbi Atık yönetimine uygun olarak, kaynağında ayrıştırma, doğru taşıma ve geçici depolama çok önemlidir. Bununla beraber, daha az atık üretmek, ülke ekonomisine katkıda bulunmak, daha sağlıklı çevre oluşturmak için tıbbi atıklardan sorumlu kişilerde farkındalık meydana getirme, olumlu bilinç oluşturma, kaynakların sürdürülebilirliği ve gelişimi açısından önem arz etmektedir

Sonuçlar: Çevre üzerinde büyük bir baskıya neden olan tıbbi atık yönetimi tek bir yaklaşımla çözülemeyecektir. Tıbbi Atık Yönetiminin başarılı ve sürdürülebilir olması için aşamalar halinde belirlenmiş yönetmeliklerin uygulanabilirliğini sağlamak, atık miktarının azaltılması için çalışmalar yapmak, hastanelerde yeterli tıbbi atık ekipmanı ve atık personeli bulundurmak, tıbbi atık personelini bilinçlendirmeye yönelik olarak eğitim programlarını düzenlemek önemlidir. Bu sayede atık maliyetinin azaltılması ile ülke ekonomisine katkı sağlanmış olacaktır.

Anahtar kelimeler: Tıbbi atık, yönetmelik, nitelikli atık personeli

1. GİRİŞ

Tıbbi atıklar sağlık kuruluşlarının tetkik ve tedavi hizmetleri sonucu oluşan diğer atıklardan ayrıştırılarak uygun biçimde bertaraf edilmesi, güvenli bir şekilde uzaklaştırılması gereken özellikli atıklardır. Bu atıkların bulaşıcı olma özelliği de yüksek olduğundan özenli bir şekilde toplanması gerekir. Tıbbi atıkların yerinde ayrıştırılması, toplanması, taşınması ve bertaraf edilmesi atık personelinin görevidir. Personelin iyi uygulamaları, çevre ve insan sağlığını tehdit eden tıbbi atıkların riskini en aza indirerek ve tıbbi atık maliyetini azalttığı görülmektedir. İyi tıbbi atık yönetimi çevre ve insan sağlığını koruduğu gibi atık bertarafı için kullanılan kaynakların da sürdürülebilirliğini sağlayarak ülke ekonomisine de katkı sağlamaktadır. Bu nedenledir ki tıbbi atıklar sistematik bir şekilde yönetilmelidir.

BULGULAR

Amaç: Bu çalışma ile çevre ve insan sağlığını korumak, ülke ekonomisine katkı sağlamak amacına yönelik olarak, atık ekipmanlarının, sarf malzemelerinin bilinçli kullanımı ve doğru atık ayrıştırması açısından tıbbi atık uygulamalarında görevli personel uygulamalarının verimlilik ve etkinliğinin incelenerek mevcut durumun belirlenmesidir. Bu amaç doğrultusunda Tıbbi Atık Yönetmeliği kapsamında ilgili Yönetmelik, Atık Yönetmeliği, T.C. Çevre Şehircilik ve İklim Değişikliği Bakanlığı yıllık atık verileri, TÜİK yıllık tıbbi atık verileri ve ikincil veri kaynakları incelenmiştir.

Son yıllarda sağlık alanındaki yenilikler, nüfusun çoğalmasına bağlı olarak sağlık tesisleri sayısının artması ve tek kullanımlık sarf malzemelerin tüketimi beraberinde tıbbi atık miktarını da artırmıştır. Sağlık kuruluşlarında tıbbi atıkların toplanması, taşınması ve geçici depolarda biriktirilmesi konusunda, Dünya Sağlık Örgütü hastane yönetiminin belli standartlar getirmiştir. Bu standartlar beş ana grupta değerlendirilmektedir. Bu sınıflandırmaya göre hastane atıkları; genel atıklar, kesiciler, kimyasal ilaçlar ve ilaç atıkları, enfeksiyona yol açan atıklar ve tehlikeli atıklar olarak sıralanmaktadır. (Tıbbi Atıkların Kontrolü Yönetmeliği 2017). Yapılan araştırmalar hastanelerden çıkan atıkların %80'inin zararsız atıklar olduğu, kalan atıkların %15'inin enfeksiyon bulaşmış atıklardan meydana geldiği, %1'lik kısmın kesici ve delici malzemelerden oluştuğu, kalanların ise kimyasal atıklar başta olmak üzere, radyoaktif ve farmakolojik atıklardan oluştuğu belirtilmektedir (WHO 2021).

Dünya Sağlık Örgütü, ayrıca tıbbi atıkların toplanması taşınması ve depolanması ile ilgili tavsiyelerde de bulunmuştur (WHO 2021).

- Atık toplama işlemlerinin öncelikle hasta odası ve servislerden başlanarak yapılmasını,

- Evsel atık niteliğindeki atıkların tıbbi atıklarla karıştırılmaması gerektiğini,

- Sağlık kurumlarının hasta odaları ve çalışılan diğer yerlerden çıkan atıkların, kullanım amacına uygun atık taşıma arabaları ile taşınması gerektiği,

- Taşıma arabalarının temizlenmesi ve dezenfekte edilmesi gerektiğine vurgu yapmaktadır. Bu atıklar hastane atıklarının toplanması ve nakli sırasında sağlık riski oluşturmaktadır. Bu yüzden de özellikle tehlike yaratacak atıkların taşınması sırasında azami dikkat gösterilmelidir.

- Hastane bünyesinde mümkünse tehlike oranı düşük olan malzemelerin kullanılması gerekmektedir. Hastane yönetimi açısından dikkat edilecek en önemli husus ise, tehlike arz eden uygulamaların, tehlike arz etmeyenlerden ayrılmasıdır. Bu nedenle zararsız atıklar değerlendirilmeli, tekrar kullanılamayan kimyasal atıklar için uygun depolama alanları oluşturulmalıdır.

- Radyoaktif maddelerle ilgili güvenli alanlar meydana getirilmeli, kimyasal nitelikteki atık grubu atık su tesisatlarından uzak tutulmalıdır. Bu tür atıklar için herhangi bir işlem yapılmamalı, uzman personellerin bulunduğu firmalara teslim edilmelidir (WHO 2021).

- Atıkların düşük seviyede olması durumunda yerleşim biriminden uzak noktalar seçilmelidir.

- Tehlikeli atık çıktıları bulunan sağlık kuruluşları, olumsuz durumları göz önüne alarak nerelerden yardım alacağı konusunda daha önceden tedbirli davranmalıdır.

- Tüm sağlık kuruluşları için atık planlamaları, hastanelerin oluşumu aşamasında tamamlanmalıdır.

- Hastanelerden çıkan atık miktarları, hasta sayısına göre değişiklik gösterebileceğinden planlamalar ona göre yapılmalıdır.

- Atıklar ayrıştırılmalı, atık toplama ile ilgili alet ve gereçler mevzuat hükümlerine uygun olmalı, geçici atık depoları atık toplama merkezlerine mümkün olduğu kadar yakın olmalıdır.

- Atıkların bertaraf yöntemleri daha önceden planlanmalıdır. Çünkü özellikle büyük miktarda hasta kapasitesine sahip olan hastaneler için kendi imkanları ile bertaraf etme yöntemi ekonomik bir durumken, bazı kuruluşlara bu maliyetli gelebilir. Bu tarz sağlık kuruluşları için ortak bir imha yerinin bulunmasında fayda sağlayacaktır. Dünya Sağlık Örgütü'nün tavsiye ettiği öneriler doğrultusunda, öncelikle atıklarla ilgili her türlü faaliyette, tüm sıkıntıları en aza indirecek uygulamalara ihtiyaç bulunmaktadır. Ayrıca atıkların toplanması, nakliyesi ve depolanması sırasında kullanılacak olan alet ve malzemelerin atık işlerine uygun olması gerekmektedir.

TIBBİ ATIKLARIN BERTARAF YÖNTEMLERİ

Tıbbi atıkların çevre ve insan sağlığına zarar vermeden güvenli bir şekilde bertaraf edilmesi için bir çok yöntem kullanılabilmektedir.

Yakma Teknolojileri:

Tıbbi Atık Yönetiminin Ekonomisi Tıbbi atıklar, fırında yakma, döner fırınlarda yakma, pirolitik fırınlarda yakma (piroliz ve gazlaştırma) şeklinde birkaç teknikle bertaraf edilebilmektedir. Bu teknoloji bir çok ülkede kullanmaktadır. Danimarka kullandığı elektriğin bir kısmı atık yakma ile elde ederken, AB ülkelerinin çoğunda ise yakma sonucu oluşan furan ve dioksin gibi zararlı emisyonların oluşması, bunların arıtılması için de pahalı cihazlara gereksinim duyulması nedeniyle birçok yakma fırını kapatılmıştır. Örneğin Almanya'da 1987'de 218 olan yakma fırını sayısı 1996'da 10 adete düşmüştür (Cansaran, 2010: 116).

Kimyasal Bertaraf Teknolojileri:

Sağlık hizmetlerinde kullanılan tıbbi ekipmanların, yerlerin ve duvarlardaki mikroorganizmaların öldürülmesi amacıyla sık olarak kullanılmakta olan kimyasal dezenfektanlar son zamanlarda tıbbi atıkların bertarafında da kullanılmaktadır.

Buhar Bertaraf Teknolojileri:

Otoklav ile sterilizasyon, atıkların yüksek sıcaklık, yüksek basınçlı buhara tabi tutulma işlemi olup, yakmadan sonra en çok kullanılan alternatif bir bertaraf yöntemidir. Düşük yatırım ve işletme masrafları nedeniyle tercih edilmektedir.

Diğer Yöntemler:

Ülkemizde son yıllara kadar en yaygın kullanılan yöntemlerden biri olan düzenli depolama dışında mikrodalga ile ışınlama (atıkları küçük parçalara bölen bir yükleme sistemi ile atıkların ışınlamaya tabi tutulması), enkapsülasyon (kübik kutular veya metal fıçı gibi konteynırlara doldurulan atıklara bağlayan bir madde ilavesi yapılarak, konteynırların sıkıca kapatılması işlemi) inert hale getirme (farmakolojik atık ve yüksek dozda (ağır) metal içeren yanma külleri için genelde uygun olan ve atıkların bertarafından önce bunların çimento veya diğer maddelerle karıştırılarak içindeki zehirli maddelerin, yüzey veya yer altı sularına karışma riskini en aza indirgenmesi işlemi) gibi birçok bertaraf yöntemi mevcuttur (Veeken, 2000: 31-44; WHO, 2013a: 112-116).

TIBBİ ATIK YÖNETİMİN MALİYETİ

Tıbbi atık yönetiminin maliyet ekonomisini incelemek için öncelikle atık değerlendirmesi yapılmalıdır. Atıklar değerlendirilirken personel uygulamalarını da izlemek gerekmektedir. Bir çok yerde personelin tıbbi atık sarf malzemelerini amacı dışında kullandığı görülmektedir.

Günlük üretilen atık miktarı ve türünün, bir sağlık tesisinin nerelerinde atık üretildiğinin ve toplama sıklığının bilinmesiyle günlük ne kadar atık kovasına, plastik torbaya, kesici alet konteynırına, depolama alanına, personele ve ekipmana ihtiyaç duyulduğu tahmin edilebilir. Günlük atık miktarı, gereksinim duyulan bertaraf tesisinin kapasitesini, vardiya sayısını veya işletme saatlerini belirler (WHO, 2013a: 168). Kurum ve kuruluşlar tarafından kullanılan atık yönetimi hiyerarşisinde 6 sistematik yaklaşım bulunmaktadır. Bunlar:

- Önleme
- Azaltma
- Tekrar kullanım
- Geri Dönüşüm
- Enerji kazanımı
- Bertaraf

Ülkemizde tıbbi atıkların güvenli yönetimi ile ilgili usul ve esaslar, Çevre ve Orman Bakanlığı tarafından hazırlanan 22 Temmuz 2005 tarih ve 25883 sayılı Resmî gazetede yayımlanarak yürürlüğe giren ‘’Tıbbi Atıkların Kontrolü Yönetmeliği’’ ile belirlenmiştir. Bu yönetmeliğe göre, sağlık tesislerinden kaynaklanan atıklar Dünya Sağlık Örgütünün genel sınıflandırmasına uygun olarak sınıflandırılır. Sağlık kuruluşlarının hemen hepsinde tıbbi atık yönetimi ile ilgili sorunlar benzer şekildedir. Atık toplama, ayrıştırma, geçici depolama, personelin atık yönetimi ile ilgili uygulamaları, alışkanlıkları eğitimi ve bilinçlenmesi, bertaraf yöntemleri, bertaraf yönteminin uygunluğu, çevresel kontrol ve izleme maliyet olarak görülmektedir. Tıbbi atık yönetiminde uygun ve sürdürülebilir bir standart oluşturabilmek için sağlık tesisinin yıllık bütçesi içinde atık yönetimi için kullanılabilir ayrı bir bütçenin olması gerekmektedir. Bir sağlık kuruluşunda atık sisteminin etkili bir şekilde yürütülmesi, sürdürülmesi ve izlenmesi ancak bu koşulla sağlanabilir. Özel bir bütçenin yokluğu olası iyileşmeleri oldukça kısıtlar (WHO, 2013a:174). Tıbbi atık yönetiminde en çok kullanılan metot kg başına fiyat uygulamasıdır. Ülkemizde tıbbi atık bertaraf ücretlerinin bazı Avrupa ülkelerinden daha yüksek olduğu alan yazındaki çalışmalarda görülmektedir. Aynı zamanda bu veriler yerel ve ulusal düzeyde planlama, bütçeleme, tedarik, atık yönetim sistemlerinin optimizasyonu ve çevresel etki değerlendirme risklerinin belirlenmesi için de kullanılabilmektedir Tıbbi atığın oluşumunu önlemek veya daha az üretmek, ayrıştırmak ve gereksiz atık bertarafını engelleyerek bertaraf ve uzaklaştırma maliyetini azaltacaktır. Tıbbi atıkların bertaraf ve uzaklaştırma maliyeti, katı atığın maliyetinden daha yüksek olduğundan tıbbi atıkları azaltmayı bir ödev haline getirir. Katı ve evsel atık, tıbbi atık ile karıştığında katı atıktan yaklaşık 20 kat daha fazla uzaklaştırma maliyeti olan tıbbi atık olarak bertaraf edilmelidir (Giacchetta ve Marchetti, 2013:66). Özellikle atıklar ayrıştırılırken personelin hangi atığın hangi sınıfa girdiğini bilmesi son derece önemlidir (Ananth vd., 2010:159).

TÜİK verilerine göre Sağlık kuruluşlarında 2012/2022 yılları arasında toplanan tıbbi atık miktarı aşağıda verilmiştir.

Tıbbi atık göstergeleri, 2012 - 2016

	2012	2014	2016
Sağlık kuruluşu sayısı	1 449	1 498	1 527
Tıbbi atık miktarı (ton)	68 929	74 495	81 024
Düzenli depolama tesisinde bertaraf edilen (ton)	50 982	50 656	54 440
Sterilize edilerek (ton)	31 697	40 161	54 440
Sterilize edilmeden (ton)	19 284	10 494	-
Belediye çöplüğünde bertaraf edilen (ton)	12 198	16 323	14 019
Sterilize edilerek (ton)	11 218	16 313	14 013
Sterilize edilmeden (ton)	980	11	6
Yakma tesisinde bertaraf edilen (ton)	5 745	7 515	12 566
Diğer (ton)(1)	5	1	-
Hasta başına ortalama tıbbi atık miktarı (kg/kişi)	0,20	0,19	0,18

Tablodaki rakamlar, yuvarlamadan dolayı toplamı vermeyebilir.

- Bilgi yoktur.

(1) Açıkta yakılan, gömülen vb. kapsanmaktadır.

Tıbbi atık istatistikleri, 2017, 2018

	2017	2018
Sağlık kuruluşu sayısı[1]	1 525	1 550
Tıbbi atık miktarı (ton)	85 987	89 454
Sterilize edilerek depolama alanlarında bertaraf edilen (ton)	78 380 (r)	82 559
Yakma tesislerinde bertaraf edilen (ton)	7 607 (r)	6 895

(1) Üniversite, doğum ve genel maksatlı hastaneler ile kliniklerini kapsar.
(r) Revize edilmiştir.

Oluşan atık miktarı, 2020, 2022 (Ton)

	Toplam atık miktarı		Tehlikeli atık miktarı		Tehlikesiz atık miktarı	
	2020	2022	2020	2022	2020	2022
Toplam	**104 739 181**	**109 237 232**	**30 770 088**	**29 380 898**	**73 969 093**	**79 856 334**
İmalat sanayi işyerleri	**23 867 866**	**27 969 021**	4 597 274	5 439 883	19 270 593	22 529 139
Termik santraller	**24 375 356**	**27 815 548**	10 012	10 512	24 365 343	27 805 036
Maden işletmeleri[1]	**27 581 875**	**26 309 170**	26 044 730	23 794 881	1 537 144	2 514 289
Organize sanayi bölgeleri	**279 067**	**323 140**	116 720	127 268	162 347	195 872
Hanehalkı[2]	**28 635 018**	**26 820 352**	1 352	8 354	28 633 665	26 811 998

Tablodaki rakamlar, yuvarlamadan dolayı toplamı vermeyebilir.
Önceki yıllarda yayımlanan Sağlık Kuruluşları Atık İstatistikleri, 2022-2026 Resmi İstatistik Programı çerçevesinde Çevre, Şehircilik ve İklim Değişikliği Bakanlığı tarafından yayımlanacaktır.
(1) Dekapaj malzemesi/ pasa hariç atık miktarıdır.
(2) Hanehalkından kaynaklı atık miktarı, Belediye Atık İstatistikleri Anketi sonuçları kullanılarak tahmin yöntemiyle hesaplanmıştır.

Çevre Şehircilik ve İklim Değişikliği Bakanlığının verilerinde de son yıllardaki tıbbi atık miktarında artış olduğu gözlenmektedir.

2017 yılında toplam tıbbi atık miktarı:98 729 ton

2018 yılında toplam tıbbi atık miktarı:107 400 ton

2019 yılında toplam tıbbi atık miktarı:109 478 ton

2020 yılında toplam tıbbi atık miktarı:125 566 ton

2021 yılında toplam tıbbi atık miktarı:135 869 ton

2022 yılında toplam tıbbi atık miktarı:130 401 ton (Çevre Şehircilik ve İklim Değişikliği Bakanlığı)

2024 YILINDA MAHALLİ ÇEVRE KURULU KARARLARI GEREĞİ UYGULANAN TIBBİ ATIK BİRİM FİYATLARI		
PLAKA NO	**İLİ**	**2024**
1	**ADANA**	2024 yılında ilimizde oluşan tıbbi atıkların toplama, taşıma ve bertaraf ücretlerinin; %80 oranı esas alınarak yapılan güncellemeye göre; **Yüreğir, Sarıçam, Seyhan, Çukurova, Karaisalı, Ceyhan, Karataş, İmamoğlu, Kozan, Yumurtalık İlçelerinde** sağlık kuruluşlarından taşıma ücreti 6,55 TL/KG+KDV, bertaraf ücreti 10,04 TL/KG+KDV ve toplamda **16.59 TL/KG+KDV** olarak, **İl Merkezine 81 KM ve üzeri uzaklıktaki Aladağ, Feke, Saimbeyli, Tufanbeyli, Pozantı İlçelerinde** sağlık kuruluşlarından taşıma ücreti 7,02 TL/KG+KDV, bertaraf ücreti 10,04 TL/KG+KDV ve toplamda **17,06 TL/KG+KDV** olarak, **Ayda 0-7 kg'a kadar** atık üreten sağlık kuruluşlarından taşıma ücreti 125,64 TL/AY+KDV, bertaraf ücreti 10,04 TL/AY+KDV ve toplamda **135,68 TL/AY+KDV** olarak, **Ayda 8-15 kg'a kadar** atık üreten sağlık kuruluşlarından taşıma ücreti 251,32 TL/AY+KDV, bertaraf ücreti 10,04 TL/AY+KDV ve toplamda **261,36 TL/AY+KDV** olarak, Tıbbi atık üreten kuruluşlardan çıkan patolojik atıkların tıbbi atık yakma tesislerinde bertaraf edilmesi gerektiğinden; İlimize en yakın patolojik atıkların bertaraf edilebileceği tesisin Ankara ilinde bulunması sebebiyle patolojik atıkların Ankara İline gönderilmesine ve **patolojik atıklar için 69,41 TL/KG+KDV + Ankara MÇK'da belirlenen bertaraf ücreti uygulanmasına**, Adana İli sınırlan içerisinde evde Periton Diyaliz tedavisi gören hastalardan toplama ve taşıma ve bertaraf bedeli alınmamasına,
6	**ANKARA**	**26/12/2023 tarihli ve 2023/85 nolu karar ile;** İlimizde uygulanacak Tıbbi Atık toplama, taşıma ve bertaraf (yakma) ücretinin 2024 yılı için; **Ayda 20 kg'a kadar** tıbbi atık üreten sağlık kuruluşları için **aylık 260 TL (KDV hariç)**, **Ayda 20 kg ve üzerinde** tıbbi atık üreten sağlık kuruluşları için **12,50 TL/kg (KDV hariç)**, **31/05/2024 tarihli ve 2024/87 nolu karar ile;** İlimizde uygulanacak Tıbbi Atık toplama, taşıma ve bertaraf (yakma) ücretinin **01/06/2024 tarihinden itibaren;** **Ayda 20 kg'a kadar** tıbbi atık üreten sağlık kuruluşları için **aylık 320 TL (KDV hariç)**, **Ayda 20 kg ve üzerinde** tıbbi atık üreten sağlık kuruluşları için **16 TL/kg (KDV hariç)**,
7	**ANTALYA**	2024 Yılı tıbbi atık bertaraf ücretinin; **Aylık 0-10 kg arası** tıbbi atık üreten tesisler için tıbbi atık toplama, taşıma ve bertaraf ücreti **150 TL/AY + KDV**, **Aylık 10 kg üzeri** tıbbi atık üreten tesisler için tıbbi atık toplama, taşıma ve bertaraf ücreti **17 TL/KG + KDV**, Kimyasalla muamele görmüş patolojik atıkların toplama, taşıma ve bertaraf ücreti **50 TL/KG + KDV** olarak belirlenmesi;

10	**BALIKESİR**	İlimiz sınırları dahilindeki sağlık kuruluşlarından ve tıbbi atık üreticilerinden kaynaklanan tıbbi atıkların toplama, taşıma ve bertaraf (sterilizasyon) ücretinin; **10 kg/ay altında** tıbbi atık üretenler için **82,95 TL/ay + KDV** (Seksen iki lira doksan beş kuruş) olarak, **10 kg/ay üzerinde** tıbbi atık üretenler için **12,20 TL/kg + KDV** (On iki lira yirmi kuruş) olarak, İlimiz sınırları dahilindeki sağlık kuruluşlarından ve tıbbi atık üreticilerinden kaynaklanan kimyasalla muamele görmüş patolojik atıkların toplanması, taşınması, depolanması ve bertaraf ücretinin **48,80 TL/kg + KDV** (Kırk sekiz lira seksen kuruş) olarak kalmasına,
16	**BURSA**	25.01.2017 tarih vc 29959 sayılı Resmi Gazetede yayımlanarak yürürlüğe giren Tıbbi Atıkların Kontrolü Yönetmeliğinin 24. Maddesi gereğince, İlimizde oluşan tıbbi atıkların Yönetmeliğin ilgili hükümlerinde belirtilen usul ve esaslar çerçevesinde toplama, taşıma, sterilizasyon ve bertaraf harcamalarının 2024 yılı için; Yönetmeliğin Ek-1 Listesinde yer alan 19. ve 30. grubun haricinde kalan sağlık kuruluşlarının atık kabul bedeli için; **16,46 TL/kg (KDV Hariç)** ücret tarifesinin uygulanmasına, Yönetmeliğin Ek-1 Listesinde yer alan 19. ve 30. gruplar arası sağlık kuruluşlarının atık kabul bedeli için; **420,49 TL/ay (KDV Hariç)** ücret tarifesinin uygulanmasına, Yönetmeliğin Ek-1 Listesinde yer alan tüm tıbbi atık üreticilerin kimyasalla muamele görmüş patolojik atıkları için yakma tesisine kadar sterilizasyon tesisinde geçici depolanması, yakma tesisine taşınması ve yakma bedeli **33,75 TL/kg (KDV Hariç)** ücret tarifesinin uygulanmasına,

17	**ÇANAKKALE**	Aşağıda belirtilen Tıbbi atık üreticilerinin 2024 yılı boyunca tıbbi atıkları toplayan ilgili Birlik Başkanlığına karşısında bulunan miktarları KDV Hariç ödemelerine, **A. Tıbbi Hizmet Veren ve Atık Üreten Üniteler (Çanakkale Katı Atık Birliğine Bağlı Belde ve Belediyeler):** Tıbbi Atık Toplama, Taşıma ve Bertaraf Ücreti (TL) (KDV) Hariç; (*) Bireysel Dahili Branş Muayenehaneleri, Sağlık Kabinleri (Sünnetçi ve Ebeler Gibi). Veteriner Hekim Muayenehaneleri (Bir Hekim Başına), Aile Sağlığı Merkezleri (Bir Hekim Başına), Diş Hekimi Muayenehaneleri (Bir Hekim Başına), Akupunktur Merkezleri, Revirler; **Aylık 217,00 TL**, (**) Bireysel Cerrahi Branş Muayenehaneleri, Veteriner Klinik ve Poliklinikleri (Bir Hekim Başına), Güzellik Ve Estetik Merkezleri, OSGB'ler; **Aylık 358,00 TL**, Yataklı Sağlık Tesisleri (Hastaneler), Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler (Poliklinikler, Tıp Merkezleri, Özel Dal Kliniği), Radyoloji, Sintigrafi, Görüntüleme Merkezleri, Dispanserler, Ana Çocuk Sağlığı Merkezleri, Fizik Tedavi Laboratuvarları, Diş Protez Laboratuvarları, Ağız ve Diş Sağlığı Merkezleri ve Hastaneleri, Hayvan Hastaneleri, Hayvan Barınma - Eğitim Yeri, Diyaliz Merkezleri, Tarım İl Müdürlükleri Veteriner Hizmetleri Şube Müdürlükleri, Toplum Sağlığı Merkezleri; **Kg başına 25,71 TL** **B. Tıbbi Hizmet Veren Üniteler (Troas Katı Atık ile Çan-Biga-Yenice ve Çevresi Katı Atık Yönetim Birliklerine Bağlı Belde ve Belediyeler):** Tıbbi Atık Toplama, Taşıma ve Bertaraf Ücreti (TL) (KDV) Hariç; (*) Bireysel Dahili Branş Muayenehaneleri, Sağlık Kabinleri (Sünnetçi Ve Ebeler Gibi), Veteriner Hekim Muayenehaneleri (Bir Hekim Başına), Aile Sağlığı Merkezleri (Bir Hekim Başına), Diş Hekimi Muayenehaneleri (Bir Hekim Başına), Akupunktur Merkezleri, Revirler; **Aylık 217,00 TL**, (**) Bireysel Cerrahi Branş Muayenehaneleri, Veteriner Klinik ve Poliklinikleri (Bir Hekim Başına), Güzellik Ve Estetik Merkezleri, OSGB'ler; **Aylık 358,00 TL**, Yataklı Sağlık Tesisleri (Hastaneler), Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler (Poliklinikler, Tıp Merkezleri, Özel Dal Kliniği), Radyoloji, Sintigrafi, Görüntüleme Merkezleri, Dispanserler, Ana Çocuk Sağlığı Merkezleri, Fizik Tedavi Laboratuvarları, Diş Protez Laboratuvarları, Ağız ve Diş Sağlığı Merkezleri ve Hastaneleri, Hayvan Hastaneleri, Hayvan Barınma - Eğitim Yeri, Diyaliz Merkezleri, Tarım İl Müdürlükleri Veteriner Hizmetleri Şube Müdürlükleri, Toplum Sağlığı Merkezi/İlçe Sağlık Müdürlüğü; **Kg başına 31,14 TL** **C. Tıbbi Hizmet Veren Üniteler (Gelibolu Yarımadası Katı Atık Yönetim Birliklerine Bağlı Belde ve Belediyeler, GÖKÇEADA):** İlimiz Gelibolu Yarımadası sınırlarında oluşan tüm tıbbi atıklar Edirne İline bağlı Keşan İlçesinde bulunan sterilizasyon tesisinde bertaraf edilmesi nedeniyle, birim fiyatlar Edirne İli Mahalli Çevre Kurulunda belirlenmesine, **D.** İlimiz sınırları içerisinde Tıbbi Atık toplama ve taşıma faaliyeti gösteren Troas Katı Atık Yönetim Birliği ile Çan-Biga-Yenice ve Çevresi Katı Atık Yönetim Birliklerinin yukarıda belirlenen tıbbi atık ücretlerinden bertaraf için Sterilizasyon tesisinin kumlu olduğu ilgili Birliğe Kg başına 8,00 TL/KDV ödemesine, **E.** Gökçeada ve Bozcaada İlçelerimizde İl Sağlık Müdürlüğümüze bağlı Devlet Hastanelerinin Tıbbi Atık Geçici Depolama Alanlarının Tıbbi Atıkların Kontrolü Yönetmeliği 12. Maddesi kapsamında Tıbbi Atıkların en fazla bir hafta kalabilecek şekilde yeniden düzenlenmesine, **F.** İlimiz genelinde oluşan kimyasal muamele görmüş patolojik atıkların toplama taşıma ve yakma tesisinde yakma bertaraf ücreti olarak ilgili Birlik Başkanlığına (Çanakkale Katı Atık Yönetim Birliği) 80,00 TL+KDV ödemelerine, **G.** Bozcaada ve Gökçeada İlçesinde Tıbbi Atıkların Kontrolü Yönetmeliği'nin 8. Maddesi kapsamında Bozcaada ve Gökçeada

		Belediyesinin, yine aynı Yönetmeliğin 9. Maddesi kapsamında Sağlık Kuruluşlarının Tıbbi Atıkların Toplanması Taşınması ve Bertaraf edilmesi hususundaki yükümlülüklerini yerine getirmesine, **H.** Periton diyaliz hastalarından (Evlerde tedavi gören) kaynaklanan tıbbi atıkların ilgili Birlik Belediyesince ücretsiz toplanmasına, **İ.** Kemik yoğunluğu ölçen muayeneler, psikiyatri ve fizik tedavi branşları muayenelerinden tıbbi atık ücreti alınmamasına,
25	**ERZURUM**	Erzurum Büyükşehir Belediyesinin 11.06.20204 tarihli ve 141110 sayılı yazılarında Tıbbi Atıkların Kontrolü Yönetmeliği kapsamında Erzurum Büyükşehir Belediyesi ile sözleşme imzalayan aile sağlığı merkezleri, özel muayenehaneler, diş hekimi muayenehaneleri vb. sağlık kuruluşlarından gelen atık miktarının az olduğu belirtilerek tıbbi atıkların evsel atıklarla birlikte atılarak insan sağlığına tehdit oluşturmasının engellenmesi için 17.01.2024 tarihli ve 82 sayılı mahalli çevre kurulu kararı ile belirlenen ücret tarifesinin revize edilmesi talep edilmiştir. Bu doğrultuda; 1. 17.01.2024 tarihli ve 82 sayılı mahalli çevre kurulu kararı ile belirlenen tıbbi atık toplama, taşıma ve bertaraf ücret tarifesinin uygulanmasının devam edilmesine, İlimizde faaliyetleri sonucu tıbbi atık oluşumuna neden olan sağlık kuruluşları için **Aziziye, Palandöken ve Yakutiye ilçelerinde** 2024 yılı tıbbi atık toplama, taşıma ve bertaraf bedelinin **15 TL/Kg (KDV hariç)**, **diğer ilçelerde** 2024 yılı tıbbi atık toplama, taşıma ve bertaraf bedelinin **17 TL/Kg (KDV hariç)** olmasına, Tıbbi atık bertaraf tesisine lisanslı araçlar ile getirilen tıbbi atıklar için 2024 yılı bertaraf bedelinin (taşıma ve toplama hariç) **10 TL/Kg (KDV hariç)** olmasına, İlimizde faaliyetleri sonucu patolojik atık oluşumuna neden olan sağlık kuruluşları tarafından sızdırmaz, kapaklı plastik kaplarda biriktirilen kimyasalla muamele görmüş **patolojik atıklar** için 2024 yılında **70 TL/Kg (KDV hariç)** olmasına, 2. 82 sayılı mahalli çevre kurulu karına ek olarak, 01.08.2024 tarihinden

		geçerli olmak üzere 2024 yılı için Yönetmeliğin Ek-1 listesi 5, 7, 17, 18, 19, 20, 26, 27, 28, 29, 30. maddelerinde yer alan; toplum sağlığı merkezleri, aile sağlığı merkezleri, dispanserler ve benzeri birinci basamak sağlık kuruluşları, ayakta teşhis ve tedavi hizmeti veren merkezler, rehabilitasyon merkezleri, fizik tedavi merkezleri, sağlık hizmeti verilen diğer sağlık kuruluşları (doktor muayenehaneleri, diş ve ağız sağlığı muayenehaneleri ve benzerleri), bakımevleri ve huzurevleri, akupunktur merkezleri, evde yapılan tedavi ve hemşire hizmetleri, güzellik, kulak delme ve dövme merkezleri, eczaneler, Ek 1 listesinde yer almayan ancak faaliyetleri sonucu tıbbi atık oluşumuna neden olan kişi, kurum ve kuruluşlardan **ayda 10 kg altı tıbbi atık üretenler için** taşıma, sterilizasyon ve bertaraf bedelinin **müessese başına aylık 150 TL (KDV hariç)**, **ayda 10 kg üstü tıbbi atık üretenler için** ise 82 sayılı çevre kurulu kararı ile belirlenen ücret tarifesinin uygulanmasına,
28	**GİRESUN**	**Büyük miktarda (20 kg/ay'dan fazla) tıbbı atık üreten** sağlık kuruluşlarından (hastaneler, ayda 20 kg'dan fazla tıbbi atık üreten ASM, TSM ve diğer birimler) kaynaklanan tıbbi atıkların toplanması, taşınması, sterilizasyonu ve düzenli depolama tesislerinde bertaraf ücreti (KDV hariç) **Şebinkarahisar, Alucra, Çamoluk İlçeleri için 21,35 TL/kg, diğer ilçeler için 20,00 TL/kg**, **Az miktarda (20 kg/ay'dan az) tıbbi atık üreten** sağlık kuruluşlarından (ayda 20 kg'dan az tıbbi atık üreten ASM, TSM, bireysel dahili branş muayenehaneleri, bireysel cerrahi branş muayenehaneleri, sağlık kabinleri (sünnetçi-ebe), ağız ve diş sağlığı muayenehaneleri vb., veteriner hekim muayenehaneleri, akupunktur merkezleri, fizik tedavi merkezleri, güzellik merkezleri, ekim yapılan gıda laboratuvarları vb. diğer birimlerden) kaynaklanan tıbbi atıkların toplanması, taşınması, sterilizasyonu ve düzenli depolama tesisinde bertaraf ücreti (KDV hariç) **206,83 TL/ay**, Herhangi bir kimyasalla muamele görmüş patolojik atıklar ile ilgili olarak 2024 yılı için taşıma, toplama ve bertaraf ücretinin **KDV hariç 96,46 TL/kg** olarak belirlenmesine,
34	**İSTANBUL**	2024 yılı için uygulanacak Tıbbi Atıkların Toplanması, Taşınması ve Bertarafı Ücretlerinin; **1. Tıbbi Atıkların Toplanması, Taşınması ve Bertarafı Ücretinin "Kilogram Başına Ödeme" yapan (Sağlık Bakanlığı Kamu Hastaneleri, Kamu Üniversite Hastaneleri, Vakıf Üniversite Hastaneleri ve Özel Hastaneler) sağlık kuruluşları için birim fiyat olarak 4,72 TL / Kg +KDV belirlenmesine,** **1.1.** Kilogram başına ödeme yapan sağlık kuruluşlarının ödeme döneminin ve tıbbi atık bertaraf ücreti tahakkuklarının hizmetin sürekliliği ve kalitesi esasında kurumların İBB ile yapacağı özel protokollerin dışında aylık olarak tahsil edilmesine, **2.** Diyaliz Merkezleri için Tıbbi Atıkların Toplanması, Taşınması ve Bertarafı Ücretinin seans başına 7,92 TL/seans (KDV Dahil) olarak belirlenmesine, **2.1.** Evlerde tedavi gören periton diyaliz hastalarından kaynaklanan tıbbi atıkların bedelsiz alınmasına, **2.2. Evlerde tedavi gören periton diyaliz hastaları için tıbbi atık poşetlerinin İBB tarafından bedelsiz verilmesine,** **2.3.** Diyaliz merkezlerinin ödeme döneminin ve tıbbi atık bertaraf ücreti tahakkuklarının hizmetin sürekliliği ve kalitesi esasında kurumların İBB ile yapacağı özel protokollerin dışında 3 aylık olarak tahsil edilmesine, **3. Tıbbi Hizmet veren ve ünite cinsine göre "Yıllık Tıbbi Atık Aidat Ücreti" alınan sağlık kuruluşları için Tıbbi Atıkların Toplanması, Taşınması ve Bertarafı Ücretinin EK-1'deki tabloda belirtildiği gibi belirlenmesine,**

		3.1. Tıbbi Hizmet Veren ve Ünite Cinsine Göre Yıllık Tıbbi Atık Aidat Ücreti Alınan Sağlık Kuruluşlarında Tıbbi Atık Bertaraf Ücretinin 31 Mart 2024 tarihine kadar ödemesine (yeni açılış yapan sağlık kuruluşları hariç), ödeme yapmayan kurum/kuruluşların İl Sağlık Müdürlüğü'ne bildirilmesine, **3.2.** Yeni açılacak olan ve Ünite Cinsine Göre Yıllık Tıbbi Atık Aidat Ücreti Alınan Sağlık Kuruluşlarında, yıllık hesaplamanın, açılış yaptığı ay itibariyle yılın kalan süresi üzerinden oranlama yapılarak hesaplanmasına ve yıl bitmeden kapanan sağlık kuruluşlarına herhangi bir ücret iadesi yapılmamasına, **3.3.** Yıllık Tıbbi Atık Aidat Ücreti Alınacak Sağlık kurum/kuruluşu olup, yukarıda Tıbbi hizmet veren üniteler kategori listesinde yer almayan sağlık kuruluşlarının hizmet talep etmesi halinde en yakın kategori tarifesi üzerinden ücretlendirilmesine, **3.4.** Müşterek muayenehanelerde hekim başına tıbbi atık kabul belgesi başvurusu yapılmasına ve hekim başına Yıllık Tıbbi Atık Aidat Ücreti alınmasına, **3.5.** Kemik yoğunluğu ölçen muayenehaneler ile psikiyatri branş muayenehaneleri ve psikiyatri merkezlerinden tıbbi atıkların bedelsiz alınmasına, **3.6.** Türk Standartları Enstitüsü (TSE) tarafından Mart 2018'de hazırlanmış olan "TS 13819 Tıbbi atık Toplama Torbası - Polietilenden (PE)" standardında yer alan kriterlere uygun tıbbi atık torbaları ve kovaların sağlık kuruluşları tarafından kullanılmasına, **3.7.** Sağlık kuruluşlarında çalışan atık toplayıcılarının; "Sağlık Kuruluşları Kaynaklı Tıbbi Atık Toplayıcısı (Seviye 3)" mesleği için "Mesleki Yeterlilik Belgesi" almasının sağlanmasına, **EK-1** - Bireysel Dahili Branş Muayenehanesi: **1.500,00 TL/yıl (KDV Dahil)** - Bireysel Cerrahi Branş Muayenehanesi: **2.400,00 TL/yıl (KDV Dahil)** - Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler - Toplam Alanı 500 m2'den Az (Poliklinikler / Tıp Merkezleri / Özel Dal Klinikleri /Sandıklara Ait Sağlık Birimleri / Havaalanı ve Gümrüklü Alanlardaki Sağlık Üniteleri / İlçe Belediyelerinin Sağlık Üniteleri vs.): **6.500,00 TL/yıl (KDV Dahil)** - Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler - Toplam Alanı 500-1.000 m2 Arası (Poliklinikler / Tıp Merkezleri / Özel Dal Klinikleri /Sandıklara Ait Sağlık Birimleri / Havaalanı ve Gümrüklü Alanlardaki Sağlık Üniteleri / İlçe Belediyelerinin Sağlık Üniteleri vs.): **11.600,00 TL/yıl (KDV Dahil)** - Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler - Toplam Alanı 1.000-3.000 m2 Arası (Poliklinikler / Tıp Merkezleri / Özel Dal Klinikleri /Sandıklara Ait Sağlık Birimleri / Havaalanı ve Gümrüklü Alanlardaki Sağlık Üniteleri / İlçe Belediyelerinin Sağlık Üniteleri vs.): **17.400,00 TL/yıl (KDV Dahil)** - Birden Çok Branş Doktoru ve Sağlık Personeli Çalışan Üniteler - Toplam Alanı 3.000 m2'den Fazla (Poliklinikler / Tıp Merkezleri / Özel Dal Klinikleri /Sandıklara Ait Sağlık Birimleri / Havaalanı ve Gümrüklü Alanlardaki Sağlık Üniteleri / İlçe Belediyelerinin Sağlık Üniteleri vs.) Üniteleri / İlçe Belediyelerinin Sağlık Üniteleri vs.): **45.600,00 TL/yıl (KDV Dahil)** - Radyoloji / Radyoterapi / Sintigrafi / Nükleer Tıp Müesseseleri / Fizik Tedavi ve Rehabilitasyon Müesseseleri / Görüntüleme ve Tanı Merkezleri: **2.400,00 TL/yıl (KDV Dahil)** - Kan ve Kan Ürünleriyle Çalışma Yapan Üniteler, Tıbbi Atık Üreten Laboratuvarlar ve Merkezler (Tıbbi Araştırma Merkezleri / Biyoteknoloji Laboratuvarları ve Enstitüleri / Kan Bankaları ve Transfüzyon Merkezleri / Biyomedikal Laboratuvarları/ Üniversite Laboratuvarları, Deney ve Test Sonucu Tıbbi Atık Üreten İşyerleri/İşletmeler, Basit Hizmet Laboratuvarları, Diş Protez Laboratuvarı, Tıbbi Malzeme Üreten Laboratuvarlar vb.):

		4.700,00 TL/yıl (KDV Dahil) - Tıbbi Tahlil Laboratuvarları (Patoloji, Mikrobiyoloji, Biyokimya) / Gıda Kontrol Laboratuvarları: **14.600,00 TL/yıl (KDV Dahil)** - Aile Sağlık Merkezleri / Ana Çocuk Sağlığı Merkezleri / Verem Savaş Dispanserleri / Birinci Basamak Muayene Merkezleri / Resmi Kurum Tabiplikleri, Revirler / Toplum Sağlığı Merkezleri / Toplum Ruh Sağlığı Merkezleri / Göçmen Sağlığı Birimleri: **1.500,00 TL/yıl (KDV Dahil)** - İş Yeri Hekimliği Yapılan Üniteler (Hekim Sayısı Kadar): **1.500,00 TL/yıl (KDV Dahil)** - Evde Tedavi Merkezleri / Yaşlı Bakım Evleri / Huzurevleri / Hemşire Hizmetleri Servisi Veren Sağlık Kuruluşları / Engelli Bakım Evleri: **1.500,00 TL/yıl (KDV Dahil)** - Bağımsız Ambulans Hizmetleri / Gezici Sağlık Servisleri (Gezici Sağlık Aracı Sayısı Kadar): **1.000,00 TL/yıl (KDV Dahil)** - Sağlık Kabinleri / Sağlık Evleri: **1.000,00 TL/yıl (KDV Dahil)** - Diş Hekimi Muayenehanesi: **2.475,00 TL/yıl (KDV Dahil)** - Diş Poliklinikleri: **9.000,00 TL/yıl (KDV Dahil)** - Ağız ve Diş Sağlığı Merkezleri: **15.000,00 TL/yıl (KDV Dahil)** - Diş Hekimliği Fakülteleri / Diş Hastaneleri: **30.000,00 TL/yıl (KDV Dahil)** - Veteriner Hekim Muayenehanesi: **2.400,00 TL/yıl (KDV Dahil)** - Veteriner Poliklinikleri / Hayvan Barınma-Eğitim Yeri / Hayvanat Bahçesi: **6.600,00 TL/yıl (KDV Dahil)** - Hayvan Hastaneleri: **16.200,00 TL/yıl (KDV Dahil)** - Hayvanlar Üzerinde Araştırma ve Deney Yapan Kuruluşlar: **2.500,00 TL/yıl (KDV Dahil)** - Güzellik Salonu İşyeri Açma ve Çalışma Ruhsatı Bulunan İşletmeler: **2.400,00 TL/yıl (KDV Dahil)** - Akupunktur / Kulak Delme / Dövme Merkezleri: **1.400,00 TL/yıl (KDV Dahil)**
35	**İZMİR**	İlimiz sınırları içerisindeki sağlık kuruluşlarından kaynaklanan tıbbi atık ve patolojik atıkların 2024 yılı için geçerli toplama, taşıma, sterilizasyon/yakma ve bertaraf bedellerinin 25.01.2017 tarih ve 29959 sayılı Resmi Gazetede yayımlanan "Tıbbi Atıkların Kontrolü Yönetmeliğimin 24. Maddesi çerçevesinde belirlenmesi hususu görüşülmüş olup, tıbbi atık toplama, taşıma, sterilizasyon ve bertaraf ücretinin **16,00 TL/kg+KDV**, patolojik atık toplama, taşıma ve yakma ücretinin **45,00 TL/kg+KDV** olarak belirlenmesine oy birliği ile,
51	**NİĞDE**	İlimiz sınırları içerisinde 2024 yılı için tıbbi atık toplama, taşıma ve bertaraf ücretinin KDV hariç aşağıda belirtilen miktarda uygulanmasına, a) İl Merkezi ve Bor İlçesinde bulunan kamu ve özel sağlık kuruluşlarından kaynaklı tıbbi atıklar için kilogram başına **19,30 TL/kg (KDV hariç)** bedel alınmasına, b) Diğer İlçe Merkezinde bulunan kamu ve özel sağlık kuruluşlarından kaynaklı tıbbi atıklar için kilogram başına **20,30 TL/kg (KDV hariç)** bedel alınmasına, c) İl ve İlçe Merkezi dışında bulunan belde ve köylerde bulunan Aile Sağlığı Merkezlerinden kaynaklı Tıbbi Atıklar için **1500 TL/YIL (KDV hariç)** bedel alınmasına, d) Patolojik atıklar için kilogram başına **50 TL/kg (KDV hariç)** bedel alınmasına, e) Türkiye Kızılay Derneği Niğde Kan Merkezi'nin tıbbi atıklarının ücretsiz bertaraf edilmesine,

73	**ŞIRNAK**	**07.03.2024 tarihli ve 2024/01 nolu karar ile;** 1. İlimizde faaliyet gösteren büyük miktarda atık üreten sağlık kurumlarından (Devlet Askeri-Özel Hastaneler) kaynaklanan 2024 yılı tıbbi atık bertaraf ücretinin 01.01.2024 tarihinden 31.12.2024 tarihine kadar Beytüşşebap İlçesi **22 TL/Kg + KDV**, Merkez ve diğer İlçeler için geçerli olmak üzere **21,5 TL/Kg + KDV** olarak belirlenmesi, 2. Tıbbi Atıkların Kontrolü Yönetmeliği'nin Ek-1 listesi 19, 26, 28 ve 30. sırasında yer alan 15 kg'ın altında tıbbi atık üreten (doktor muayenehaneleri, ağız ve diş sağlığı merkezleri, akupunktur merkezleri, güzellik merkezleri, bu listede yer almayan ancak faaliyetleri sonucu tıbbi atık oluşumuna neden olan kişi, kurum ve kuruluşlar) tıbbi atık üreticisi özel ve resmi sağlık kuruluşlarından yılda bir defaya mahsus olmak üzere 01.01.2024 tarihinden itibaren 31.12.2024 tarihine kadar geçerli olmak üzere tıbbi atık ücretinin **3745 TL/Yıl + KDV** olarak belirlenmesine, (15 kg'ın üzerinde atık üreten sağlık kuruluşları kendisine en yakın devlet hastanesi için belirlenen fiyat üzerimden ücretlendirilecektir.), 3. 01.01.2024 tarihinden itibaren 31.12.2024 tarihine kadar geçerli olmak üzere Aile Sağlığı Merkezleri (ASM) ve Toplum Sağlığı Merkezleri (TSM) için tıbbi atık ücretlerinin; - 1 ve 2 hekim bulunanlar **345 TL/Ay + KDV** - 3 ve 4 hekim bulunanlar **692 TL/Ay + KDV** - 4'ten fazla hekim bulunanlar **925 TL/Ay + KDV** olarak belirlenmesine, 4. Kimyasalla işlem görmüş patolojik atıkların Yeşil Yaşam Çevre Tek. İnş. Nak. San. ve Tic. Ltd. Şti. firması tarafından Ankara ilinde bulunan ITC Atık Bertaraf tesisine gönderilmesi ve 2024 yılı bertaraf ücretinin **93 TL/Kg + KDV** olarak belirlenmesine, **12.07.2024 tarihli ve 2024/02 nolu karar ile;** 1. İlimizde faaliyet gösteren büyük miktarda atık üreten sağlık kurumlarından (Devlet Askeri-Özel Hastaneler) kaynaklanan 2024 yılı tıbbi atık bertaraf ücretinin 01.07.2024 tarihinden 31.12.2024 tarihine kadar Beytüşşebap İlçesi **26,9 TL/Kg + KDV**, Merkez ve diğer İlçeler için geçerli olmak üzere **26,4 TL/Kg + KDV** olarak belirlenmesi, 2. Tıbbi atıkların Kontrolü Yönetmeliği'nin Ek-1 listesi 19, 26,28 ve 30. sırasında yer alan aylık 15 kg'ın altında tıbbi atık üreten (doktor muayenehaneleri, ağız ve diş sağlığı merkezleri, akupunktur merkezleri, güzellik merkezleri, bu listede yer almayan ancak faaliyetleri sonucu tıbbi atık oluşumuna neden olan kişi, kurum ve kuruluşlar) tıbbi atık üreticisi özel ve resmi sağlık kuruluşlarından yılda bir defaya mahsus olmak üzere 01.07.2024 tarihinden itibaren 31.12.2024 tarihine kadar geçerli olmak üzere tıbbi atık ücretinin **4670 TL/Yıl + KDV** olarak belirlenmesine, (15 kg/ay 'ın üzerinde atık üreten sağlık kuruluşları kendisine en yakın devlet hastanesi için belirlenen fiyat üzerinden ücretlendirilecektir.), 3. 01.07.2024 tarihinden itibaren 31.12.2024 tarihine kadar geçerli olmak üzere Aile Sağlığı Merkezleri (ASM) ve Toplum Sağlığı Merkezleri (TSM) için tıbbi atık ücretlerinin; - 1 ve 2 hekim bulunanlar **430 TL/Ay + KDV** - 3 ve 4 hekim bulunanlar **863 TL/Ay + KDV** - 4'ten fazla hekim bulunanlar **1153 TL/Ay + KDV** olarak belirlenmesine, 4. Kimyasalla işlem görmüş patolojik atıkların Yeşil Yaşam Çevre Tek. İnş. Nak. San. ve Tic. Ltd. Şti. firması tarafından Ankara ilinde bulunan ITC Atık Bertaraf tesisine gönderilmesi ve 01.07.2024 tarihinden itibaren 31.12.2024 tarihine kadar geçerli olmak üzere bertaraf ücretinin **115 TL/Kg + KDV** olarak belirlenmesine,

TÜİK verilerine göre 2010 yılında ülkemizde yılda 6o bin ton tıbbi atık toplanmakta iken 2022 yılı tıbbi atık miktarı sadece İstanbul da 32 362 ton'dur. Atık üretimi oranları; sağlık hizmetinin yoğunluğuna, konuma (kır veya kent), sağlık tesisinin ve kliniğin türüne, tek kullanımlık ürünlerin kullanım büyüklüğüne, atık sınıflandırma politikalarına ve düzenlemelerine, ayrıştırma ve atık minimizasyonu uygulamalarına, tedarik politikalarına ve ülkelerin gelişmişlik düzeylerine göre değişkenlik arz etmektedir. Tıbbi atığın oluşumunu önlemek veya daha az üretmek, ayrıştırmak ve gereksiz atık bertarafını engelleyerek bertaraf ve uzaklaştırma maliyetini azaltacaktır. Tıbbi atıkların bertaraf ve uzaklaştırma maliyeti, katı atığın maliyetinden daha yüksek olduğundan tıbbi atıkları azaltmayı bir ödev haline getirir. Katı ve evsel atık, tıbbi atık ile karıştığında katı atıktan yaklaşık 20 kat daha fazla uzaklaştırma maliyeti olan tıbbi atık olarak bertaraf edilmelidir (Giacchetta ve Marchetti,2013:66). Özellikle atıklar ayrıştırılırken personelin hangi atığın hangi sınıfa girdiğini bilmesi son derece önemlidir (Ananth vd.,2010:159). Yakma, tıbbi atıkların bertarafında en güvenli yöntem olup, ülkemizde İzmit Büyükşehir Belediyesi İzmit Atık ve Artıkları Arıtma ve Yakma Değerlendirme A.Ş. (İZAYDAŞ) ile İstanbul Büyükşehir Belediyesi İstanbul Çevre Koruma ve Atık Mad. Değ. San. ve Tic. A.Ş. (İSTAÇ A.Ş.). Tıbbi Atık Yakma Tesisleri tıbbi atıkları yakarak bertaraf etmektedir (Çevre ve Orman Bakanlığı, 2008: 379.).

SONUÇ

Tıbbi atık yönetiminin temel amacı insan sağlığı ve çevreye zarar vermeden en ekonomik şekilde atıkların ayrıştırılması, ayıklanması ve kullanılacak şekilde geri dönüştürülebilenlerin ayrılması önem arz etmektedir. Tıbbi atık yönetim hiyerarşisinin birinci maddesi olan ÖNLEME en etkin tıbbi atık bertaraf maliyet azaltma uygulamasıdır. Bu yolla hem atık miktarı hem de hacmi azaltılacaktır. Bu uygulamanın birincil sorumluları tıbbi atık üreticisi sağlık personeli ve tıbbi atık toplayıcı, taşıyıcı, depolayıcı atık personelleridir. Sağlık çalışanlarının ve atık personelinin uygulamalarının maiyet etkisi olumlu ya da olumsuz olarak yansımaktadır.

Alan yazına bakıldığında tıbbi atık yönetimi ile ilgili çok sayıda çalışma yapıldığı görülmektedir. Bu çalışmaların tamamında tıbbi atık yönetimi konusundaki tıbbi atık bertarafı maliyetinin düşürülmesi için ortak fikir; iyi bir tıbbi atık yönetim stratejisinin oluşturulması, personel uygulamalarının iyileştirilmesi ve sürdürülebilmesine ilişkin eğitimin önemi vurgulanmıştır. Maliyetin azaltılması için tıbbi atık miktarını azaltmak adına tek kullanımlık malzemeler yerine tekrar kullanılabilir sarf malzemelerinin kullanılması ve tıbbi atık ekipmanlarının amacı dışında kullanılmaması önerilmektedir. Biyo-tehlikeli tıbbi atıkların atığın oluştuğu yerde doğru bir şekilde ayrıştırılması, sürekli izleme faaliyetlerinin ve raporların hazırlanarak sorunlara çözüm bulunması önemli tasarruf kaynağıdır. Personelin tıbbi atık bertaraf yöntemlerinin maliyeti hakkında bir bilgisi ya da farkındalığı yoktur. Johnson ve arkadaşları tarafından yapılan bir araştırmada enfeksiyöz tıbbi atıkların yeniden ayrıştırılması sonucu bu atıkların %61'nin genel atık olduğu görülmüştür. Personel eğitiminden sonra ise doğru tepkiler %44 artmıştır. Hastanede enfeksiyöz tıbbi atık uzaklaştırma oranının %48 azaldığı tespit edilmiştir.

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HYPOTHERMIC INJURIES IN PLASTIC SURGERY

ABSTRACT

Hypothermic injuries, although more commonly associated with environmental exposure, can occur in plastic surgery when tissues are exposed to cold for prolonged periods during surgical procedures. This can happen due to the use of cooling techniques such as cryotherapy, cold compresses, or ice packs, which are routinely applied to reduce inflammation, swelling, and bruising after surgery. However, if these methods are used improperly or for too long, they can lead to localized hypothermia, causing damage to the skin, subcutaneous tissues, and even deeper structures. Potential complications include frostbite-like necrosis, delayed wound healing, and nerve damage. In more severe cases, the damage can lead to long-term complications such as fibrosis or chronic pain. Certain areas of the body, particularly those with poor blood supply, such as the extremities, fingers, toes, and regions with thin skin, are more prone to these injuries. In reconstructive plastic surgery, especially in procedures involving microsurgery, maintaining adequate blood flow to grafts or tissue flaps is crucial. Hypothermia can compromise this circulation, increasing the risk of tissue ischemia and failure of the reconstruction. Preventing hypothermic injuries requires careful temperature regulation, limiting exposure time to cold, and ensuring adequate monitoring during and after the procedure. Additionally, the recognition of early signs of cold-induced damage is essential for timely intervention, which may include controlled rewarming, topical treatments, or pharmacological management to mitigate further damage. Future research focusing on optimizing temperature control and minimizing the risks of hypothermic injuries in plastic surgery will be key to improving surgical outcomes and patient safety.

Keywords: Hypothermic injuries, plastic surgery, tissue necrosis, flap

PLASTİK CERRAHİDE HİPOTERMİK YARALANMALAR

ÖZET

Hipotermik yaralanmalar, genellikle çevresel soğuk maruziyeti ile ilişkilendirilse de, plastik cerrahide de dokuların uzun süre soğuğa maruz kalması sonucunda meydana gelebilir. Bu tür yaralanmalar, şişlik, iltihaplanma ve morarmayı azaltmak amacıyla yaygın olarak kullanılan kriyoterapi, soğuk kompres veya buz torbası gibi soğutma yöntemleri sırasında ortaya çıkabilir. Ancak, bu yöntemlerin yanlış kullanımı veya uzun süreli uygulanması, lokalize hipotermiye neden olabilir ve bu da ciltte, alt dokularda ve daha derin yapılarda hasara yol açabilir. Donma benzeri doku nekrozu, yara iyileşmesinde gecikme ve sinir hasarı gibi komplikasyonlar görülebilir. Daha ciddi vakalarda, hasar fibrozis veya kronik ağrı gibi uzun vadeli sorunlara neden olabilir. Vücutta kan akışının yetersiz olduğu bölgeler, özellikle ekstremiteler, parmaklar, ayak parmakları ve ince deriye sahip bölgeler, bu yaralanmalara karşı daha duyarlıdır. Rekonstrüktif plastik cerrahide, özellikle mikrocerrahi gerektiren işlemlerde, greftler veya doku fleplerine yeterli kan akışının sağlanması çok önemlidir. Hipotermi, bu dolaşımı bozarak doku iskemi riskini artırabilir ve rekonstrüksiyonun başarısız olmasına neden olabilir. Hipotermik yaralanmaları önlemek için soğuk uygulama sürelerinin dikkatlice izlenmesi, sıcaklık kontrolünün sağlanması ve işlem sırasında ve sonrasında sürekli takip yapılması gereklidir. Ayrıca, soğuk kaynaklı hasarın erken belirtilerini tanımak, zamanında müdahale açısından hayati öneme sahiptir. Bu müdahaleler arasında kontrollü yeniden ısıtma, topikal tedaviler veya farmakolojik yaklaşımlar bulunabilir. Plastik cerrahide hipotermik yaralanmaların riskini en aza indirmek ve hasta güvenliğini artırmak için gelecekte bu alanda yapılacak araştırmalar büyük önem taşımaktadır.

Anahtar Kelimeler: Hipotermik yaralanma, plastik cerrahi, doku nekrozu, flep

HİPOTERMİK YARALANMALAR

GİRİŞ VE TARİHÇE

And Dağları'ndaki 5000 yıllık mumya bilinen en eski hipotermik yaralanma vakası olarak kayıtlara geçmiştir. 1812-1813 yılları arasında Fransa-Rusya savaşı sırasında Napolyon'un başcerrahı Jean Larrey çoklu donma vakalarını yazdığı kitapta bildirmiştir.

PATOFİZYOLOJİ

Tüm hipotermik yaralanmaların temelinde ısı kaybı mevcuttur. Isı kaybı; Buharlaşma, İletim, Isı yayılımı, Işıma olmak üzere 4 temel yolla meydana gelmektedir.

ISI KAYBI MEKANİZMALARI

Isı kaybı mekanizmalarını tek tek inceleyecek olursak Buharlaşma ya da diğer adı ile Evaporasyon ısının su tarafından doğrudan absorpsiyonu ile meydana gelmektedir.

İletim yani Kondüksiyon Daha soğuk bir cisimle temas ile meydana gelirken,

Isı yayılımı ya da diğer adı ile Konveksiyon Su akıntısı ya da hava akımı ile ısı kaybı mekanizması ile gerçekleşmektedir.

Işıma yani Radyasyon Isının vücuttan havaya kaybı yoluyla olmaktadır.

Soğuğu fark edebilme yetisinde azalma olan ve Tehlike altında barınak arayamayan insanlar donma ve hipotermik yaralanmalar açısından yüksek risk altındadır. Bu gruba uyan çocuklar ve bebekler aynı zamanda titreme reflekslerinin olmaması ve yüksek yüzey alanlar nedeni ile artmış risk altındalardır. Aynı zamanda kütanöz dolaşımda vazodilastasyona neden olacak durumlar hipotermik yaralanmalara zemin hazırlamaktadır.

Donmalar en sık 30-49 yaş aralığındaki erkeklerde görülmektedir. Hipotermik yaralanmalar açısından risk faktörleri İngizlizce kaynaklarda Donmanın I'ları olarak belirtilmektedir.

Hipotermik yaralanmalar en sık olarak ekstremitelerin distalinde yani el ve ayaklarda görülmektedir. Yine dış çevre ile yakın temas halinde bulunan Burun, çene, kulak lobülü, yanak, dudak yüksek risk altındadır. Oturarak donmalarda Gluteal alan, perine; Kayakçılar ise Penis donmalarına rastlanabilmektedir.

Hipotermik yaralanmaların boyutu temel olarak ısı kaybının hangi çabuklukta olduğu, Dokuda buz kristallerinin olup olmaması, Buz kristallerinin yerine bağlıdır.

Ancak Temas süresi, Mevcut sıcaklık değeri, ıslak/kuru soğuğa maruziyet, Soğuk suda bekleme, Rüzgar, hastanın giyinme derecesi yaralanmanın boyutunu değiştirmektedir.

Hastaya bağlı bazı faktörler de hipotermik yaralanmanın boyutunu değiştirebilmektedir. Örneğin Raynaud Sendromu, periferik vasküler hastalıklar, Nöropatiler, Kronik tütün kullanımı ve vazodilatasyona neden olması nedeni ile akut alkol tüketimi yaralanma boyutlarını artırabilmektedir.

HİPOTERMİK YARALANMA BOYUTU – 3

Donma hızı düşünüldüğünde Hızlı Donmalarda Hücre içinde buz kristalleri, doğrudan hücre ölümü meydana gelirken, Yavaş Donmalarda Hücre dışında buz kristalleri, hücre dışına

osmotik sıvı kaçışı, dehidratasyon olmaktadır. Yüksek irtifada ise Azalmış ADH nedeni ile artmış dehidratasyon, soğuk diürezi meydana gelmektedir.

HIZLI DONMA

Hızlı donmalarda da yavaş donmalarda da Buz kristalleri mevcut olabilmektedir. Ancak hızlı donmalarda Buz Kristalleri Hücre içinde yerleşmiştir. Hızlı donmalar Genel olarak daha iyi prognozludur.

HIZLI DONMA – FROSTNIP

Hızlı donmaların ilk grubu olan frostnip yani soğuk sızısında Deride solukluk, hafif ağrı ve bölgesel uyuşmalar mevcuttur. Buz kristalleri **yok**tur. Soğuk sızısı Hızlı soğumanın geri dönüşlü evresidir ve hafif bir soğuk yaralanmasıdır. Soğuk sızısına Kışın elin soğuktan uyuşması örnek verilebilir.

HIZLI DONMA – FLASHFREEZE

Bir başka hızlı donma örneği Ani donma ya da diğer adı ile Flashfreezedir. Ani donmada Dokular çok hızlı bir şekilde soğumaktadır. Buz kristalleri hücre içinde mevcuttur. Ani donmaya Kışın metal bir çubuğa dilin, elin yapışması örnek verilebilir.

YAVAŞ DONMA

Yavaş donmalarda da hızlı donmalarda olduğu gibi Buz kristalleri vardır ya da yoktur. Ancak buz kristalleri oluşmuş ise bu kristaller Hücre dışındadır. Genel olarak hızlı donmalara göre daha kötü prognozludur.

PERNİYO

Perniyo ya da diğer adı ile Chilblains; Donmaya yakın soğuğa tekrarlayan maruziyetler nedeni ile meydana gelmektedir. Hızlı donmalara göre Daha ciddi bir soğuk yaralanmasıdır. Tekrarlı hipotermi sonucu bölgesel ağrılı ve kaşıntılı kırmızı / mor lezyonlar oluşmaktadır. Ancak etkilenen dokularda Buz kristalleri yok

SOĞUK ISIRMASI

Soğuk ısırması; Donuk ya da daha yaygın adı ile Frostbite olarak literatürde adlandırılmaktadır. Yavaş hızda ancak ciddi soğuma ile karakterizedir. Hücre dışında buz kristalleri mevcuttur. Doku sıcaklığı - 0,5°C ile -2,2°C arasına geldiğinde buz kristalleri oluşmaya başlamaktadır. Ancak frostbite'ta Doku Donması 2°C'de bile olabilmektedir.

Frostbite; Hücre dışında osmotik basınç artışı, Hücre içinden dışına doğru sıvı hareketi ve Hücre zarında delinmeler ile karakterizedir. Damar içinde oluşmuş buz kristalleri doğrudan vasküler hasara ve damar içi buz çökeltilerine neden olmaktadır. Yeniden ısıtma ise Dokuların donuk damarlardan yüzeyele doğru tabakalar halinde çözülmesi ile sonuçlanmaktadır.

Yavaş donmalarda donma ilişkili endotel hasarı gerçekleşmiş ise kapillerlerin sızdırması, lökositlerin ve mast hücrelerinin damar dışına çıkması meydana gelmektedir. 6-24 saatte bül oluşumu meydana gelmektedir. Ve Dermal vasküler hasar varsa bu büller Hemorajik karakterde olmaktadır.

DONMANIN EVRELERİ

Donmalarda evreleme ısıtmadan 24 saat sonra yapılmaktadır.

1. Derece donuklarda: Hiperemi ve Bozulmamış duyu varken, Bül yoktur. Doku kaybı beklenmemektedir. Hastaneye yatış gerektirmemektedir.

2. Derece donuklarda; Distal falanksta bül mevcuttur ve Sıvı içeriği serözdür. Parmakta yumuşak doku kaybı, tırnak deformitesi meydana gelebilmektedir. 2.derece donma itibari ile artmış amputasyon riski nedeniyle Hastaneye yatış endikasyonu bulunmaktadır.

3. Derece donuklarda; Doku ödemlidir, Proksimal falanksta hemorajik büller mevcuttur ve Zonklama tarzı ağrı vardır. Parmakta kemik doku kaybı olasıdır. Fonksiyonel sekel riski mevcuttur.

4. Derece donuklarda; Karpal / Tarsal alanda lezyonlar vardır. Siyanotik deri rengi ve Hemorajik büller mevcuttur. Derin dokuların donması sonucu Ekstremite amputasyonu, sepsis riski artmıştır. Haftalar içinde mumyalaşma belirtileri oluşmaktadır.

TEDAVİ İLKELERİ // 1

Donmaların tedavisine bakıldığında Tekrar donma riski var ise → HASTAYI ISITMAmak gerekmektedir. Çünkü Çoklu donma – çözülme döngüleri sonucu Doku hasarı aritmetik değil, geometrik artmaktadır. Ayrıca Etkilenen bölge ısıtıcı sıcak cisim ile (ışıma yoluyla) ISITILMAMALIDIR.

Hastayı sıcak ortama alarak hastanın Rüzgar teması kesilmeli, ıslak kıyafetler kuruları ile değiştirilmelidir. Donuk alana ovalama yapılmamalıdır. Ek olarak Parmaktan yüzük benzeri takılar çıkarılmalıdır.

Tedavide Afterdrop Fenomeni her zaman akılda tutulmalıdır. Bu durum Hasta ikinci defa ısıtılırken düşünülmelidir. Afterdrop Fenomeni hastanın santral olarak ısıtılmasının periferik vazodilatasyona neden olması ve devamında Periferdeki soğumuş kanın Hızla santrale dönmesi sonucu santral hipotermiye neden olması ile karakterizedir.

Akut tedavide hasta Travma hastası olarak kabul edilmelidir. Periferden önce santral sıcaklık 35 °C olmalıdır. Bu amaçla hasta 30 dakika – 1 saat aralığında 40-42 °C su banyosunda ısıtılmalıdır. Sıcak suya Batikon ya da klorheksidin eklenebilir.

Hastanın ısıtılmasında hedef Pembe rengin geri dönmesidir ve bu noktada tedavi sonlanabilir. Isınma sırasında aktif egzersiz ile eklem açıklığı korunabilir. Şiddetli ağrısı olan hastalara Narkotik analjezik ilaçlar verilebilir. Daha ciddi donmalarda ise Isıtılmış IV sıvılar hastaya verilebilmektedir.

Aspirin 75 – 300 mg; Reolojik etkisinden yani damar içi akışkanlığı artırıcı etkisinden faydalanılabilmektedir. İbuprofen 400 mg po 2x1 Isıtma çok ağrılı ise verilebilmektedir. Etkilenen ekstremiteye Gevşek atel uygulanmalı ve ekstremite yüksekte tutulmalıdır. Vazokonstrüksiyona neden olduğundan Çikolata, kahve, sigara yasaklanmalıdır.

BÜLLERİN TEDAVİSİ

Büllerin tedavisi konusu tartışmalıdır. Patlamamış seröz büller → Eklem hareketini bozuyor ise aspire edilmelidir. Patlamamış hemorajik büller → Kendi haline bırakılmalıdır. Patlamış büller → Debride edilmeli, basitrasinli ya da gümüş sülfadiazinli merhem ile günlük pansuman yapılmalıdır.

ANTİBİYOTERAPİ

Antibiyotik verilip verilmeyeceği hastaya göre seçilmelidir. Genelde Penisilin türevleri yeterli olmaktadır. Malnütrisyon, alkolizm, evsiz hasta gibi durumlarda antibiyoterapi oral olarak verilmelidir. Ancak Yüksek irtifa, 3. ve 4. derece donuk, Bilinen enfeksiyon, selülit, Travma gibi durumlarda antibiyoterapi IV olarak verilmelidir.

TETANOZ PROFLAKSİSİ

Rutin kılavuza göredir ancak Genelde gerekli değildir.

PROGNOZ

Hipotermik yaralanmalarda prognoz etkilenen doku derinliği ile ilişkilidir. Doku nekrozu yüzeyel ise Derin dokular korunmuştur. Isıtma sonrası duyunun geri dönüşü İyi prognoz göstergesidir. Donma sonrası Amputasyon Donma derecesinden çok temas süresi ile bağlantılıdır. Aynı zamanda Seri fotoğraflar takipte faydalıdır.

GÖRÜNTÜLEME

Arteriyel kateterizasyon ile Vazospazm tanı ve tedavisi mümkündür. MR anjiyografi / DSA anjiografi ile Doğrudan oklüzyon seviyesi ve demarkasyon hattı belirlenebilmektedir. Yaralanma sonrası 2. günde uygulanan Üç fazlı T^{99} kemik sintigrafisi ile ciddi risk altındaki doku belirlenebilir.

SONUÇ

Ciddi donma belirtileri gösteren stabil hastalar mutlaka 12 saat içinde Girişimsel Radyoloji'ye danışılmalıdır. tPA ve heparin ya da iloprost tedavisi bu hastalara uygulanabilmektedir. Bu agresif protokol ile Doku kaybı ve amputasyon oranında anlamlı azalma elde edilebilmektedir.

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ANALYSIS OF RADIATION DOSE LEVELS FOR PATIENT CAREGIVERS IN PET/CT UNITS

ABSTRACT

A PET/CT system is a nuclear imaging technique that provides both functional (PET) and anatomical (CT) information in a single examination. The most commonly used radioisotope for imaging is fluorine-18 (F-18), which has a half-life of 109 minutes. After the injection of F-18 fluorodeoxyglucose (FDG), a pair of 511 keV annihilation photons is emitted in opposite directions from the patient.

Most PET/CT patients are elderly or have poor general health conditions, requiring assistance. In many cases, their companions remain with them throughout the imaging process, even waiting together in the designated rest area.

This study seeks to assess the radiation exposure experienced by individuals accompanying and assisting patients during the imaging procedure following the radiopharmaceutical injection. Measurements were taken at different locations and times. The dose rate was recorded for one patient at three different time points using a GM counter to analyze radiation decay at these points. Radiation dose rates were measured immediately after injection, one hour later, and just before the patient was discharged.

According to the measurements, the average dose rate varied depending on time and distance from the patient. However, in compliance with both international and national radiation safety regulations, the radiation dose to the companion of the patient does not pose a significant risk. There is no major radiation hazard for individuals in close contact with the patient for approximately two hours following the F-18 FDG injection during the PET/CT imaging process.

Keywords: *Radiation dose rate, PET/CT, radiation safety*

1. INTRODUCTION

In recent years, the application of nuclear medicine techniques—particularly positron emission tomography (PET)—has expanded significantly due to its diagnostic value in a variety of diseases, including vascular disorders and malignancies. PET enables the visualization of metabolic activity at the cellular level, offering a valuable tool for functional and molecular diagnostics. This imaging modality integrates the principles of nuclear medicine with biochemical processes, allowing clinicians to assess not only the anatomical structure but also the functional and physiological characteristics of organs and tissues.

What distinguishes PET from other nuclear imaging methods is its unique ability to visualize cellular metabolism, rather than simply tracking the distribution of radiopharmaceuticals. A small amount of a radioactive tracer—called a radiopharmaceutical—is injected into the patient, highlighting metabolic activity in tissues, often before structural changes become visible. This feature allows PET to play a critical role in the early detection of diseases such as cancer and inflammation.

To enhance diagnostic precision, PET is now often integrated with CT in a hybrid PET/CT system, combining functional and anatomical imaging in a single session. While software-based image registration is an alternative for aligning separately acquired PET and CT scans, it frequently presents challenges in accuracy and practicality. The use of integrated PET/CT hardware minimizes these issues, reducing misalignment and improving consistency, especially in oncological applications.

On the other hand, a fundamental principle in radiation protection is to keep exposure "as low as reasonably achievable" (ALARA). This concept is universally recognized and aims to minimize unnecessary radiation exposure while considering social, technical, and economic factors. To support this principle, effective dose limits have been established to ensure that individuals are not exposed to harmful levels of ionizing radiation over time (Berberoglu, K., 2019, Uslu Erdemir, R., 2022, Günay, O., 2018., Kır, K. M., 2022, Şenışık AM, 2023). The International Commission on Radiological Protection (ICRP) provides guidance on safe exposure levels, and national regulations often reflect these standards in Table 1.1.

Table 1.1: Radiation Dose Rate Measurement Limits

	Effective Doses
Patients	No limits
Attendant	Adult - 5 mSv/y
	Child < 1 mSv/y
Radiation workers	20 mSv/y
Public	<1 mSv

In line with these recommendations, the present study investigates the radiation dose levels to which caregivers or accompanying relatives may be exposed during F-18

fluorodeoxyglucose (FDG) PET/CT examinations. To assess this, radiation dose rates were measured at various time intervals and distances following the radiopharmaceutical injection using a Geiger-Müller (GM) counter. The rationale behind this study stems from the fact that many patients undergoing PET/CT scans are physically limited due to their medical conditions and require continuous assistance from a companion throughout the procedure. By evaluating the radiation exposure risk to these companions, this study aims to contribute to improved radiation safety practices in clinical PET/CT settings.

2. MATERIAL AND METHOD

This study was conducted in the Nuclear Medicine PET/CT Department of Kütahya Health Sciences University Training and Research Hospital. Patients undergoing F-18 fluorodeoxyglucose (FDG) PET/CT examinations were included, with a total of 25 individuals (13 female, 12 male) participating in the study.

Following the injection of the F-18-FDG radiopharmaceutical, external radiation dose rates were measured from the anterior side of each patient at four different distances—25 cm, 50 cm, 100 cm, and 200 cm—from three anatomical reference points: the head, chest, and feet. These measurements were taken at three distinct time intervals: immediately after injection, approximately 60 minutes post-injection (before imaging), and at around 180 minutes post-injection (before discharge).

The study protocol was approved by the Kütahya Health Sciences University Research Ethics Committee, and written informed consent was obtained from all participants.

To observe variations in dose rate over time and distance, data were collected in a structured manner across the defined spatial and temporal intervals. Measurements were carried out using an ERD RX-70 Analog Survey Meter (Geiger-Müller type), which had been calibrated by the Nuclear Regulatory Authority (NDK) in 2024 to ensure measurement accuracy and compliance with safety standards.

3. RESULT

Radiation dose rates were assessed at distances of 25 cm, 50 cm, 100 cm, and 200 cm from the patient's head, chest, and foot, with measurements conducted at three time intervals: immediately following the radiopharmaceutical injection, approximately 60 minutes after injection (before imaging), and just before patient discharge, around 180 minutes post-injection.

The data revealed a consistent decline in radiation dose rate as the distance from the source—namely, the patient—increased. This trend supports the well-established principle that radiation intensity diminishes in inverse proportion to distance (Sarihan and Abamor, 2022; Berberoğlu, 2019; Uslu Erdemir, 2022; Günay, 2018; Güneş, 2019). While a decrease in measured dose is evident even between 25 cm and 50 cm, the reduction becomes more pronounced at greater distances, such as 100 cm and 200 cm, as illustrated in Table 3.1 and Table 3.2.

Furthermore, it was observed that radiation levels measured at the head and foot regions were significantly influenced by the radiation emitted from the chest area, particularly at a distance of 200 cm. At this point, the dose values recorded at the head and foot were nearly equivalent to those at chest level, indicating overlapping exposure effects at increased distances.

Table 3.1 Radiation dose rate according to the different times at different distances

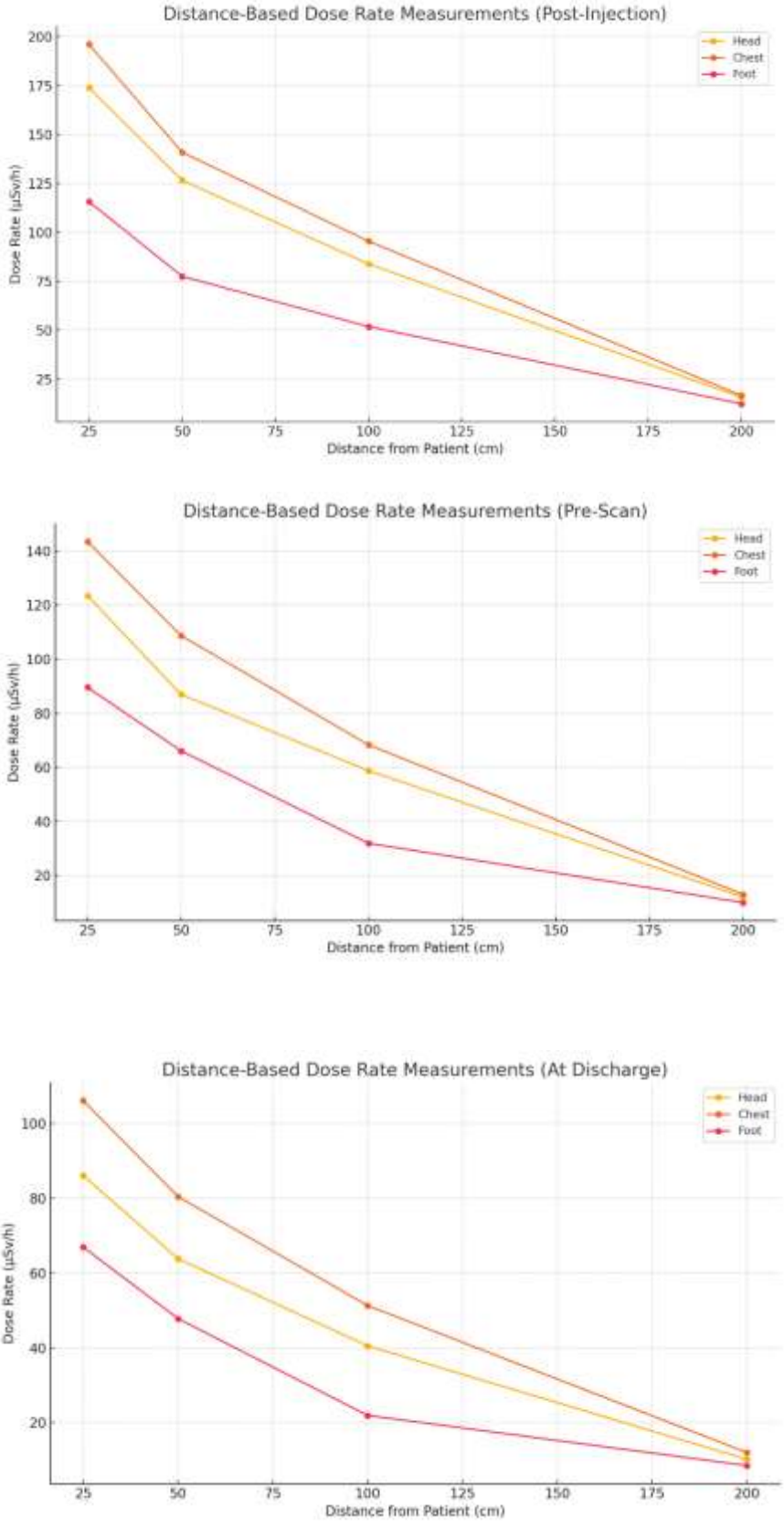
		25 cm (µSv/h)	50 cm (µSv/h)	100 cm (µSv/h)	200 cm (µSv/h)
1 min. After Enjection	**Head**	173,91	126,52	83,86	15,65
	Chest	196,08	140,86	95,47	16,6
	Foot	115,65	77,47	51,82	12,34
60 min. After Enjection	**Head**	123,47	86,95	58,78	12,08
	Chest	143,47	108,69	68,34	13,04
	Foot	89,56	66,08	31,91	10
120 min. After Enjection	**Head**	86,08	63,82	40,52	10,17
	Chest	106,08	80,43	51,3	12
	Foot	66,9	47,8	21,91	8,52

Most of the PET/CT patients are old or in need of someone to help them during the imaging. In this study, we want to calculate and evaluate the caregivers' or relatives' radiation dose exposure from the patients during the process when they have to close the patients. In Table 3.2, the total radiation exposure doses are seen from different distances. Distance and time are important for the caregivers or patients' relatives, as radiation, them are affected in Figure 3.1. According to the International Commission on Radiological Protection (ICRP), attendant adult doses must be under 5 mSv/y. In light of this information, through the process of imaging and before discharging patients almost 3 hours after injection, it would not pose a radiation health risk for guards.

Table 3.2 Total radiation dose rate according to the different times at different distances

	25 cm (µSv/h)	50 cm (µSv/h)	100 cm (µSv/h)	200 cm (µSv/h)
After Enjection	485,64	344,85	231,15	44,59
Before Imaging	356,5	261,72	159,03	35,12
Before Patient Discharge	259,06	192,05	113,73	30,69
Total	1,10 mSv/y	0,79 mSv/y	0,50 mSv/y	0,11 mSv/y

Figure 3.1: Dose Rate Measurements According to Distance and Time



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WEIGHT-BASED PROPERTIES OF OSTRICH EGG

ABSTRACT

The present study was conducted with the objective of determining the various traits of ostrich eggs, including albumen+yolk weight, shell weight and thickness, shape index, and the number and density of shell pores, based on egg weight obtained through weighing. The eggs were collected from two ostriches raised in a private farm located in the Antakya district of Hatay province during the 2021–2022. Each egg was weighed on the day of collection to determine its total weight. Based on the measured egg weights and using equations previously developed for other poultry species, estimations were made for egg length, egg width, egg surface area, and the total number of shell pores. The mean egg weight was determined to be 1272.67±38.97 g, with an average albumen+yolk weight of 1116.96 g, and shell weight of 116.71 g. Additionally, the mean shell thickness was 1.28 mm, the shape index was 69.56%, and the elongation ratio was 1.438. The estimated pore number ranged from 38,064.88 to 106,078.91, and the pore density varied between 69.70 and 193.66 pores/cm². This study provides important preliminary data indicating that structural and compositional traits of ostrich eggs can be estimated non-destructively.

Keywords: *shell index, content weight, elongation, volume*

DEVEKUŞU YUMURTASININ AĞIRLIK BAZLI ÖZELLİKLERİ

ÖZET

Çalışmada devekuşu yumurtalarının tartımla elde edilen yumurta ağırlığı bazlı hesaplanan ak+sarı ağırlığı, kabuk ağırlığı ve kalınlığı, şekil indeksi, kabuk gözenek sayı ve yoğunluğu özelliklerinin belirlenmesi amacıyla yapılmıştır. Çalışmada 2021-2022 yıllarında Hatay ili Antakya ilçesinde özel bir tesiste yetiştirilen iki dişi devekuşlarına ait yumurtalar kullanılmıştır. Yumurtalar toplandıkları gün tartılarak yumurta ağırlığı saptanmıştır. Tartılarak belirlenen bu yumurta ağırlığı baz alınarak çeşitli kanatlı hayvan yumurtalarında belirlenen denklemler yardımıyla; yumurta boyu, yumurta eni, yumurta yüzey alanı, kabuk gözenek sayısı hesaplanmıştır. Devekuşu yumurta ağırlığı ortalama 1272.67±38.97 g, ak+sarı ağırlığı 1116.96 g ve kabuk ağırlığı 116.71 g olarak saptanmıştır. Ayrıca 1.28 mm kabuk kalınlığı, %69.56 şekil indeksi, 1.438 uzama, 38064.88 - 106078.91 adet gözenek sayısı ve 69.70 - 193.66 adet/cm^2 gözenek yoğunluğu belirlenmiştir. Bu çalışma Devekuşu yumurtasının yapısal özelliklerinin özellikle kırılmadan tespit edilebileceğini verebilmek adına önemli bir ön çalışmadır.

Anahtar kelimeler: *kabuk indeksi, İçerik miktarı, Uzama, hacim*

Giriş

Yumurta, kanatlı hayvanlarda embriyonik gelişim için gerekli besin ve korumayı sağlayan; biyolojik, morfolojik ve fizyolojik özelliklerin incelenmesine olanak tanıyan önemli bir üründür. Dünyanın en büyük kuş türü olan devekuşu (Struthio camelus), hem biyolojik özellikleri hem de ekonomik potansiyeli nedeniyle son yıllarda artan bir ilgiyle karşılaşmaktadır. Güney Afrika kökenli olan bu tür, adaptasyon kabiliyetinin yüksek olması nedeniyle dünyanın farklı bölgelerinde yetiştirilebilmektedir. Özellikle et verimi, deri ve yumurta üretimi açısından devekuşu, alternatif hayvansal üretim kaynaklarından biri haline gelmiştir (Sales ve Janssens, 2003; Horbańczuk, 2000).

Devekuşu uçma yeteneği olmayan Afrika'ya özgü bir kuş türüdür. Uzun boyun ve bacakları ile diğer kuşlardan yüksek canlı ağırlığı ile önemli farklılık göstermektedir. Devekuşu yetiştiriciliğinden elde edilen yumurta, et ve deri öne çıkan ürünlerdir. Devekuşu yumurtaları ortalama 1100–1900 g ağırlığında ve yetişkin bir devekuşunun vücut ağırlığının yaklaşık %1.2'sine karşılık gelmektedir (Van Schalkwyk et al., 2020). Devekuşu yumurtası mat beyaz ve kalın kabuklu özellik göstermektedir. Devekuşu yumurtasının yapısında sarı, ak, kabuk zarları ve kabuk bulunmaktadır (Gonzalez ve ark. 1999). Diğer kanatlı türlerine göre çok daha büyük boyutlara sahip olan devekuşu yumurtaları, kalın kabuk yapısı ve yüksek besin içeriğine sahiptir (Dzoma et al., 2020). Bu yapıların her birinden elde edilen özellik değerleri kalite ve üretimdeki verim düzeylerinin belirlenmesinde önemli faktörlerdir. Devekuşu yumurta kalite özelliklerinin belirlenmesinde yumurtaların kırılmaması elde edilecek civciv sayısının artırılması adına gerekli bir işlemdir. Çünkü devekuşlarında yumurta üretimi mevsimsel olup genelde sürü devamlılığı amacıyla kuluçka işleminde kullanılmaktadır. Yumurta oluşumu, dişi bireyin üreme kanalında yaklaşık 48 saatlik bir süreçte tamamlanmakta ve yumurtlama sıklığı ortalama iki günde bir şeklinde gözlemlenmektedir (Sahan et al., 2003).

Üretim verimliliği ve embriyonik gelişim açısından yumurta kalitesinin belirlenmesi büyük önem taşımaktadır. Yumurta kalite özelliği dış ve iç kalite özellikleri olarak ikiye ayrılmaktadır. Dış kalite özellikleri yumurta ağırlığı, yumurta boyu ve yumurta eni gibi yumurta kırılmadan belirlenen özelliklerin yanında kabuk ağırlığı ve kabuk kalınlığı gibi kırılarak belirlenen özellikleri kapsamaktadır (Altuntaş & Şekeroğlu, 2008; Tullett, 1984). İç kalite özellikleri yumurta akı ve sarı ile ilgili ağırlık, uzunluk ve yükseklik belirleme işlemi için yumurtanın kırılması gerekmektedir. Yumurta ağırlığı, yumurta boyu ve yumurta eni gibi özellikler baz alınarak oluşturulan denklemler ile bazı kalite özellikleri hesaplanabilmektedir (Paganelli ve ark. 1974; Narushin ve Romanov 2002; Sezer, 2007; Gualtieri ve Tartari, 2016). Mevsimsel üretim yapan ve sınırlı sayıda yumurta elde edilen türlerde ve özellikle devekuşunda her bir yumurtanın biyolojik ve ekonomik değeri göz önünde bulundurulduğunda, bu yöntemlerin bazı sakıncaları bulunmaktadır. Bu nedenle, yumurta bütünlüğünün korunarak yapılabilecek matematiksel modelleme teknikleri önem kazanmaktadır. Bu modellemelerde, yumurta ağırlığı temel alınarak morfolojik ve fiziksel özellikler tahmin edilebilmektedir (Rahn ve Paganelli, 1989; Board ve Scott, 1980).

Geleneksel yöntem olarak tanımlanan terazi ve kumpas ile yapılan bazı çalışma sonuçları verilmiştir. Devekuşu yumurta ağırlığı 1470.8 g, yumurta yüzey alanı 604.1 cm^2, yumurta eni 12.7 cm, yumurta boyu 16.0 cm, kabuk ağırlığı 242.5 g ve zarlı kabuk kalınlığı 0.19 cm olarak bildirilmiştir (Christensen ve ark. 1996). Shanmuga Sundaram ve ark. (2018) tarafından devekuşu yumurta ağırlığı 1237.33 g, yumurta boyu 14.92 cm, yumurta eni 11.67 cm, kabuk ağırlığı 222.50 g, kabuk kalınlığı 2.87 mm, ak ağırlığı 720.00 g ve sarı ağırlığı

283.33 g olarak tespit etmişlerdir. Devekuşu yumurtalarının kabuk kompozisyonunu, %53.9'unu yumurta akı, %26.7'sini yumurta sarısı ve %19.4'ünü kabuk oluşturmaktadır (Sahan et al., 2003; Melesse et al., 2021). Morfometrik açıdan devekuşu yumurtalarının uzunluğu 14–18 cm, genişliği 12–15 cm arasında değişmekte ve şekil indeksi %83–86 civarındadır (Altuntaş ve Şekeroğlu, 2008; Mugo et al., 2022). Kabuk kalınlığı ise genellikle 1.7–2.1 mm arasında olup, ortalama kabuk ağırlığı 231–243 gr. civarındadır (Horbańczuk, 2000; Gualtieri ve Tartari, 2016). Yumurtanın elipsoidal yapısını belirlemede kullanılan şekil indeksi, kuluçka süresince embriyonun gaz değişimi, dönme hareketleri ve ısı transferi gibi fizyolojik süreçlerini doğrudan etkilemektedir (Narushin et al., 2021).

Çalışmada devekuşu yumurtalarının tartımla elde edilen yumurta ağırlığı bazlı hesaplanan ak+sarı ağırlığı, kabuk ağırlığı ve kalınlığı, kabuk gözenek sayı ve yoğunluğu özelliklerinin belirlenmesi amacıyla yapılmıştır.

Materyal ve Metotlar

Çalışmada kullanılan devekuşu yumurtaları 2021-2022 yıllarında Hatay ili Antakya ilçesinde özel bir tesiste yetiştirilen iki dişi devekuşlarından temin edilmiştir. Yumurtalar yumurtlandığı gün toplanmış ve bireysel olarak tartılarak 14 adet yumurtanın yumurta ağırlığı saptanmıştır.

Yumurta ağırlığı baz alınarak bütün yumurtanın diğer parçalarına ait ağırlık, kalınlık, uzunluk, genişlik ve gözenek sayısı gibi özellikler matematiksel formüller yardımıyla hesaplanmıştır. Kullanılan matematiksel formüller farklı kanatlı tür yumurtalarında yapılan çalışmalar sonucu bulunmuş olup özellikler ve matematiksel formüller aşağıda sunulmuştur (Paganelli ve ark., 1974, Reddy ve ark. 1979, Hoyt ve ark., 1979, Rahn ve Paganelli 1988, Rahn ve Paganelli, 1989, Rahn ve Paganelli, 1990, Rahn ve ark. 1980, Narushin 2005, Alaşahan ve ark.2019);

Yumurta Boyu (mm) = $14.7 \times (\text{Yumurta ağırlığı})^{0.341}$

Yumurta eni (mm) = $11.3 \times (\text{Yumurta Ağırlığı})^{0.327}$

Yumurta yüzey alanı (cm^2) = $4.835 \times (\text{Yumurta ağırlığı})^{0.662}$

Gözenek Sayısı-1 (Adet) = $304 \times (\text{Yumurta ağırlığı})^{0.767}$

Gözenek Sayısı-2 (Adet) = $1041 \times (\text{Yumurta ağırlığı})^{0.504}$

Gözenek Sayısı-3 (Adet) = $3520 \times$ (Yumurta ağırlığı / Kuluçka süresi)

Kabuk Ağırlığı (g) = $0.0524 \times (\text{Yumurta ağırlığı})^{1.113}$

Yumurta kabuk indeksi (g/100 cm^2) = (Yumurta kabuk ağırlığı / Yumurta yüzey alanı) × 100

Yumurta ağırlığı baz alınarak hesaplanan değerler kullanılarak matematiksel formüller yardımıyla gözenek yoğunluğu ve kabuk hacmi belirlenmiştir;

Gözenek Yoğunluğu 1 (Gözenek/cm^2)= (Gözenek Sayısı-1 / Yumurta yüzey alanı)

Gözenek Yoğunluğu 2 (Gözenek/cm^2)= (Gözenek Sayısı-2 / Yumurta yüzey alanı)

Gözenek Yoğunluğu 3 (Gözenek/cm^2)= (Gözenek Sayısı-3 / Yumurta yüzey alanı)

Kabuk hacmi (cm^3) = Yumurta yüzey alanı / yumurta boyu



Resim 1. Dişi Devekuşu görseli



Resim 2. Yumurta ağırlık tartım görseli

İstatistiki Analizler;

Çalışmada yumurta özelliklerine ait veriler IBM SPSS Statistics 22 programında tanımlayıcı istatistik yapılarak tablolarda sunulmuştur.

Bulgular

Devekuşu yumurta ağırlığı ortalama 1272.67 g olup Tablo 1'de yumurta şekil özellikleri sunulmuştur. Devekuşu yumurta şekil indeksi %69.56 (%69.43-69.75) ve uzama değeri 1.438 (1.434-1440) olduğu saptanmıştır. Ayrıca devekuşu yumurta ak+sarı ağırlığı 1116.96 g ve kabuk ağırlığı 148.76 g olarak belirlenmiştir (Tablo 2).

Tablo 1. Devekuşu yumurta şekil özellikleri

Özellikler	Ortalama	Minimum	Maximum
Yumurta Ağırlığı (g)	1272.67	1040.00	1442.00
	Ağırlık bazlı yumurta şekil özellikleri		
Yumurta boyu (mm)	167.79	157.08	175.60
Yumurta eni (mm)	116.71	109.56	121.92
Şekil indeksi	69.56	69.43	69.75
Elongasyon	1.438	1.434	1.440

Tablo 2. Devekuşu yumurta parça özellikler

Özellikler	Ortalama	Minimum	Maximum
Yumurta Ağırlığı (g)	1272.67	1040.00	1442.00
	Ağırlık bazlı yumurta parça özellikleri		
Ak+sarı ağırlığı	1116.96	920.52	1270.11
Kabuk ağırlığı (g)	148.76	119.48	171.89
Ak+Sarı Oranı (%)	88.26	88.08	88.51
Kabuk Oranı (%)	11.74	11.49	11.92

Devekuşu yumurtasına ait kabuk özellik değerleri Tablo 3'te sunulmuştur. Kabuk kalınlığı 1.28 mm, yumurta yüzey alanı 546.63 cm^2, yumurta kabuk indeksi 27.14 g/100 cm^2, gözenek sayısı 38064.88-106078.91 adet ve gözenek yoğunluğu 69.70-193.66 adet/cm^2 olarak belirlenmiştir.

Tablo 3. Devekuşu yumurta kabuk özellikleri

Özellikler	Ortalama	Minimum	Maximum
Yumurta Ağırlığı (g)	1272.67	1040.00	1442.00
	Ağırlık bazlı yumurta ağırlık ve oran özellikleri		
Kabuk kalınlığı (mm)	1.28	1.17	1.35
Yumurta yüzey alanı (cm^2)	546.63	480.48	596.53
Yumurta kabuk indeksi (g/100 cm^2)	27.14	24.87	28.82
Kabuk hacmi (cm^3)	32.55	30.59	33.97
Gözenek sayısı 1 (adet)	38064.88	34517.20	40.697.64
Gözenek sayısı 2 (adet)	72778.98	62652.46	80500.75
Gözenek sayısı 3 (adet)	106078.91	87161.90	120853.33
Gözenek yoğunluğu 1 (adet/cm^2)	69.70	68.22	71.84
Gözenek yoğunluğu 2 (adet/cm^2)	133.06	130.40	134.95
Gözenek yoğunluğu 3 (adet/cm^2)	193.66	181.41	202.59

Tartışma

Tartarak belirlenen devekuşu yumurta ağırlığı 1272.67 g (1040-1442 g) olup yumurta ağırlığı baz alınarak matematiksel formülle hesaplanan yumurta boyu 167.79 mm ve yumurta eni 116.71 mm bulunmuştur. Ayrıca çalışmada hesaplanan yumurta boyu ve eni

değerleri kullanılarak yumurtanın şeklini tanımlamada kullanılan şekil indeksi %69.56 ve uzama 1.438 olarak tespit edilmiştir (Tablo 1). Devekuşu yumurta ağırlığı 1450-1650 g arasında (Gonzalez ve ark, 1999), 1470.8 g (Christensen ve ark, 1996), 1618 g (1215-1887 g) (Şahan ve ark, 2003), 1237.33 g (Shanmuga Sundaram ve ark, 2018) olduğu bildirilmiştir. Yumurta şekil indeksi daha önce yapılan çalışmalarda %82.86 (Selvan ve ark, 2014), %78.28 (Shanmuga Sundaram ve ark, 2018) ve %83.51 (%80.37-%85.33) (Brassó ve Komlósi, 2021) olarak verilmiştir.

Çalışmamızda ağırlığı ortalama 1272.67 g olan devekuşu yumurtasında kabuk ağırlığı 148.76 g (oranı %11.74) ve ak+sarı ağırlığı 1116.96 g (%88.26) olarak belirlenmiştir (Tablo 2). Yumurta kanalında oluşan bütün yumurta kabuk, kabukaltı zarları, ak ve sarı parçalarının birleşimi sonucu oluşmaktadır. Bütün yumurtadaki bu parçaların ağırlık ya da oranları Christensen ve ark (1996) tarafından 1470.8 g ağırlığındaki bir yumurtada kabuk ağırlığını 242.5 g ve Shanmuga Sundaram ve ark (2018) tarafından 1237.33 g ağırlığındaki yumurtada 222.50 g kabuk ağırlığı, 720 g ak ağırlığı ve 283.33 g sarı ağırlığı şeklinde saptanmıştır.

Çalışmada yumurta ağırlığı baz alınarak matematiksel formülle hesaplanan kabuk kalınlığı 1.28 mm olup 1.17-1.35 mm arasında değiştiği belirlenmiştir (Tablo 3). Devekuşu yumurtası ile yapılan çalışma sonuçlarında yumurta kabuk kalınlığı Keffen and Jarvis, (1985) 1.79-1.83 mm, Gonzalez ve ark, (1999) 1.87-1.88 mm arasında, Christensen ve ark, (1996) zarlı kabuk kalınlığını 0.19 cm ve zarsız kabuk kalınlığını 0.17 cm, Şahan ve ark, (2003) 1.94 mm (1.8-2.0 mm), Brand ve ark, (2012) 1.76 mm ve Shanmuga Sundaram ve ark, (2018) 2.87 mm olarak bildirilmiştir.

Devekuşu yumurta yüzey alanı 546.63 cm^2 (480.48-596.53 cm^2) olarak saptanmıştır (Tablo 3). Bu özelliği belirleyen bazı çalışma sonuçlarında 604.1 cm^2 (Christensen ve ark, 1996), 464.97 cm^2 (Nedomová and Buchar, 2013) ve 473.10- 532.41cm^2 arasında değiştiği ortalama 494.03 cm^2 (Brassó ve Komlósi, 2021) olduğu ifade edilmiştir.

Çalışmada devekuşu yumurtasında farklı üç matematiksel formülle belirlenen santimetrekare yüzey alana düşen gözenek sayısı ortalama 69.70 adet/cm^2, 133.06 adet/cm^2 ve 193.66 adet/cm^2 olmuştur (Tablo 3). Gözenek yoğunluğunu Christensen ve ark, (1996) ortalama 18.3 (20.2-17.7), Brand ve ark, (2012) 57.1 adet/cm^2 ve Brassó ve Komlósi, (2021) 18.75 adet/cm^2 (18.12-19.71) olarak belirlemişlerdir.

Sonuçlar

Sonuç olarak, bu çalışmada ölçümle belirlenen yumurta ağırlık değeri baz alınarak devekuşu yumurtalarına ait bazı kalite özellikleri yumurta kabuk bütünlüğü bozulmadan matematiksel formül yardımıyla hesaplanmıştır. Devekuşu yumurtasının kabuk ağırlığı ve kalınlığı değerleri diğer literatür sonuçlarından düşük saptanmıştır. Ayrıca devekuşu yumurtasının özellikle yumurta uzunluğu, yumurta genişliği, kabuk kalınlığı ve kabuk ağırlığı için küçük yumurtalarda belirlenen matematiksel formüllerin büyük devekuşu yumurtasında literatür değerlerinden düşük sonuç verdiği gözlenmiştir.

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EXPERIENCE WITH TOTALLY IMPLANTABLE VENOUS ACCESS PORTS IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

ABSTRACT

Totally implantable venous access ports (TIVAP) are widely preferred for oncology patients requiring chemotherapy. The most common cause of port removal in hematological malignancy patients is infection, followed by dysfunction. The aim of this study is to evaluate single center experience of TIVAP in patients with hematologic oncology. 126 patients who were followed up in the hematology-oncology department of the tertiary oncology hospital and who had port catheters inserted in the interventional radiology unit between January 2019- January 2022 were evaluated retrospectively. Post-procedure control radiographs of the patients were evaluated for early complications and localization suitability**.** Additionally, patients' port catheter follow-ups were evaluated for infection and dysfunction. 68 (54%) of the patients were male and 58 (46%) were female. The age range of the patients was 18-65, and the average age was calculated as 41,3. 60 patients were followed up with a diagnosis of acute myeloid leukemia, 30 with acute lymphocytic leukemia, 24 with non-Hodgkin lymphoma, 10 with Hodgkin lymphoma, and 2 with multiple myeloma. In the control radiograph examination taken after the procedure, the port location was appropriate in 124 patients and the port catheter ended in the right ventricle in 2 patient. No early complications were observed in any of the patients. Port infection developed in 14 patients and the average time to develop port infection was calculated as 3,4 weeks. Port infection rates are higher in hematological malignancy patients compared to other malignancy patient groups. Although the use of port catheters is common in patients with hematological malignancy, caution should be exercised in terms of possible port infection.

Keywords: TIVAP, hematologic malignancies, complications

Introduction

Totally implantable venous access ports (TIVAPs) are widely used in oncology patients who require long-term intravenous therapies such as chemotherapy, parenteral nutrition, or transfusion support. They offer a reliable, safe, and patient-friendly alternative to external catheters, particularly in individuals requiring frequent vascular access (1). In patients with hematological malignancies, however, TIVAP use may be associated with specific complications due to prolonged neutropenia and immunosuppression. Among these, infection remains the most common reason for port removal, followed by mechanical dysfunction (2,3). Use of TIVAPs allows long-term administration of veinotoxic compounds, improves

patient quality of life and reduces risk of infection.(4) Neutropenia on the day of implantation and the number of chemotherapy lines after IVAP insertion were independent risk factors for IVAP-related bloodstream infections(6).Hematologic malignancy, hypoalbuminemia, leukopenia, and diabetes mellitus at the time of port placement were independent risk factors for early port infections.(7) This study aims to share the experience of a tertiary oncology center regarding the safety, efficacy, and complication profile of TIVAP use in patients with hematological malignancies.

Materials and Methods:

This retrospective study included 126 patients with hematological malignancies who had TIVAPs inserted under fluoroscopic guidance by the interventional radiology unit between January 2019 and January 2022. All patients were being followed in the hematology-oncology department of a tertiary oncology hospital. Baseline demographic data, diagnosis, and procedural details were recorded. Immediate post-procedural chest radiographs were reviewed for proper catheter tip placement and early complications such as pneumothorax or hemothorax. Port catheters can be inserted through central veins such as subclavian and jugular veins. In practice, the subclavian vein may be preferred because of its proximity to the vena cava and right atrium. However, the possibility of development of pneumothorax is high (1-3.2%) in subclavian vein puncture with the Seldinger method.(5) In our study, jugular vein was used primarily and no pneumothorax was detected in this intervention line due to the routine use of ultrasonography. During follow-up, TIVAPs were assessed for two major complications: infection (confirmed by clinical signs and positive blood or port cultures) and catheter dysfunction (defined as inability to infuse or aspirate). Time to complication development was calculated from the date of implantation.

Results:

Of the 126 patients, 68 (54%) were male and 58 (46%) female. The median age was 41.3 years (range: 18–65). The most common diagnoses were:

Acute Myeloid Leukemia (AML): 60 patients (47%)

Acute Lymphoblastic Leukemia (ALL): 30 patients (24%)

Non-Hodgkin Lymphoma: 24 patients (19%)

Hodgkin Lymphoma: 10 patients (8%)

Multiple Myeloma: 2 patients (1%)

Post-procedure chest radiographs confirmed appropriate catheter tip location in 124 patients (98%), while in 2 patients (2%), the catheter tip was found to be in the right ventricle and repositioning was required. No immediate complications such as pneumothorax, hemothorax, or arrhythmias were observed.







During follow-up:

Port-related infection occurred in 14 patients (11%), with a mean time to onset of 3.4 weeks post-implantation. All required systemic antibiotic treatment, and in 5 cases (36%), port removal was necessary.

Catheter dysfunction was documented in 8 patients (6%), with a mean onset of 17.25 weeks. Most cases were managed with thrombolytic therapy or catheter repositioning, but 2 ports were explanted due to persistent dysfunction.

Conclusion-Discussion:

TIVAPs are a reliable and generally safe vascular access option for patients with hematological malignancies. In our cohort, the overall complication rate was acceptable, with infections being the most frequent issue encountered. Prompt management of complications and close follow-up are crucial for maintaining port function and minimizing treatment delays in this vulnerable patient population. Further studies with longer follow-up and larger cohorts could help identify patient-specific risk factors to optimize TIVAP management strategies.

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HEALTH LITERACY AND WOMEN'S HEALTH

ABSTRACT

Health literacy is important for a person to know and implement what they need to do and what they need to avoid during the process of improving their current health in their communication with a healthcare professional. It enables individuals to take an active role and responsibility in the decision-making process regarding their own health status. As the level of health literacy decreases, the person's effective communication with healthcare professionals progresses negatively and this situation hinders the individual's ability to make decisions regarding their health. Health literacy is affected by many factors such as socio-demographic, cultural, healthcare system, etc. When the concept of gender is considered, especially among socio-demographic characteristics, health literacy in women has a special importance. Women are the cornerstone of society and also reflect the level of social, political, technological and economic development. A high level of health literacy in women is very important for both themselves, their environment and society because it provides them with the opportunity to understand, comprehend and use health-related information and to make appropriate decisions on necessary issues. One-on-one communication should be established with women in each life period, women should be reached through various channels and their knowledge levels should be increased and healthy life behaviors should be developed. Health workers have important duties in this regard. When the importance of the relationship between women's health and health literacy is considered in terms of public health nursing, services should be carried out with a team approach in a preventive and health-promoting manner. From this perspective, the public health nurse has undeniable roles in the team.In this process, women should be considered as a whole with their environment. The necessary consultancy should be provided. When the studies conducted in this field are examined, it becomes clear that the health literacy levels in women are not sufficient and should be improved by supporting them with various means.

Keywords: Health Literacy, Women's Health, Public Health, Nursing

SAĞLIK OKURYAZARLIĞI VE KADIN SAĞLIĞI

ÖZET

Sağlık okuryazarlığı kişinin sağlık çalışanıyla kuracağı iletişimde ,mevcut sağlığının düzelme sürecinde yapması gerekenleri ve uzak durması gerekli konuları bilmesi ve uygulaması adına önem arz etmektedir. Kişilerin kendi sağlık durumları üzerinde karar verme süreçlerinde etkin rol ve sorumluluk almalarını sağlar. Sağlık okuryazarlık seviyesi düştükçe kişinin sağlık çalışanları ile etkili iletişimi olumsuz yönde ilerler ve bu durum bireyin sağlığı ile ilgili kararlar almasını sekteye uğratır. Sağlık okuryazarlığı sosyo-demografik, kültürel , sağlık sistemi vb. birçok faktörden etkilenmektedir. Sosyo-demografik özelliklerden özellikle cinsiyet kavramı ele alındığında kadınlarda sağlık okuryazarlığı ayrı bir öneme sahip olmaktadır. Kadın toplumun temel taşı olmakla beraber sosyal, siyasal, teknolojik ve ekonomik gelişmişlik düzeyini de yansıtmaktadır. Kadınlarda sağlık okuryazarlık düzeyinin yüksek seviyede olması hem kendisi hem çevresi ve toplum için çok önemlidir çünkü sağlık ile ilgili bilgileri anlama, kavrama, kullanma ve gerekli konularda uygun kararlar alabilmek için kendisine fırsat sağlar. Kadınlar ile her yaşam dönemlerine özgü bire bir iletişim halinde bulunulmalı çeşitli kanallar vasıtası ile kadınlara ulaşılarak bilgi düzeylerinin artırılması sağlanarak sağlıklı yaşam davranışları geliştirilmelidir. Bu konuda öncelikli olarak sağlık çalışanlarına önemli görevler düşmektedir. Halk sağlığı hemşireliği açısından kadın sağlığı ve sağlık okuryazarlığı ilişkisinin önemi ele alındığında hizmetler ağırlıklı olarak koruyucu ve sağlığı geliştirici biçimde ekip anlayışı ile yürütülmelidir. Bu çerçeveden bakıldığında ekipte halk sağlığı hemşiresinin yadsınamaz rolleri vardır. Bu süreçte kadın çevresiyle bir bütün olarak ele alınmalıdır. Gerekli danışmanlık sağlanmalıdır. Bu alanda yapılan çalışmalar incelendiğinde kadınlarda sağlık okuryazarlık düzeylerinin yeterli olmadığı çeşitli vasıtalarla desteklenerek iyileştirilmesi gerçeği ortaya çıkmaktadır.

Anahtar Kelimeler: Sağlık Okuryazarlığı , Kadın Sağlığı ,Halk Sağlığı ,Hemşirelik

GİRİŞ

Sağlık okuryazarlığı bir bireyin hem kendisi hem ailesi ve çevresi için sağlığını ,benliğini anlaması ,değerlendirmesi ,gerektiğinde kararlar alabilmesi ,sağlık hizmetlerinden ihtiyaçları doğrultusunda en iyi şekilde faydalanabilmesi adına yadsınamaz bir öneme sahiptir (Akça ve ark. 2020). Günümüzde değişen ve gelişen koşullar teknoloji ve ortamlar sağlık okuryazarlığını farklı bir konuma ve noktaya taşımaktadır (Ilgaz 2021). Bu sebeple sağlık okuryazarlık düzeylerinin geliştirilmesi özellikle kadınlarda ve devamında tüm bireylerde ne denli gerekli olduğu gerçeği karşımıza çıkmaktadır. Kadınlar temelde ailenin ,toplumun kilit noktası olması sebebiyle öncelikle kadınların sağlık okuryazarlık düzeylerinin iyileştirilmesi gerçeğine dikkat çekilmektedir Böylece bu durum sağlık hizmetlerinden etkin bir şekilde yararlanmayı, sağlık sorunlarında kararlar alabilmeyi ve hem çevresi hem de sağlık çalışanı ile etkili iletişim kurabilme davranışını bireye kazandırır (Dağlar ve Oksay, 2022).

Sağlık okuryazarlığı kavramı ilk kez 1974 yılında kullanılmıştır. Simonds tarafından “Health Education as Social Policy” isimli makalede kavram yer almıştır .Nutbeam 1998 yılında Dünya Sağlık Örgütü (DSÖ) adına bir sözlük hazırlamıştır. “Sağlığın Geliştirilmesi Sözlüğü” adlı çalışmasında (Health Promotion Glossary) "Bir bireyin sağlıkla ilgili bilgiye ulaşması, anlaması ve sağlığını geliştirici yönde bu bilgiyi kullanması için motivasyonunu ve yeteneğini belirleyen sosyal ve bilişsel beceriler" şeklinde tanımlanmıştır. Amerikan Tıp Derneği (AMA) ise sağlık okuryazarlığını 1999 yılında hazırladığı raporda “bireylerin sağlıkla ilgili mesajları okuyabilmesi, ilaç kutularının üzerini okuyup anlaması, sağlık çalışanları tarafından söylenenleri anlayıp yapabilmesi” olarak tanımlamıştır (Turan ve Söylemez 2023).T.C. Sağlık Bakanlığının hazırladığı Sağlığın Teşviki ve Geliştirilmesi Sözlüğü’nde “Sağlık okuryazarlığı; bireylerin, iyi sağlığı teşvik edecek ve sürdürecek şekilde bilgiye erişme, bilgiyi anlama ve kullanma becerisi ve motivasyonunu belirleyen bilişsel ve sosyal becerileri temsil eder. “ tanımına yer verilir (Yorulmaz ve Sezer 2021).

Sorensen ve arkadaşları 2012 yılında sağlık okuryazarlığı üzerine yapılan tanımlar için geniş çaplı bir analiz yapmışlar .Yapılan analizde (okuryazarlıkla bağlantılı, insanların sağlık durumlarıyla ilgili olarak günlük yaşamlarında kararlar almak, yaşam kalitelerini arttırmak/sürdürmek için sağlıklarını geliştirme ve hastalıkları önleme amacıyla gerekli sağlık bilgisine erişme, anlama, değer biçme ve bilgiyi kullanmayı sağlayacak bilgi, motivasyon ve yeterlilik) şeklinde geniş bir tanım ortaya koymuşlardır (Yorulmaz ve Sezer 2021)

SAĞLIK OKURYAZARLIĞININ ÖNEMİ

AMA, DSÖ, Uluslar arası Göç Örgütü (IOM) raporlarında Sağlık okuryazarlığı ve bireylerin sağlık sonuçları arasındaki var olan ilişkinin önemi yer almıştır . Sağlık okuryazarlığı kişinin sağlık çalışanıyla kuracağı iletişimde ,mevcut sağlığının düzelme sürecinde yapması gerekenleri ve uzak durması gerekli konuları bilmesi ve uygulaması adına önem arz etmektedir (Derbent ve ark 2023). Yeterli ve yetersiz sağlık okuryazarlığına sahip bireyler arsında bir karşılaştırma yapıldığında yetersiz sağlık okuryazarlık düzeyine sahip bireylerde gereksiz hastane kullanımı ,tahliller ,yatış oranı ve sürelerinde artışlar yine acil servislerin gereği dışında kullanımlarının arttığı görülmüş bu durum ise sağlık sektöründe harcamalarda fazlaca artışlara ve iş gücü kayıplarına neden olmuş ve halen olmaktadır (Kıvanç ve ark 2018).

Kişilerin kendi sağlık durumları üzerinde karar verme süreçlerinde etkin rol ve sorumluluk almaları büyük önem arz etmektedir. . Bireyin bu süreçte aktif rol almasında asıl amaç ;stres ve anksiyete seviyesini düşürmektir(Tekbaş ve ark.2023). Sağlık okuryazarlık seviyesi düştükçe kişinin sağlık çalışanları ile etkili iletişimi olumsuz yönde ilerlemektedir. (Akan 2023).

DÜNYA VE TÜRKİYEDEKİ SAĞLIK OKURYAZARLIK DÜZEYLERİ

Sağlık Bakanlığı tarafından "Türkiye Sağlık Okuryazarlığı Düzeyi ve İlişkili Faktörleri Araştırması" yapılan adlı çalışmada sosyo_demografik ,sosyo_ekonomik ve kitle iletişim araçlarının kullanımının sağlık okuryazarlığı hangi düzeyde etkilediği araştırılmıştır (Özkan 2018). Çalışma 6.228 hane ile yapılmış olup TSOY-32 ölçeği uygulanmıştır. %30,9'u yetersiz, %38'i sınırlı, %23,4'ü yeterli, %7,7'si ise ileri düzey olduğu tespit edilmiş olup yaklaşık 10 kişiden yedisinin sağlık okuryazarlık seviyesinin düşük olduğu anlaşılmaktadır. Sağlık okuryazarlık seviyesi düştükçe hastalık ve kronik hastalık oranlarında yükselmeler yaşandığı ,sağlık okuryazarlık düzeyinin artırılması ile bu konuda başarılı sonuçlar elde edileceği tespit edilmiştir.Kadınların %35,3 ,erkeklerin %26,4 oranında yetersiz sağlık okuryazarlık düzeyine sahip olduğu bulunmuştur. 65 yaş üzeri yaşlılar değerlendirildiğinde 10 kişiden 9 unda sağlık okuryazarlığının yetersiz olduğu tespit edilmiştir. (T.C.Sağlık Bakanlığı 2020)

Avrupa Sağlık Okuryazarlığı Araştırması (HLS-EU), 8.000 kişilik bir örneklem (ülke başına 1.000) temelinde sekiz ülkedeki sağlık okuryazarlığı düzeylerini inceledi. Sonuçlar, Hollanda'da katılımcıların %28,7'sinin yetersiz sağlık okuryazarlığına sahip olmasından, Bulgaristan'da %62,1 gibi çok daha yüksek seviyelere kadar değişiyordu . Genel olarak, sekiz ülke genelinde katılımcıların %47,6'sı yetersiz veya sorunlu sağlık okuryazarlığı seviyeleri gösterdi. Japonya'da yetersiz sağlık okuryazarlığı düzeyinin %49,9 olduğu, %85,4'ünün ise "sınırlı" sağlık okuryazarlığına sahip olduğu bulunmuştur. Tayvan'da genel olarak Avrupa'dakinden biraz daha yüksek bir sağlık okuryazarlığı düzeyi bulunmuştur. Amerika' da yapılan çalışmada yetişkin Amerikalıların yaklaşık %36'sının sınırlı sağlık okuryazarlığına sahip olduğu tespit edilmiştir. İngiltere'de 2015 yılında yapılan bir çalışmada ise insanların %43'ünün metin içeren sağlık bilgilerini yetersiz anladığı tahmin edilirken, sayısal beceriler gerektiğinde bu rakam %61'e yükselmiştir. Genel olarak, 18 Ekonomik İşbirliği ve Kalkınma Örgütü (OECD) ülkesinden elde edilen kanıtlara ilişkin bir inceleme, nüfusun en az üçte birinin grupta düşük sağlık okuryazarlığı yaşayabileceğini göstermiştir.Ulusal sağlık okuryazarlığı değerlendirmeleri Çin'de 2008'den beri yürütülmektedir. O zamandan beri, sağlık okuryazarlığı oranı 2019'da %6,48'den %19,17'ye yükselmiştir. Ülkede sağlık okuryazarlığını artırmak için çok sayıda politika çabası belgelenmiştir ve özellikle nüfustaki sağlık okuryazarlığı seviyesi Sağlıklı Çin bir göstergesidir (Health literacy around the world 2021). Avustralya 2018'de HLQ(Sağlık Okuryazarlığı Anketi) anketine dayalı bir Sağlık Okuryazarlığı Anketi gerçekleştirmiştir. Çalışmada katılımcıların %97'sinin sağlıklarını yönetmek için yeterli bilgiye sahip olma konusunda hemfikir olduğunu veya kesinlikle hemfikir olduğunu, %96'sının ise sağlık hizmeti sağlayıcıları tarafından anlaşıldıklarını ve desteklendiklerini hissettiği tespit edilmiştir.(Health literacy around the world 2021)

SAĞLIK OKURYAZARLIĞINI ETKİLEYEN FAKTÖRLER

Sağlık okuryazarlığını daha iyi kavrayabilmek için etkileyen faktörleri ve devamında sonuçlarının bilinmesi gerekmektedir (Semerci ve ark.2023) .Sağlık okuryazarlığı sosyo-demografik, kültürel , sağlık sistemi vb. birçok faktörden etkilenmektedir. Sosyo-demografik özelliklerden özellikle cinsiyet kavramı ele alındığında kadınlarda sağlık okuryazarlığı ayrı bir öneme sahip olmaktadır. Kadın toplumun temel taşı olmakla beraber sosyal ,siyasal ,teknolojik ve ekonomik gelişmişlik düzeyini de yansıtmaktadır (Öztürk 2020). Kadınlarda sağlık okuryazarlık düzeyinin yüksek seviyede olması hem kendisi hem çevresi ve toplum için çok önemlidir çünkü sağlık ile ilgili bilgileri anlama ,kavrama ,kullanma ve gerekli konularda uygun kararlar alabilmek için kendisine fırsat sağlar (Semerci ve ark.2023).

SAĞLIK OKURYAZARLIĞINI GELİŞTİRMEK NEDEN ÖNEMLİDİR ?

Toplumlarda sağlık okuryazarlığının artırılması, vatandaşların kendi sağlıklarını iyileştirmede aktif rol oynamaları, sağlık için toplumsal eylemlere başarılı bir şekilde katılmaları ve hükümetleri sağlık ve sağlık eşitliğini ele alma sorumluluklarını yerine getirmeye zorlamaları için gereken temeli sağlar.Sağlık okuryazarlığının tüm toplumlarda, özellikle de marjinalleşmiş toplumlarda teşvik edilmesi, sağlık eşitsizliklerinin azaltılması ve 2030 Sürdürülebilir Kalkınma Gündemi'nde özetlenen daha geniş sosyal, ekonomik ve çevresel hedeflere ulaşılması yolunda ilerlemenin hızlandırılması açısından hayati önem taşımaktadır. DSÖ, üye devletlere kişisel, örgütsel ve sistemsel düzeylerde sağlık okuryazarlığının etkili yönetimi ve teşvikini sağlamak için teknik destek ve rehberlik sağlayarak sağlık okuryazarlığını teşvik eder ve iyileştirir (Dünya Sağlık Örgütü , 2023).

KADIN SAĞLIĞI NEDİR?

Bir kadının anne karnındaki yaşamından itibaren çocukluktan yaşlılığa ,ölüme kadar hayat boyu tüm süreçlerde var olan sağlık hizmetlerini kapsamaktadır.Tüm bu süreçler boyunca kadın sağlığının korunup geliştirilmesi gereklidir. Kadınların fiziksel ,psikososyal ve tüm yönlerden tam bir iyilik halinde olması kadın sağlığını ifade etmektedir (Erci 2020).

KADIN SAĞLIĞININ ÖNEMİ

Kadın sağlığını değerlendirirken ve bakım verirken yaşı ,ailesi ,kültürü ,eğitimi , sağlık okuryazarlık düzeyi ,dini ,sosyal yapısı ,duygusal ve fiziksel durumunu göz önünde bulundurmak son derece önemlidir. Bu nedenle kadının sağlığı toplumların sosyal ,siyasal ,teknolojik ve ekonomik gelişmişlik düzeyini de yansıtmaktadır (Öztürk ve ark 2022) . Dünyada ülkelerin gelişmişlik seviyeleri belirlenirken kadın sağlığı ve kadının toplumdaki konumu önemli etkilere sahiptir(Akın ve Türkçelik 2018).

KADIN SAĞLIĞINI ETKİLEYEN FAKTÖRLER

Kadın sağlığı ;aile ve toplumdan kaynaklanan psiko-sosyal faktörler ,kadının bireysel sağlık durumu ,doğurganlık davranışı ,sağlık hizmetlerinin kalitesi gibi pek çok faktörden etkilenmektedir. Kadın sağlığı çoğunlukla eğitim ,istihdam ,toplumsal konumu ,gelir durumu kent ve kır ayrımı ,ve kültürel özellikler gibi ,içinde bulunduğu koşullarca şekillendirilmektedir. Kadının toplumdaki yeri yaşam kalitesini belirleyen en önemli faktörlerden biridir (Ay ve ark. 2023).

Eğitim

Eğitim toplum içinde kadının rolünü ve konumunu belirleyen bir konudur. Ülkemiz açısından bakıldığında ise eğitim kadınlar açısından yıllardan beri süregelen en önemli sorunlar arasında yerini almaktadır(Şimşek 2022). Kadınların eğitim seviyeleri düştükçe karar alma konusunda başkalarına bağımlı oldukları ,sağlık alanında hizmetlerden yeteri kadar faydalanmadıkları ve bu konuda çeşitli korku ve endişelerinin mevcut olduğu ,kendi yaşamları konusunda yeterince özgür olmadıkları var olan sorunlar arsında yerini almaktadır (Ay ve ark. 2023). Türkiye İstatistik Kurumu (TÜİK) 2023 verilerine göre ; Ortalama eğitim süresi kadınlarda 8,5 yıl olduğu tespit edilmiştir (TÜİK 2023).

Çalışma Hayatı

Kadınların çalışma hayatındaki varlıkları eğitim konusunda olduğu gibi onları birçok konuda özgür kılmaktadır. Kadınların çalışma hayatındaki varlıkları gelir- gider konusunda söz sahibi olmalarına, daha iyi şartlara sahip olarak yaşamlarını devam ettirmelerine olanak verir. (Toker ve Çıtak 2021).TÜİK 2022 verilerine göre ; Yükseköğretim mezunu kadınların işgücüne katılım oranı %68,8 olduğu, kadınların istihdam oranının erkeklerin yarısından daha az olduğu tespit edilmiştir (TÜİK 2022).

Toplumsal Cinsiyet ve Eşitsizliği

Toplumsal cinsiyet biyolojik farklılıklardan değil ,kadın ve erkek olarak toplumun bizi nasıl gördüğü ,nasıl algıladığı ,nasıl düşündüğü ve davranmamızı istediği ile ilgili bir kavramdır (Öztürk 2020).Toplumsal cinsiyet eşitsizliğinin neden olduğu konuların başında sağlık ile ilgili konular gelmektedir(Semerci ve ark. 2023). Bu konuda en önemli alan üreme sağlığıdır (Öztürk 2020).

Şiddet

Şiddet insanlık tarihinin bugüne kadar sahip olduğu sorunların başında gelmektedir. Toplumun tüm yaş gruplarının sağlığını tehdit eden bir olgudur (Doğrucan ve Yıldırım 2020). Kadına yönelik şiddetin her toplumda ve her dönemde olduğu bilinmektedir. Kadınların binlerce yıl öncesinde de fiziksel şiddete uğradığına dair veriler bulunmaktadır (Öztürk 2020) .

KADIN SAĞLIĞININ GELİŞTİRİLMESİ NEDEN ÖNEMLİDİR?

Kadınlar hayatları boyunca cinsiyet ,sağlık ,şiddet ,eğitim gibi çeşitli konularda sorunlarla karşı karşıya kalmaktadır. Bunların yanında üstlenmiş oldukları rollerden kaynaklı olarak sürekli stres yaşayabilmektedirler. İş hayatında erkeklere göre daha az rol alırlar ve yaşadıkları toplumun kültürel yapısından kaynaklı baskıya maruz kalmaları ruhsal sorunlar

yaşamalarına neden olabilir .Kadınların yaşadıkları sorunlar karşısına kendileri daha rahat ve doğru ifade edebilmeleri konusunda sağlık çalışanlarına önemli bir sorumluluk düşmekte bu konuda kişiyi cesaretlendirerek kendini tam anlamıyla ifade etmesini sağlamalı ve sağlık hizmetlerinden ihtiyacı doğrultusunda faydalanması sağlanmalıdır. Sağlıklı kadın ;sağlıklı çocuk ,aile, toplumdur (Şimşek 2022).

KADIN SAĞLIĞI VE SAĞLIK OKURYAZARLIĞI

Kadının sağlık okuryazarlık düzeyinin yüksek olması sağlık düzeyinin ,refahının ve esenliğinin daha iyi olması ile ilişkili bulunmuştur. Sağlık okuryazarlığı birçok sosyo_demografik özellik ile yakından ilişkilidir. Kadınlar ile her yaşam dönemlerine özgü bire bir iletişim halinde bulunulmalı çeşitli kanallar vasıtası ile kadınlara ulaşılarak bilgi düzeylerinin artırılması sağlanarak sağlıklı yaşam davranışları geliştirilmelidir . Bu konuda öncelikli olarak sağlık çalışanlarına önemli görevler düşmektedir (Dağlar ve ark .2022).

SONUÇ VE ÖNERİLER

Bu alanda yapılan çalışmaları incelediğimizde ; Akça E. ve arkadaşlarının "Gebelerde Sağlık Algısı, Sağlık Okuryazarlığı Ve İlişkili Faktörler "adlı yapmış oldukları çalışmada gebelerin eğitim ve gelir durumları ile sağlık algısı ve okuryazarlığı düzeyleri arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur. Ayrıca gebelerin sağlık okuryazarlıkları yükseldikçe sağlık algılarının iyileştiği belirlenmiştir (Akça ve ark 2020). Tahrani ve arkadaşlarının İran-Meşhed'de yapmış oldukları "kadınların sağlık okuryazarlığı ve bazı ilgili faktörler "adlı çalışmasında kadınların üçte birinden fazlasının yetersiz veya sınırda sağlık okuryazarlığı vardı. Kadınların aile ve toplum sağlığındaki önemli rolü ve sağlık okuryazarlığının bu önemli rol üzerindeki etkisi göz önüne alındığında, onlarda sağlık okuryazarlığı becerilerini teşvik etmek için eğitim programları tasarlamak ve uygulamak gereklidir sonucuna ulaşılmıştır (Tehrani ve ark 2021). Amare ve arkadaşlarının Etiyopya'daki Ilu Ababor Halk Sağlığı tesislerinde Kadın Sağlığı Okuryazarlığı ve Kadın ve Çocuk Sağlığı Bakımıyla İlgili Faktörler adlı 411 katılımcıyla yaptıkları bu çalışmada kadınların %71,3 ünün yetersiz sağlık okuryazarlığına sahip olduğu bulunmuştur. Yeterli anne sağlığı okuryazarlığı oranının kentsel kadınlarda kırsal kadınlara göre 12,2 kat daha yüksek olduğunu bulunmuştur. Vajinal doğum yapan kadınların sezaryenle doğum yapan kadınlara göre yeterli anne sağlığı okuryazarlığına sahip olma olasılığı 0,24 kat daha az olduğu ,doğum öncesi dört veya daha fazla kontrol yaptıran annelerin doğum öncesi kontrol yaptırmayan ya da daha az yaptıran annelere oranla sağlık okuryazarlık oranları daha yüksek bulunmuştur (Amare ve ark 2024).

2019 yılında Aydın ve Aba 'nın yapmış olduğu "Annelerin Sağlık Okuryazarlığı Düzeyleri ile Emzirme Öz-Yeterlilik Algıları Arasındaki İlişki "adlı çalışmalarında annelerin sağlık okuryazarlık düzeyi yükseldikçe emzirme öz –yeterlilik algılarının da yükseldiği tespit edilmiştir. Bu sebeple gebelik sürecinden başlanarak annelerin bu konuda bilgi düzeylerini artırılarak doğru davranış kazanmaları sağlanabilmektedir (Aydın ve Aba 2019). Aktan ve Özdemir'in 2020 yılında Ankara 'da bir üniversite hastanesinin kadın hastalıkları bölümünde yapmış oldukları" Klimakterik dönemdeki kadınların sağlık okuryazarlığı düzeyi" adlı çalışmalarında kadınların sağlık okuryazarlık düzeyleri yeterli düzeyde bulunmamış ve geliştirilmesi gerektiği vurgulanmıştır (Aktan ve Özdemir 2020). Öztürk ve arkadaşlarının 2021 yılında yapmış oldukları "Sağlık Okuryazarlığı Düzeyi Doğum Sonu

Anneye Yönelik Yapılan Geleneksel Uygulamaları Etkiler mi? " adlı çalışmalarında yaşı büyük olan annelerin geleneklere daha bağlı olduğu ,annelerin sağlık okuryazarlık düzeylerinin yüksek olduğu ve sağlık okuryazarlık düzeyi ile doğum sonu uygulamalar arasında anlamlı bir ilişki bulunmadığı tespit edilmiştir (Öztürk ve ark 2021).

Pazarözyurt ve Özkan 'ın 2023 yılında yapmış olduğu "Gebelerin Sağlık Okuryazarlığı ile Öz Bakım Gücü Arasındaki İlişkinin Değerlendirilmesi" adlı çalışmalarında gebelerin sağlık okuryazarlığı ile öz bakım gücü arasında anlamlı yüksek bir ilişki bulunmuş ve sağlık personelinin gebeleri gerekli kaynak ve desteklere yönlendirerek bu konuda gelişmeler sağlanması vurgulanmıştır (Pazarözyurt ve Özkan 2023). Premusz ve arkadaşlarının 2024'te Macaristan 'da yapmış oldukları" Kadınların Üreme Sistemleri Hakkındaki Bilgilerinin Belirleyicileri Olarak Sosyo-Ekonomik ve Sağlık Okuryazarlığı Eşitsizlikleri: Kesitsel Bir Çalışma" adlı çalışmalarında Kadınların üreme sistemleri ve sağlık okuryazarlık düzeylerinde eşitsizlikler bulundu ve gebe kalma olasılığının en yüksek olduğu yaşta bilginin anlamlı olarak en düşük olduğu görüldü. Bu nedenle, hedeflenen eğitime ek olarak sağlık okuryazarlık düzeylerinin de iyileştirilmesi gerektiği vurulandı (Premusz ve ark 2024). Harsch ve arkadaşlarının 2021 yılında yapmış oldukları " Afganistan Gazni 'deki kadınlar arasında sağlık okuryazarlığı ve sağlık davranışları " adlı çalışmalarında kadınların sağlık okuryazarlığı diğer Asya ülkeleriyle karşılaştırıldığında oldukça düşük bulunduğu aynı zamanda yaş eğitimle bağlantılı olduğu tespit edilmiştir. Çalışma sağlık okuryazarlığının bir halk sağlığı sorunu olarak kabul edilmesinin Afganistan ve krizlerden etkilenen diğer düşük gelirli ülkelerde ele alınması çağrısında bulunmaktadır (Harsch ve ark 2021). Leila ve arkadaşlarının 2020'de yapmış olduğu "Sağlık merkezlerine bağlı gebelerde gebelik döneminde sağlık okuryazarlığı düzeyinin bakım kalitesinin iyileştirilmesine etkisinin araştırılması" adlı çalışmalarında gebe kadınlarda sağlık okuryazarlığı puanı ortalamasının sınır aralıkta olduğunu görülmüştür. Sağlık okuryazarlığı yüksek olan kişiler diğer kadınlara göre anlamlı derecede daha fazla doğum öncesi danışmanlık almış ve planlı gebelik yaşamıştır . Gebe kadınlarda sağlık okuryazarlığı düzeyi olumsuzdur. Toplumdaki kadınlarda yüksek sağlık okuryazarlığı düzeyinin gebelik bakımının kalitesinin artmasına yol açabileceği göz önüne alındığında, kadınlarda sağlık okuryazarlığını artırmak için sağlık hizmeti sağlayıcıları tarafından toplumda düzenli eğitimlere daha fazla dikkat edilmesi önerilir şeklinde vurgulanmıştır (Leila ve ark 2020). Sonuç olarak kadınlarda sağlık okuryazarlık düzeylerinin yeterli olmadığı çeşitli vasıtalarla desteklenerek iyileştirilmesi gerçeği ortaya çıkmaktadır.

Halk sağlığı hemşireliği açısından kadın sağlığı ve sağlık okuryazarlığı ilişkisinin önemi ele alındığında hizmetler ağırlıklı olarak koruyucu ve sağlığı geliştirici biçimde ekip anlayışı ile yürütülmelidir. Bu çerçevede halk sağlığı hemşiresinin vazgeçilmez rolü vardır. Bu süreçte kadın çevresiyle bir bütün olarak ele alınmalıdır. Sahip oldukları sosyoekonomik ,kültürel yapıları göz önünde bulundurulmalıdır. Karşılıklı güven sağlanarak gerekli danışmanlık sağlanmalıdır (Erci 2020).

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SLEEP QUALITY AND AFFECTING FACTORS IN MENTAL ILLNESSES

ABSTRACT

PURPOSE: The purpose of this review is to examine sleep quality and affecting factors in mental illnesses.

RESULTS: Sleep quality is defined by factors such as sleep depth, duration, efficiency after waking up, vitality and general well-being. The concept of sleep quality is frequently used in sleep studies and provides effective benefits in distinguishing the differences between good and bad sleep. Good sleep allows the individual to remain energetic and perform high throughout the day, while also helping them feel mentally and psychologically comfortable. On the other hand, poor sleep quality can bring about problems such as sleepiness and daytime sleepiness. This situation can create negative effects such as difficulty in concentrating, decreased perception and impaired cognitive functions in individuals, leading to a decrease in general functionality. When the factors affecting sleep quality in mental illnesses are examined; it is stated that depressive symptoms, anxiety symptoms, psychotic features, high neuroticism level, impulsivity, history of suicide attempt, stress experienced in the last 6 months, childhood trauma exposure and anticonvulsant drug use reduce sleep quality. It is also emphasized that the eating habits and intestinal microbiota of individuals with mental illnesses also affect sleep quality.

CONCLUSION: As a result, sleep quality is seen as an important factor affecting the functionality of individuals with mental illness. For this reason, nurses should evaluate sleep quality while providing care to individuals with mental illness, identify factors affecting sleep quality, and take initiatives to increase sleep quality, which can contribute to the increase in nursing care.

Keywords: Mental Illness, Psychiatric Nursing, Sleep Quality

RUHSAL HASTALIKLARDA UYKU KALİTESİ VE ETKİLEYEN FAKTÖRLER

ÖZET

AMAÇ: Bu derlemenin amacı ruhsal hastalıklarda uyku kalitesi ve etkileyen faktörleri irdelemektir.

BULGULAR: Uyku kalitesi; uykunun derinliği, süresi, uyandıktan sonraki verimlilik, zindelik ve genel iyilik hali gibi unsurlarla tanımlanmaktadır. Uyku kalitesi kavramı, uyku araştırmalarında sıkça kullanılmakta ve iyi ile kötü uyku arasındaki farkları ayırt etmede etkin fayda sağlamaktadır. İyi uyku, bireyin gün boyunca enerjik kalmasını ve yüksek performans göstermesini sağlarken, aynı zamanda zihinsel ve psikolojik açıdan da rahat hissetmesine yardımcı olmaktadır. Öte yandan, kötü uyku kalitesi, uykululuk hali ve gündüz uyuklama gibi sorunları beraberinde getirebilir. Bu durum, bireylerde dikkat toplamada zorluk, algılamada azalma ve bilişsel işlevlerde bozulma gibi olumsuz etkiler yaratarak genel işlevsllikte bir düşüşe yol açabilir. Ruhsal hastalıklarda uyku kalitesini etkileyen faktörler incelendiğinde; depresif belirtiler, anksiyete belirtileri, psikotik özellikler, yüksek nörotiklik düzeyi, dürtüsellik, suisid girişimi öyküsü, son 6 ay içinde yaşanan stresler, çocukluk çağı travma maruziyeti ve antikonvülzan ilaç kullanımının uyku kalitesini düşürdüğü belirtilmektedir. Ayrıca ruhsal hastalığı olan bireylerin beslenme alışkanlıkları ve bağırsak mikrobiyotasının da uyku kalitesi üzerinde etkisi olduğu vurgulanmaktadır.

SONUÇ: Sonuç olarak ruhsal bozukluklarda uyku kalitesi ruhsal hastalığı olan bireylerin işlevselliğini etkileyen önemli bir etmen olarak görülmektedir. Bu sebeple hemşirelerin ruhsal hastalığı olan bireylere bakım verirken uyku kalitesini değerlendirmeleri, uyku kalitesini etkileyen faktörleri tespit etmeli, uyku kalitesini arttırmaya yönelik girişimlerde bulunmaları hemşirelik bakımının artmasına katkı sağlayabilir.

Anahtar Kelimeler: Psikiyatri Hemşireliği, Ruhsal Hastalık, Uyku Kalitesi

GİRİŞ

Uyku, temel insan gereksinimlerinden olan solunum, yeme, içme ve boşaltım kadar önemli bir fizyolojik gereksinim olarak kabul görmektedir. Uyku bireyi stres ve sorumluluklardan soyutlayarak rahatlatan, ruhsal ve fiziksel yönden dinlendiren, organizma için koruyucu, yenileyici ve toparlayıcı, sağlıklı ve uzun bir yaşam için gerekli olan bir süreç olarak tanımlanır (11). Uyku, iki ana evreden oluşmaktadır. Uykunun İlk evresi, yavaş göz hareketlerinin gözlendiği Non-REM (hızlı olmayan göz hareketi) evresi olarak ifade edilmektedir. İkinci evresi ise, göz hareketlerinin yoğun olduğu REM (hızlı göz hareketi) evresidir. Uykunun Non-REM evresi, dört aşamadan oluşmaktadır. İlk aşama, tam bir uyku hali değildir ve kişi bu evrede uyanıklık hissi yaşayabilir. İkinci aşamada ise, kişi birinci evreye göre daha derin bir uykuya dalmaktadır. Üçüncü aşamada, derin uykuya geçiş gözlemlenir. Dördüncü aşamada ise, derin uyku daha da artmaktadır ki; bu evrede kişinin kan basıncı, solunumu ve nabzı normalin altına düşer, kaslar gevşer ve kişi dinlenme aşamasına geçer. Bu aşamanın uzun sürmesi, bireyin genel sağlığı üzerinde olumlu bir etki sağlayabilmektedir (4).

Uyku kalitesi, bireyin verimli bir uyku sonrası tatmin içinde uyanması olarak tanımlanabilir. İyi bir uyku, kişinin gün boyunca uyanık kalmasını ve yüksek performans sergilemesini sağlarken, aynı zamanda zihinsel ve psikolojik olarak da rahat hissetmesine katkıda bulunabilmektedir. Kısa uyku süreleri ve verimsiz uyku, düşük uyku kalitesinin belirtilerindendir. Uyku sorunları yaşayan bireyler, gün içinde sık sık uykuya dalma eğiliminde olabilirler; bu da işlevsellikte düşmeye yol açabilir (2). Uyku kalitesindeki azalmalar, bireylerin sağlığını olumsuz yönde etkilerken, toplumsal düzeyde iş gücü kaybı gibi sonuçlar doğurabilmektedir (12). Uyku kalitesi, fizyolojik faktörlerden (yaş, sirkadiyen ritim, beden kitle indeksi, non-rem, rem), psikolojik faktörlerden (stres, anksiyete, depresyon) ve çevresel faktörlerden (oda sıcaklığı, teknolojik alet kullanımı) etkilenebilmektedir. İyi bir uyku kalitesi, bireyin olumlu davranışlar sergilemesine yardımcı olurken, kötü uyku kalitesi olumsuz davranışlara yol açabilmektedir (19).

Uyku kalitesinin, ruhsal hastalığı olan bireylerde duygusal durumunun düzenlenmesiyle yakından ilişkili olduğu bilinmektedir. Ruhsal hastalıkların çoğunda, uykunun hem niteliğinde hem de niceliğinde yaşanan bozulmalar yaygın şikayetler arasında yer alabilmektedir. Özellikle depresyon, şizofreni, madde kullanım bozukluğu, bipolar bozukluk ve anksiyete bozuklukları gibi birçok ruhsal hastalık, uyku problemleri ile birlikte görülebilir ve bu durum hastalığın seyrini etkileyebilir (11).

Psikiyatri kliniklerinde iyi bir uykunun sağlanmasında uyku hijyeninin önemi dikkat çekmektedir. Bu bağlamda, sigara, çay ve kahve gibi uyarıcı maddelerin kısıtlanması gibi bazı önlemler alınsa da sirkadiyen sistem üzerinde etkili olan gün ışığına erişmede sınırlılık ve çevresel gürültüler uyku kalitesini olumsuz yönde etkileyebilmektedir. (8).

Ruhsal hastalığa sahip bireylerin uyku kalitesi, hastaların hastalığa uyumunu ve tedavi sürecine katılımını doğrudan etkilediği için büyük öneme sahiptir. Terapötik bir ortamın oluşturulması ve sürdürülmesi, psikiyatri hemşiresinin temel görevlerinden biri olarak belirtilmektedir. Psikiyatri hemşiresi, uyku düzeninin sağlanması için yapılandırılmış bir ortam oluşturarak üzerine düşen bu rolü yerine getirebilir. Yapılandırılmış ortam, hastaların gündüz yatak kıyafetleriyle dolaşmamalarını, gündüz uyumamalarını, akşam yemeğinden sonra belirli bir saatte yatmalarını ve sabah belirli bir saatte kalkmalarını sağlamayı içermektedir. Ayrıca hemşireler, gece akut dönemler dışında (örneğin madde bağımlılığı gibi durumlarda) vital bulguların alınmaması, odaların kapılarının camlı olması veya odalarda

kamera bulunması durumunda hemşirenin gerektiğinde camdan veya kameradan hasta takibi yapması gibi uygulamalarla ruhsal, fiziksel ve psikolojik uyku düzenlerinin sağlanmasına katkıda bulunabilir (14).

Ruhsal hastalıklarda uykuyu etkileyen risk faktörleri belirlenmiş olmalı ve bu risk faktörlerinin kuruma uygunluğu düşünülerek hizmet sunumu planlanmalıdır. Her psikiyatrik tanıya göre uyku kalitesi farklı düzeyde etkilenebilmektedir. Var olan her tanının uyku yapısındaki bozulmasını çözmek amacıyla, vaka-kontrol, kohort, deneysel araştırmalar gibi daha detaylı çalışmaların yapılmasına ihtiyaç olduğu görülmektedir. (20).

GELİŞME

Ruhsal Hastalıklarda Uyku Kalitesi

Uyku kalitesi psikotik durumların ortaya çıkmasında ve sürdürülmesinde nedensel bir role sahiptir ayrıca ruhsal hastalıklar ile iki yönlü ilişkiler göstermektedir. Uyku kalitesinde yaşanan bozulma, psikotik durumları da içeren psikopatolojik durumlarda en sık görülen şikayetler arasında yer almaktadır (26). Uyku kalitesi ve ruh sağlığı arasındaki ilişki uzun süredir incelenmektedir. Elde edilen veriler ruhsal hastalıklarla uyku kalitesinin ilişkili olduğunu doğrulamaktadır (16,21).

Uyku kalitesi bipolar bozukluk (27), depresyon, anksiyete bozuklukları (1) ve psikoz (22) gibi ruh sağlığı bozukluğu teşhisi konan hastalarda düşük saptanmaktadır (7). Düşük uyku kalitesinin anksiyete, depresyon (1), değişen bilişsel işlev (6) ve dikkat eksikliği / hiperaktivite bozukluğu (15) gibi ruhsal hastalıklarla ilişkili olduğu bulunmuştur. Kötü uyku kalitesi ile depresyon ve anksiyete arasında bazı mekanizmaların olduğu tespit edilmiştir. Örneğin, kortikolimbik devre, duygusal reaktivite ve düzenlemedeki zorluklarla ilgili düşük uyku kalitesinden etkileniyor gibi görünmektedir (3).

Meule ve arkadaşları (2023) tarafından Almanya'da Temmuz 2014- Eylül 2020 tarihleri arasında 11.226 hasta ile yapılan gözlemsel bir çalışmada ruhsal hastalığa sahip 10 farklı hasta grubunun, hastaneye yatıştan taburculuğa kadar uyku kalitesi incelenmiş. Tüm tanı gruplarında uyku kalitesinde bozulma görülmüş. Travma ile ilişkili bozukluğu olan hastaların en düşük, obsesif kompulsif bozukluğu olan hastaların ise en yüksek uyku kalitesine sahip olduğu saptanmıştır (17).

Scott ve arkadaşlarının (2021) yayınladığı çalışmada uyku kalitesinin arttırılması depresyon ve anksiyete üzerinde orta büyüklükte olumlu etki, stres üzerinde küçük-orta ölçekli olumlu etki ve son olarak pozitif psikoz semptomları üzerinde küçük olumlu etkiler oluşturmuştur (25).

Ruhsal Hastalıklarda Uyku Kalitesini Etkileyen Faktörler

Psikiyatri servislerinde hastalara yönelik düzenli güvenlik kontrolü, rahatsız edici ışık ve gürültü gibi çevresel faktörlerin uyku kalitesini olumsuz etkileyebileceği bildirilmektedir (29). Bu faktörlerin yanı sıra uyarıcı ve ilgi çekici aktivite eksikliği, hapsedilme hissi ve ilaç tedavisi gibi zorunlu bakım da uyku kalitesinde aynı olumsuz etkiye sebep olabilir (10).

Saunders ve arkadaşları (2013) bipolar bozuklukta uyku kalitesini etkileyen sosyodemografik ve klinik özellikleri araştırılmış. Ötimik bipolar hastalarda uyku kalitesi; depresif belirtiler, anksiyete belirtileri, psikotik özellikler, yüksek nörotiklik düzeyi,

dürtüsellik, suisid girişimi öyküsü, son 6 ay içinde yaşanan stresler, çocukluk çağı travma maruziyeti ve antikonvülzan ilaç kullanımı ile ilişkili bulunmuştur (24).

Wagner-Skacel ve arkadaşları (2020) yayınladıkları çalışmada psikiyatri hastalarının beslenme alışkanlıkları ve bağırsak mikrobiyotasının uyku kalitesi üzerinde etkisi olduğu vurgulanmış. Ayrıca yeme alışkanlıklarının da uyku kalitesini çift yönlü olarak etkileyebileceği saptanmıştır (30).

Müller ve arkadaşlarının (2016) yayınladıkları çalışmada şizofreni spektrum bozuklukları, madde kullanım bozuklukları, anksiyete/depresif bozuklukları olan 18-65 yaş arası hastalarda, hastaneye yatış sonunda subjektif uyku kalitesi ve ortalama uyku süresi araştırılmış. Subjektif uyku kalitesi uyku süresi ile anlamlı olarak ilişkili bulunmuş ancak yaş, cinsiyet veya tanısal alt grup ile anlamlı bir ilişki bulunmamış (18).

Ruhsal Hastalıklarda Uyku Kalitesini Arttırmaya Yönelik Hemşirelik Müdahaleleri

Psikiyatri servisinde hemşirelerin ruhsal bozukluğa sahip hastalara yönelik uyku hijyeni eğitimi ve çevresel düzenlemeleri içeren müdahalelerinin, uyku kalitesini anlamlı şekilde arttırdığı gözlemlenmektedir (28). Aynı şekilde hemşirelerin hastalar ile olumlu ilişkiler kurmaları, çevresel stresörleri azaltmaları ve motivasyon teknikleri kullanmaları, hastalarda uyku kalitesini olumlu etkilemektedir (5).

Yıldırım Üşenmez ve Kavak Budak'ın (2024) yayınladığı çalışma şizofreni tanılı bireylerde nefes ve gevşeme egzersizleri eğitiminin psikolojik iyi oluş ve uyku kalitesi üzerine etkisini belirlemek amacıyla yapılmış. Çalışmaya şizofreni tanısı almış 64 birey (deney grubunda 31 ve kontrol grubunda 33) katılmış. Deney grubundaki bireylere grup eğitimi şeklinde 6 seans nefes ve gevşeme egzersizleri eğitimi verilmiş, kontrol grubundaki bireylere ise herhangi bir eğitim uygulanmamış. Deney grubundaki bireylerin nefes ve gevşeme egzersiz eğitimi sonrası psikolojik iyi oluş toplam puan ortalamasının arttığı, uyku kalitesi toplam puan ortalamasının ise azaldığı belirlenmiş. Sonuç olarak şizofreni tanılı bireylerde nefes ve gevşeme egzersizleri eğitimi, psikolojik iyi oluş ve uyku kalitesini arttırmada etkili bir müdahale olarak kullanılabilir ve hemşirelik bakım planına entegre edilebilir (31).

Uğurlu ve arkadaşlarının (2018) psikiyatri servisinde yatan 51 hasta ile yaptığı çalışmaya göre; uyku kalitesi düşük hastaların uyku kalitesini arttırmak için eğitimler verildi. Eğitimde uykuyu bozan alışkanlıklar, uyku düzenindeki değişiklikler, uyku ve rahatlama konuları yer aldı. Katılımcılara müzik terapisi, kitap okuma, ılık duş alma, ılık süt içme, sohbet etme ve televizyon izleme gibi müdahaleler hakkında bilgi verildi. Eğitim sonunda hastaların uyku kalitesinde iyileşme gözlenmiştir (28).

Samadi ve arkadaşlarının (2021) yapmış olduğu çalışmada majör depresyonlu hastalarda lavanta uçucu yağı ile aromaterapinin uyku kalitesi üzerine etkisi incelenmiş. Uyku bozukluğu olan seksen majör depresif hasta deney ve kontrol grubu olarak ikiye ayrılmış. Deney grubuna lavanta yağı kontrol grubuna ise plasebo olarak badem yağı solutulmuş. Girişim sonrası katılımcıların uyku kalitesi ölçüldüğünde deney grubunun uyku kalitesi kontrol grubuna göre daha yüksek bulunmuştur (23).

İçel ve Başoğlu'nun (2021) yapmış olduğu çalışmada Toplum Ruh Sağlığı Merkezi'ne kayıtlı olan ve haftanın belirli günlerinde merkeze devam eden kronik psikiyatri hastalarının ilerleyici kas gevşetme eğitimi ve müzik terapisinin öfke düzeyi ve uyku kalitesi üzerine etkileri incelenmiş. 3 ay boyunca haftada 2 seans olmak üzere 24 seanslık bir program

uygulanmış. Bu programda deney grubuna ilk 15 dakika progresif kas gevşetme teknikleri kullanılarak egzersiz yaptırılmış ardından 45 dakika boyunca müzik terapisi uygulanmış. Yapılan müdahalenin uyku kalitesini iyileştirmede etkili olduğu ortaya konmuştur (9).

Örsal ve arkadaşları (2019) ise psikiyatri servisinde yatan hastalarda müzik terapisi ve gevşeme eğitiminin uyku kalitesi üzerine etkilerini incelemiş ve uyku kalitesi puanları üzerinde herhangi bir etkisi olmadığını bulmuşlardır (20).

Korkmaz Aslan ve Ekinci'nin (2022) yapmış olduğu çalışmada şizofreni hastalarında yapılandırılmış egzersiz programının yaşam ve uyku kalitesine etkisi incelenmiş. Örneklemi basit rasgele örnekleme yöntemi ile belirlenmiş olup, 30'u araştırma, 31'i kontrol grubu olmak üzere toplam 61 hasta çalışmaya dâhil edilmiş. Şizofreni hastalarına uygulanan yapılandırılmış egzersizin yaşam ve uyku kalitesini artırdığı belirlenmiş (13).

SONUÇ

Ruhsal hastalığa sahip bireylerin uyku kalitesi, hastaların hastalığa uyumunu ve tedavi sürecine katılımını doğrudan etkilediği için büyük öneme sahiptir. Terapötik bir ortamın oluşturulması ve sürdürülmesi, psikiyatri hemşiresinin temel görevlerinden biri olarak belirtilmektedir. Psikiyatri hemşiresi, uyku düzeninin sağlanması için yapılandırılmış bir ortam oluşturarak üzerine düşen bu rolü yerine getirebilir.

Ayrıca, ruhsal hastalıklarda uyku kalitesini etkileyen risk faktörleri belirlenmiş olmalı ve bu risk faktörlerinin kuruma uygunluğu düşünülerek hizmet sunumu planlanmalıdır. Her psikiyatrik tanıya göre uyku kalitesi farklı düzeyde etkilenebilmektedir. Var olan her tanının uyku yapısındaki bozulmasını çözmek amacıyla, vaka-kontrol, kohort, deneysel araştırmalar gibi daha detaylı çalışmaların yapılmasına ihtiyaç olduğu görülmektedir. (20).

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ISOLATED CORONARY SINUS ATRESIA WİTH DIRECT DRAINAGE OF CARDIAC VEINS INTO THE LEFT ATRIUM: A RARE ANATOMICAL VARIANT IDENTIFIED BY CARDIAC CT

ABSTRACT

Objective

Coronary sinus (CS) atresia is a rare congenital anomaly, often associated with other cardiac abnormalities. Isolated CS atresia is extremely uncommon and is usually detected incidentally. In this report, we present a case of isolated CS atresia with abnormal drainage of cardiac veins into the left atrium, evaluated through advanced imaging findings.

Methods

A thirty-nine-year-old male patient presented to our hospital with intermittent chest pain. Transthoracic echocardiography revealed normal cardiac chamber sizes and valve structures. Pulmonary artery pressure was measured as 25 mmHg. Coronary CT angiography showed no coronary artery pathology, but a phase discrepancy and venous structures were noted in the posterior left atrium. Further evaluation demonstrated direct drainage of the posterior interventricular vein, great cardiac vein, and left marginal vein into the left atrium, along with an atretic coronary sinus. No associated congenital anomalies such as persistent left superior vena cava (PLSVC) or atrial septal defect were observed.

Results

On multi-slice CT and 3D volumetric imaging, the CS ostium was not visualized. Cardiac veins were shown to drain into the left atrium through separate ostia. This condition has been reported in only one previous case in the literature. In our case, the independent drainage of coronary veins into the left atrium represents a noteworthy and rare anatomical variant.

Conclusion

Isolated CS atresia is often asymptomatic but may pose significant anatomical challenges during electrophysiological procedures and pacemaker lead placement. Cardiac CT and MRI are reliable imaging modalities for detecting such congenital variants and provide crucial information for interventional planning.

Keywords: Coronary sinus, atresia, left atrium, cardiac veins, CT angiography, congenital anomaly

KORONER SİNÜS ATREZİSİNE BAĞLI SOL ATRİYUMA KARDİYAK VEN DRENAJI: KARDİYAK BT İLE TANIMLANAN NADİR BİR ANATOMİK VARYANT

ÖZET

Amaç

Koroner sinüs (CS) atrezisi nadir görülen konjenital bir anomalidir ve genellikle başka kalp anomalileri ile birliktelik gösterir. İzole CS atrezisi ise oldukça enderdir ve çoğunlukla tesadüfen saptanır. Bu çalışmada, göğüs ağrısı şikayeti ile başvuran bir hastada saptanan izole CS atrezisi ve kardiyak venlerin sol atriyuma anormal drenajı sunulmuş, görüntüleme bulguları eşliğinde değerlendirilmiştir.

Materyal ve Yöntem

Otuz dokuz yaşında erkek hasta, ara ara gelişen göğüs ağrısı nedeniyle hastanemize başvurdu. Yapılan transtorasik ekokardiyografide kalp boşlukları ve kapak yapıları normal olarak değerlendirildi. Pulmoner arter basıncı 25 mmHg ölçüldü. Koroner BT anjiyografi çekiminde koroner arterlerde patoloji saptanmazken, sol atriyum içinde belirgin faz farkı ve posterior yerleşimli venöz yapılar dikkat çekti. İleri değerlendirmede, posterior interventriküler ven, büyük kardiyak ven ve sol marjinal venin doğrudan sol atriyuma drene olduğu ve koroner sinüsün atrezik olduğu belirlendi. Persistent sol superior vena cava (PLSVC) veya atriyal septal defekt gibi eşlik eden diğer konjenital anomalilere rastlanmadı.

Bulgular

Çok kesitli BT ve 3D volumetrik görüntülerde CS ostiyumu izlenemedi. Koroner venlerin sol atriyuma ayrı ostiyumlarla döküldüğü gösterildi. Bu durum literatürde yalnızca bir olguda benzer şekilde tanımlanmıştır. Bizim vakamızda, koroner venlerin doğrudan ve ayrı açıklıklarla sol atriyuma drenajı bu nadir varyant açısından dikkat çekicidir.

Sonuç

İzole CS atrezisi genellikle asemptomatik seyretse de, özellikle elektrofizyolojik girişimler ve kalıcı pacing sistemlerinin yerleştirilmesinde önemli anatomik zorluklara neden olabilir. Kardiyak BT ve MRG, bu tür konjenital varyantların saptanmasında güvenilir yöntemlerdir ve girişimsel planlama açısından kritik rol oynar.

Anahtar Kelimeler: Koroner sinüs, atrezisi, sol atriyum, kardiyak ven, BT anjiyografi, konjenital anomali

Giriş

Kardiyak venöz kanın büyük bir kısmı koroner sinüs (CS) ve kolları yoluyla sağ atriyuma geri döner. Gerçek anatomik CS, sol atriyumun oblik veni (Marshall veni) ile büyük kalp veninin birleştiği yerde Vieussens valfinden sağ atriyumdaki CS ostiyumuna kadar uzanan kısa bir venöz gövde olarak tanımlanır. CS ostiumu, vena kava inferior ile alt triküspit kapak arasında yer alır. Çoğu zaman açıklık, CS valfi veya Thebesian valfi olarak adlandırılan, sağ sinüs valfinin embriyolojik bir kalıntısı olan endokardiyal doku kıvrımı tarafından korunur [1].

Materyal Metod

Koroner BT Anjiyografi (CCTA) Protokolü

Kliniğimizde rutin olarak gerçekleştirilen koroner BT anjiyografi (CCTA) işlemleri, yüksek teknolojili çift kaynaklı (dual-source) BT cihazı ile yapılmaktadır. Bu cihaz, 128 × 2 kesitli dedektör yapısına ve birbirine 95 derecelik açıyla yerleştirilmiş iki X-ışını tüpüne sahiptir (Somatom Definition Flash, Siemens Healthcare, Almanya). Bu teknik yapı sayesinde yüksek zamansal çözünürlük elde edilmekte, özellikle kalp gibi hareketli organların değerlendirilmesinde artefaktlar minimize edilmektedir.

İnceleme öncesinde, hastanın kalsiyum skorlaması (Ca skoru) yapılmaktadır. Bu amaçla, Agatston skorlamasına uygun şekilde, kontrastsız olarak 3 mm kesit kalınlığında görüntüler alınır. Bu çekimler, standart prospektif EKG tetiklemeli bir protokol ile ve 120 kVp tüp voltajı kullanılarak gerçekleştirilir. Bu aşamada hem kalp damarlarında kalsifikasyon olup olmadığı belirlenmekte, hem de geniş bir görüş alanı (FOV) ile toraksın tamamını kapsayan detaylı kesitsel görüntüler elde edilmektedir. Böylece sadece kardiyak yapılar değil, aynı zamanda akciğerler, mediasten ve plevra gibi ekstrakardiyak alanlarda da önemli bulgular saptanabilmektedir.

Bu ilk görüntüleme aşamasının ardından, hastaya intravenöz iyot bazlı kontrast madde uygulanarak CCTA işlemi gerçekleştirilir. Kontrast madde enjeksiyonu trifazik bir protokolle yapılmaktadır:

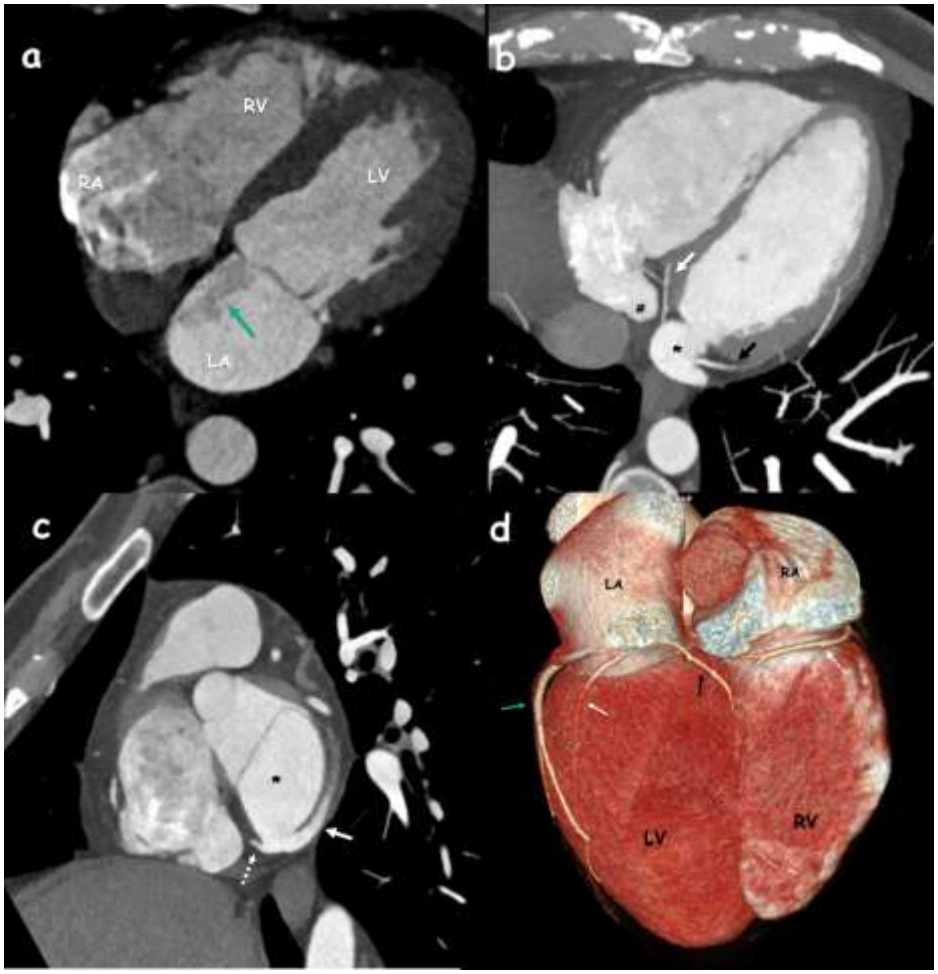
1. İlk fazda saf kontrast madde,
2. İkinci fazda kontrast-saline karışımı,
3. Üçüncü fazda ise saf serum fizyolojik uygulanmaktadır. Bu yaklaşım, optimal damar opasifikasyonu sağlamakta ve artefaktları azaltmaktadır.

Tarama alanı, ilk elde edilen kalsiyum skoru görüntüleri temel alınarak belirlenir ve karina düzeyinden başlayarak kalbin diyafragmatik yüzeyine kadar uzanır. Böylece tüm koroner arter ağacı optimal düzeyde görüntülenmiş olur.

Bu çalışmaya dâhil edilen tüm hastalar, yukarıda tanımlanan standart CCTA protokolüne göre görüntülenmiş olup, radyolojik veriler elektronik veri kayıt sisteminden retrospektif olarak analiz edilmiştir. Olgu için BT görüntüleri hem aksiyel hem de multiplanar reformats (MPR) ve 3 boyutlu hacimsel rekonstrüksiyonlarla değerlendirildi.

Olgu Sunumu

39 yaş erkek hasta ara ara meydana gelen göğüs ağrısı nedeniyle hastanemize başvurdu. Yapılan ekokardiyografide tüm kalp boşlukları normal genişlikte, duvar kalınlıkları ve hareketleri normal olup eser triküspit yetersizliği tespit edildi. tra üzerinden alınan pabS: 25 mmHg, diğer kapak yapı ve akımlar normal, interventriküler ve interatrial septum intakt olarak değerlendirildi. Çekilen koroner arter bt anjiyografide koroner arterler normaldi. Çıkım veya seyir anomalisi yoktu. Çıkan aort çapı 25 mm, pulmoner trunkus çapı 26 mm ölçüldü ve pulmoner hipertansiyon lehine değerlendirildi. Sol atriyum içerisinde özellikle posteriorda heterojenite ve faz farkı dikkati çekmekteydi. Ancak interatrial septumda defekt izlenmedi. Hastada koroner sinüsün (CS) atrezik olduğu ve sol atriyuma posteriordan dökülen posterior interventriküler ven, major sol kardiak ven ve sol marjinal ven mevcuttu. Hastada CS atrezisine eşlik eden persistent left superior vena cava (PLSVC) gibi herhangi bir vasküler patoloji saptanmadı. Tanı izole CS atrezisi ve kardiyak venlerin sol atriyuma anormal drenajı olarak kondu (Figür 1).



Figür 1. a: Sol atriyum içinde koroner venöz dönüşe sekonder heterojenite (ok), b: middle kardiyak vein (beyaz ok) ve left marjinal vein (siyah ok) in sol atritum (*) bağlantısı ve oblitere koroner sinüs (#) görülüyor, c: great cardiac vein (beyaz ok) ve orta kardiyak venin (kesikli ok) sol atriyuma (*) dökümü kısa aks görüntüler, d: 3D volum rendering görüntülerdekoroner sinüs atrezisi, kardiyak venlerin sol atriyuma (renkli oklar) drenajı izleniyor.

Tartışma

Literatürde izole CS atrezisi, venöz drenaj yolları ve bu durumlarla ilişkilendirilmiş durumlar tanımlanmıştır. Chen ve ekibi [2] tarafından rapor edilen bir vakada, geniş koroner fistül nedeniyle tüm koroner venöz drenajın sağ pulmoner artere PLSVC aracılığıyla döküldüğü rapor edilmiştiir. Foale ve ark. [3], izole CS atrezisi vakasında kardiyak venlerin sol ve sağ atriyuma ayrı ayrı drene olduğunu rapor etmişlerdir. Rao ve meslektaşları [4] ise izole CS atrezisi ve sol ventriküle kardiyak venöz drenajın çoklu koroner-kameral fistül bağlantıları ile gerçekleştiği bir hastayı raporlamışlardır. Ayrıca literatürde CS atrezisi ile pulmoner artere kardiyak venlerin drene olduğu [5], PLSVC, Scimitar sendromu, ASD ile birlikte CS atrezisinin bir arada bulunduğu [6,7] vakalar bildirilmiştir. Yolcu ve ekibi [8], CS atrezisi ve koronokameral fistül birleşen 2 vaka raporlamışlardır. Özge ve meslektaşları [9] ise yenidoğan bir bebekte hipoplastik sol kalp sendromu ve CS atrezisi olan venöz drenajın PLSVC aracılığıyla sağ atriuma döküldüğü bir durumu rapor etmişlerdir. Bizim vakamızda ise CS atrezisi ve kardiyak venlerin sol atriyuma drenajı mevcut olup literaturde yalnızca bir vaka raporunda 58 yaşındaki aralıklı göğüs ile başvuran kadın hastada tanımlanmıştır [10]. Ancak bizim vakamızda koroner venler sol atriyuma ayrı ostiumlar ile dökülmekte olup bu açıdan ilktir.

Sonuç

İzole koroner sinüs atrezisi klinik ve fizyolojik olarak büyük bir sorun oluşturmaz; ancak aritmileri teşhis ve tedavi edebilmek için genellikle çeşitli teşhis ve haritalama manevraları CS aracılığıyla gerçekleştirilir. LV elektrot teli yerleştirmedeki başarısızlık bazen kateterlerin CS'ye yerleştirilememesiyle ilişkilendirilir [1]. Bu nedenle, CS'nin kesin bir tanımı ve anormallik yelpazesinin tanınması, bu prosedürlerin güvenli ve başarılı sonucunu sağlamak için çok önemlidir. Kardiyak BT ve kardiyak MRG, CS'nin anatomisini tanımlamada güçlü görüntüleme yöntemleri olarak ortaya çıkmıştır. Kardiyak BT ve MRG, boyutu ve komşu yapılarla ilişkisi de dahil olmak üzere CS'nin kesin morfolojisini değerlendirme yeteneğine sahiptir. Her iki yöntem de CS'ye erişen girişimsel kardiyologlara ve cerrahlara değerli tanı ve yönetim bilgileri sağlar [11].

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SPONTANEOUS SUBCUTANEOUS EMPHYSEMA IN A COPD PATIENT: A CLINICAL NURSING CASE REPORT

ABSTRACT

Aim: This study aims to present the nursing monitoring process and care approaches in an intensive care unit (ICU) patient diagnosed with chronic obstructive pulmonary disease (COPD) who developed spontaneous subcutaneous emphysema during hospitalization.

Method: This study was designed as a case report. Based on this case's clinical course and nursing follow-up, a nursing care algorithm for managing subcutaneous emphysema was developed.

Result: A 78-year-old male patient with a history of COPD was admitted to the ICU due to respiratory distress. During hospitalization, spontaneous subcutaneous emphysema was detected, characterized by swelling in the neck and chest areas and palpable crepitus under the skin. Nursing monitoring included frequent assessment of vital signs, oxygen saturation, respiratory effort, and the extent of subcutaneous air spread. Nursing interventions were implemented, such as positioning the patient in a Semi-Fowler's position, optimizing oxygen therapy, and monitoring peripheral circulation.

Conclusion: Subcutaneous emphysema, although rare, can pose significant risks in COPD patients. Early recognition and systematic nursing interventions are vital for preventing potential complications. Training ICU nurses on early detection protocols for subcutaneous emphysema could significantly enhance patient outcomes and safety. The nursing care algorithm developed based on the presented case is intended to serve as a practical guide for nursing management of similar patients with subcutaneous emphysema.

Keywords: Subcutaneous Emphysema, Nursing Care, Intensive Care Unit

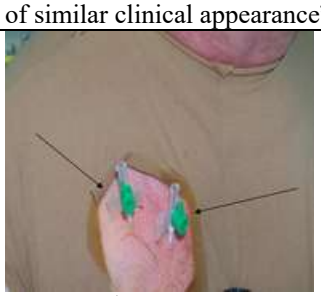
Introduction

Subcutaneous emphysema is when air enters the tissues and soft tissues under the skin. It usually occurs in the soft tissues of the chest wall or neck, but can also occur in other parts of the body[1, 2]. It can occur spontaneously or as a complication of trauma, pneumothorax, infection, malignancy or surgical procedures [2-4]. The prevalence of subcutaneous emphysema is between 0.43% and 2.34%. The most common and visible symptom is swelling around the neck with pain in the chest. Other symptoms include tender sore throat, neck pain, difficulty swallowing, shortness of breath, wheezing and bloating [2, 5]. If it involves deeper tissues of the chest and abdominal wall, it becomes a serious, stressful and life-threatening condition. It can be complicated by restriction of full lung reexpansion and can lead to high airway pressure, severe respiratory acidosis and ventilatory failure [5, 6].

The Case

A 78-year-old male patient with a history of COPD was admitted to the emergency department. He was admitted to the chest intensive care unit due to respiratory distress. During hospitalization, spontaneous subcutaneous emphysema characterized by swelling in the neck and chest regions and palpable crepitus under the skin was detected. In the table below, all the findings and applications seen in the patient are shown according to the stages.

Algorithm Step	Visual	Explanation
1. CAA is considered if subcutaneous swelling and 'snow crunch' (crepistation) is felt on palpation[7, 8].		It is the main physical examination finding for the diagnosis of subcutaneous emphysema after trauma or in a patient with a chest tube.
2. Vital signs, state of consciousness and respiration are assessed[9, 10].		Regular monitoring is recommended due to the risk of hypoxemia and respiratory distress.
3. Oxygen supplementation is initiated if oxygen saturation is < 92%[10, 11].		92% is frequently used as the clinical threshold for the need for oxygen support.
4. CAA spread is monitored by hourly palpation (face, neck, trunk)[7 ,8].	 Subcutaneous emphysema	The spread of CAA can affect respiratory function, monitoring of the process is critical. The patient is followed in semi-fowler position. In case saturation 89, oxygen support is provided to the patient. Peripheral circulation is monitored by the nurse.
5. If there is increased CAA + respiratory distress, it is reported to the physician [7].		It can turn into a life-threatening condition; it is essential to inform the physician for early intervention.

6. The standard treatment for symptomatic CAA is chest tube placement to ensure adequate air drainage. The intercostal passage of the tube should not be dissected too much in order not to allow air to escape under the skin (tube location and connections are checked)[8, 12-13].	 Figure 1. Chest tube of a patient with subcutaneous emphysema, air outlet (foam) formation in the chest tube[1] "exemplified because of similar clinical appearance"	Coughing profusely in chest tube patients allows the lung to expand and interrupt parenchymal air leakage, thus preventing the airflow that causes emphysema. Checking for air leakage is critical to prevent emphysema from increasing. The patient is taught breathing exercises by the nurse. In this case, pursed-lip exercise was applied. In the literature, pursed-lip exercise is reported to reduce shortness of breath and improve quality of life in people with severe respiratory diseases [23-24].
7. Insertion of intracaps into the skin By inserting large lumen intracaps into the areas with less subcutaneous adipose tissue at the level of the 2nd-3rd costae on the anterior chest surface and leaving the plastic part under the skin, the air escaping under the skin is drained more quickly by creating pathways for the air under the skin to come out[1, 4, 14 19, 22].	 Figure 2. [1] "exemplified because of similar clinical appearance"  Figure 3. Subcutaneous angiocatheter placement in a patient with subcutaneous emphysema [14]. "exemplified because of similar clinical presentation"	In this procedure, injection needles can also be used instead of intracaps. It is important to monitor the needles for the safety of the patient.
8. Fasciotomy In common CAAs, a subcutaneous incision about 2 centimeters long extending to the fascia in the pectoral region under the clavicle on the anterior chest[1, 14-16].	 Figure 4. Fasciotomy application in a patient with subcutaneous[1] "exemplified because of similar clinical presentation"	The aim of the procedure is to create an outlet for air under the skin. This incision should be kept open throughout the day with povidone-iodine or soaked gauze.

9. Manual patting of the skin If an intraket or fasciotomy has been opened, the air under the skin is directed to these air drainage pathways by manual patting. Thus, faster air drainage is provided[1, 14].		This is a quick and easy method, but it is necessary to repeat the procedure at intervals.
10. The patient is informed, anxiety is assessed, support is provided [7, 17].		CAA symptoms may cause anxiety in the patient and information and support is recommended.
11. All findings and practices are recorded [18].		Recording in intensive care is mandatory for patient safety and quality of follow-up.

Discussion

Subcutaneous emphysema may develop as a result of conditions such as thoracic trauma, protrusion of the tube outside the intercostal space during chest tube insertion, central venous catheterization, bronchoscopy, intubation, tracheostomy, head and neck surgeries, diagnostic and surgical procedures related to the esophagus, and high-pressure mechanical ventilation in patients with COPD. It is seen as rupture of the alveoli followed by air leakage into the interstitial tissues surrounding the pulmonary vessels. Leaking air moves into the hilus and soft tissue of the neck and chest wall, leading to pneumomediastinum and subcutaneous emphysema[15, 19-20].

In our case, the patient was diagnosed with chronic obstructive pulmonary disease and was discharged after a hospitalization of approximately two weeks.

Spontaneous subcutaneous emphysema characterized by swelling in the neck and chest and palpable crepitus under the skin was detected. The patient's vital signs were evaluated. He was conscious and his blood pressure was 156/92 mm Hg, pulse rate was 108 beats/minute, respiratory rate was 32 breaths/minute and oxygen saturation was 92% with 10 L/minute O2 using an oxygen mask with reservoir bag. The patient had decreased breath sounds in both lung fields and edema from the right chest cavity to the face was greater than in the left chest cavity. The patient was consulted by the pulmonologist to the thoracic surgeon for chest tube insertion on the left side, the area with more air accumulation. As a nurse, sterile drape, chest tube, sterile 2.0 rope for fixation, sterile scalpel, batikon, jetocaine (for numbness of the area), sterile gloves, sterile clamp, sterile sponge and plaster were prepared. Vital signs and monitoring of the patient were continued.

After chest tube insertion, it is critical for the nurse to prevent life-threatening complications, provide effective drainage and maintain patient safety. The tube should be in place and intact, there should be no leakage in the drainage system, suture sites should be monitored, the patient's position (semi-fawler) and the amount and color of the drainage from the chest tube should be monitored hourly. The respiration of the patient with a chest tube should also be monitored [21]. Our patient had a chest tube on the left side and foams were forming in the tube due to emphysema. Drainage system and respiration were monitored in the patient's comfortable position. After intubation, the patient's blood pressure was 136/72 mm Hg, pulse rate was 78 beats/minute, respiratory rate was 26 breaths/minute and oxygen saturation was 98% with 4 L/minute O2 using an oxygen mask with reservoir bag.

It is the process of creating pathways for the air under the skin to escape with the attempt of placing an intraket on the skin. It is a treatment method recommended in different case examples in the literature[1, 4, 14, 19, 22]. After the procedure performed by the physician, the nurse should adjust the patient's position to facilitate breathing (semi-fawler). The position of the intracaps should be checked regularly. The location of the intracaps is very important in terms of ensuring the drainage of the air under the skin. As a nurse, it will ensure patient safety to monitor the entrance sections of the intracaps or cannulas for infection during this procedure and to monitor and stabilize the number of intracaps and cannulas against the possibility of the materials falling and damaging the in-bed patient. Our patient had 18 intracaps to facilitate subcutaneous air drainage. The patient was informed about both the location of the intracaps and to ensure patient safety. Skin patting method was used to facilitate air outflow.

Fasciothemia procedure is to create a pathway for the escape of subcutaneous air in patients with diffuse subcutaneous emphysema by making a subcutaneous incision extending up to the fascia approximately 2 centimeters in length in the pectoral region under the clavicle on the anterior chest face[1, 14-16]. As a nurse, it is important to monitor the incision site for infection after this procedure and to ensure the evacuation of air under the skin by monitoring the patency of the area. Especially after intracutaneous and fasciothemia applications, the literature recommends manual patting of the skin to move the air under the skin to help direct the air to the open areas. Our patient had fasciotemia under the right and left clavicle. As in intracutaneous intracutaneous application, the skin patting method was utilized to facilitate the flow of subcutaneous air.

In this case, pursed-lip exercise was applied. In the literature, pursed-lip exercise is reported to reduce shortness of breath and improve quality of life in people with severe respiratory diseases [23-24].

OBSERVATION	NANDA[25]	NIC[26]	NOC[27]	OUTCOME
Distortion of respiratory pattern due to subcutaneous air invasion and pain	Ineffective Breathing Pattern	Monitoring Respiratory Rate, Evaluation of Lung Sounds Positioning (Semi-Fowler) Teaching breathing exercises (pursed-lip)	Respiratory pattern - Lung sounds - Improvement of respiratory rate	With positioning and respiratory monitoring, the patient's respiratory pattern was regulated, respiratory rate approached normal and lung sounds were obtained more clearly.
Subcutaneous spread of subcutaneous air, Skin tension, Intraket-injection needle insertion, Chest tube insertion, Fasciotomy	Risk of Impairment of Tissue Integrity	Monitoring Skin Integrity Positioning Follow-up of intraket-injection needles (control is ensured in case they come out or fall into the bed) Ensuring that the fasciothemia is open, not closed	Ensuring tissue integrity Monitoring of edema Prevention of complications Protection of the airway	Subcutaneous air invasion was limited, skin tension was not increased and no complications in skin integrity developed.
Patient tension and respiratory distress due to the intensive care environment	Anxiety	Monitoring anxiety levels, Supportive communication, Breathing exercise training	Level of anxiety, Adaptation, Emotional state	With respiratory support, patient education and supportive communication, the level of anxiety visibly decreased and the patient became more compliant.
Subcutaneous Air Monitoring	Impaired gas exchange (due to restriction of lung expansion by subcutaneous air)	Oxygen therapy, Monitoring respiratory function, Positioning (Semi-fowler)	Respiratory status, Oxygen saturation, Respiratory effort	After the intervention, the patient's SpO_2 levels stabilized, respiratory effort decreased and dyspnea regressed.

The patient was under observation in the intensive care unit for 14 days. The patient was informed before and after all procedures. Informed consent was signed and permission was obtained from the institution. All procedures performed were recorded.

Conclusion

Although subcutaneous emphysema is rare, it may pose significant risks in patients with COPD. Early diagnosis and systematic nursing interventions are vital to prevent potential complications. Educating ICU nurses on early detection protocols for subcutaneous emphysema may significantly improve patient outcomes and safety. The nursing care algorithm developed based on the case presented is intended to serve as a practical guide.

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BREAST CA RISK LEVELS AND CANCER SCREENING BEHAVIORS IN WOMEN LIVING IN RURAL AREAS OF TURKEY: A DESCRIPTIVE AND CORRELATIONAL STUDY

ABSTRACT

Objective: This study was conducted to determine the breast cancer risk levels and cancer screening behaviors of women living in rural areas of Turkey.

Materials and Methods: This descriptive and correlational study was conducted between May and October 2024. The study was conducted with 407 women aged 30 years and older living in a district in northern Turkey using convenience sampling method. The research data were obtained through "Personal Information Form" and "Breast Cancer Risk Assessment Form" through face-to-face interviews. The data obtained were analyzed by statistical methods such as Mann Whitney U, Kruskal Wallis, analysis of variance (ANOVA) and t test.

Results: As a result of the study, it was determined that 76.7% of the women had low risk, 20.4% had intermediate risk and 2.9% had high risk for breast cancer. 89.9% of women have heard of breast self-examination, 27.8% do it every three months and 25.6% do not do it. Among the female participants, 84.8% had heard of clinical breast examination and 60.4% had not done it. It was determined that 56.5% and 72.7% of the female participants did not undergo mammography and breast ultrasound, respectively. Statistically significant associations were found between mammography, menopause, age, body type, menstrual age, estimated breast cancer risk and risk score.

Conclusıon: It was found that the majority of women had a low risk level for breast cancer, only one-fourth of the women regularly practiced regular MMR, a little more than one-third of the women practiced MMR, and very few women had regular mammography. It was concluded that the risk scores of women who had mammograms, menopausal women, women with low education level, women who were not working and women who perceived the risk as high were significantly higher. Women in the high-risk group should be informed, and referrals should be made by raising awareness for early diagnosis methods.

Keywords: Breast cancer, Women, Rural area, Risk Level, Cancer Screening.

TÜRKİYE'NİN KIRSALINDA YAŞAYAN KADINLARDA MEME CA RİSK DÜZEYLERİ VE KANSER TARAMA DAVRANIŞLARI: TANIMLAYICI VE İLİŞKİ ARAYICI ARAŞTIRMA

ÖZET

Amaç: Bu çalışma Türkiye'nin kırsalında yaşayan kadınların meme kanseri risk düzeylerini ve kanser tarama davranışlarını belirlemek amacıyla yapılmıştır.

Materyal ve Yöntem: Tanımlayıcı ve İlişki arayıcı tipte yapılan bu araştırma Mayıs-Ekim 2024 tarihleri arasında yürütülmüştür. Türkiye'nin kuzeyinde bir ilçede yaşayan ve kolayda örnekleme yöntemi ile 30 yaş ve üzeri 407 kadınla yürütülmüştür. Araştırma verileri, yüz yüze görüşme tekniğiyle"Kişisel Bilgi Formu" ve "Meme Kanseri Risk Değerlendirme Formu" aracılığıyla elde edilmiştir. Elde edilen veriler, Mann Whitney U, Kruskal Wallis, varyans analizi (ANOVA) ve t testi gibi istatistiksel yöntemlerle analiz edilmiştir.

Bulgular: Çalışma sonucunda kadınların %76.7'sinin meme kanseri açısından düşük riskli, %20.4'ünün orta ve %2.9'unun ise yüksek riskli olduğu belirlenmiştir. Kadınların %89.9'u kendi kendine meme muayenesini duymuş olup %27.8'i üç ayda bir yaparken %25.6'sı yapmamaktadır. Kadın katılımcıların %84.8'i klinik meme muayenesini duymuş olup %60.4'ü yaptırmamıştır. Kadın katılımcıların %56.5'i mamografi, %72.7'si meme ultrasonu çektirmediği belirlenmiştir. Mamografi çektirme, menopoza girme, yaş, beden yapısı, menstrual yaş ve tahmin edilen meme kanseri riski ile risk puanı arasında istatistiksel olarak anlamlı ilişki bulunmuştur.

Sonuç: Araştırmada, kırsal bölgede yaşayan kadınların çoğunun meme kanseri açısından düşük riskli olduğu, ancak tarama davranışlarının yetersiz kaldığı belirlenmiştir. Kadınların çoğu KKMM ve KMM'yi duymuş olmasına rağmen bu yöntemleri düzenli uygulamamaktadır. Mamografi ve ultrason çektirme oranları da düşüktür. Mamografi yaptırma davranışı ile yaş, menopoz durumu, beden yapısı, menstrual yaş ve risk düzeyi arasında anlamlı ilişki bulunmuştur. Bu bulgular, kırsal bölgelerde meme kanseri farkındalığını artıracak ve taramayı teşvik edecek müdahalelere ihtiyaç olduğunu göstermektedir.

Anahtar Kelimeler: Meme CA, Kadınlar, Kırsal alan, Risk Düzeyi, Kanser Tarama.

GİRİŞ

Meme kanseri, dünya genelinde ve Türkiye'de kadınlar arasında en sık görülen malign tümörlerden biridir ve kadın kanserleri arasında en yüksek ölüm oranına sahip hastalıklar arasında yer almaktadır.[1] Dünya Sağlık Örgütü'ne (DSÖ) göre 2020 yılında dünya çapında 2,3 milyon yeni meme kanseri vakası tespit edilmiş ve yaklaşık 685 bin kadın meme kanseri nedeniyle hayatını kaybetmiştir.[2] Türkiye'de ise Sağlık Bakanlığı verilerine göre meme kanseri, kadınlarda en sık karşılaşılan kanser türü olup, her 4 kanser vakasından biri meme kanseridir.[3]

Meme kanseri gelişiminde etkili olabilecek birçok risk faktörü bulunmaktadır. Bu faktörlerin bazıları bireyin kontrolü dışında yer almakta olup; yaş, kadın cinsiyeti, ailede meme kanseri öyküsü, mamografik meme yoğunluğu, genetik mutasyonlar ve üreme öyküsüne ilişkin özellikler bu gruba dahildir. [4-6] Diğer yandan, bazı risk faktörleri birey tarafından değiştirilebilir niteliktedir. Örneğin; 30 yaş sonrasında gerçekleşen ilk gebelik, fiziksel hareketsizlik, alkol kullanımı, menopoz sonrası obezite, menopozal hormon tedavisi kullanımı ve düşük sosyo-ekonomik düzey bu grupta yer alır.[7] Ayrıca, çeşitli çalışmalarda sigara tüketimi ve gece vardiyasında çalışma gibi faktörlerin de meme kanseri ile ilişkili olabileceği belirtilmiştir.[8,9]

Erken tanı, meme kanserinde yaşam süresini artırmada en etkili yöntemlerden biridir. Erken evrede tespit edilen meme kanseri vakalarında beş yıllık sağkalım oranı %90'ın üzerindedir.[10] Meme kanserinin erken tanısında yaygın olarak kullanılan tarama yöntemleri kendi kendine meme muayenesi (KKMM), klinik meme muayenesi (KMM) ve mamografidir. Ancak kırsal bölgelerde yaşayan kadınların bu tarama hizmetlerine erişimi, çeşitli sosyoekonomik, kültürel ve yapısal nedenlerle sınırlı kalabilmektedir.[11] Yüksek risk grubundaki kadınlar için meme kanseri gelişimini önlemeye yönelik çeşitli tarama yöntemleri ve takip protokolleri önerilmektedir.[12] Türkiye'de Ulusal Kanser Tarama Programı kapsamında belirlenen tarama protokolüne göre; 20–40 yaş arası kadınlara ayda bir KKMM ve iki yılda bir KMM, 40–69 yaş arası kadınlara ise ayda bir KKMM, yılda bir KMM ve iki yılda bir mamografi çekimi yaptırmaları önerilmekte ve ücretsiz olarak faydalanmaları sağlanmaktadır.[13] Meme kanserine bağlı morbidite ve mortalite oranları, ülkelerin gelişmişlik düzeyine göre değişiklik göstermektedir. Gelişmiş ülkelerde meme kanseri insidansı yüksek olmakla birlikte, erken tanı ve etkin tedavi olanakları sayesinde mortalite oranları düşüktür. Buna karşılık, az gelişmiş ülkelerde meme kanserine bağlı ölümlerin daha yüksek oranda gerçekleştiği bilinmektedir. Bu ülkelerde, toplumda meme kanseri risk faktörlerinin saptanması ve erken tanı ile tarama programlarının yaygınlaştırılması özellikle önem taşımaktadır.[14-16]

Kırsal kesimde yaşayan kadınlar, sağlık okuryazarlığı düzeyinin düşük olması, geleneksel toplumsal roller, sağlık hizmetlerine fiziksel erişimin zor olması gibi faktörler nedeniyle meme kanseri riskini yeterince algılayamamakta ve tarama davranışlarını düzenli olarak gerçekleştirmemektedir.[17] Bu durum, meme kanserinde geç tanıya ve mortalite oranlarının artmasına neden olmaktadır. Bu araştırma, Türkiye'nin kırsal bölgelerinde yaşayan kadınların meme kanseri risk düzeylerini belirlemek ve bu risk ile kanser tarama davranışları arasındaki ilişkiyi incelemek amacıyla yapılmıştır. Çalışmanın sonuçları, kırsal kesimde kanser taramalarını artırmaya yönelik halk sağlığı politikalarının oluşturulmasına katkı sağlayacaktır.

GEREÇ VE YÖNTEM

Araştırmanın Tipi: Kırsalda yaşayan kadınların meme CA risk düzeyleri ve kanser tarama davranışlarının belirlenmesi amacıyla tanımlayıcı ve ilişki arayıcı tipte gerçekleştirilmiştir.

Araştırmanın Evren- Örneklemi: Türkiye'nin kuzeydoğusundaki bir ilçede yaşayan ve olasılıklı olmayan rastgele örnekleme yöntemlerinden biri olan kolayda örnekleme yöntemi kullanılarak çalışmaya dâhil edilen 30 yaş üstü 407 kadın katılımcıyla 20 Mayıs- 20 Ekim 2024 tarihleri arasında tamamlanmıştır.

Araştırmaya Kabul Kriterleri;

1. 30 yaş üstü kadınlar,

2. Meme kanseri olmayan,

3. Sözel iletişim kurulabilen,

4 Anket formundaki soruları algılamasını ve doğru şekilde cevaplandırmasını engelleyecek şekilde fiziksel ve ruhsal sağlık durumu kötü olmayan,

5. Araştırmaya katılmaya istekli olanlar.

Veri Toplama Araçları: Araştırma verileri, kadınlarla yüz yüze görüşme tekniği kullanılarak "Kişisel Bilgi Formu" ve "Meme Kanseri Risk Değerlendirme Formu" ile toplanmıştır.

Kişisel Bilgi Formu: Araştırmada kullanılan veri toplama formu, literatür taraması sonucunda araştırmacılar tarafından geliştirilmiştir.[18-20] Formda; kadınların yaş, medeni durum, eğitim düzeyi, meslek ve gelir durumu gibi sosyodemografik özelliklerinin yanı sıra, doğurganlık öyküsü, menopoz durumu, erken tanı yöntemlerine ilişkin bilgi ve uygulamaları ile meme kanseri risk algıları yer almaktadır.

Meme Kanseri Risk Değerlendirme Formu: Bu çalışmada, Amerikan Kanser Birliği tarafından geliştirilen ve Türkiye'de T.C. Sağlık Bakanlığı tarafından kabul edilerek kullanımı önerilen "Meme Kanseri Risk Değerlendirme Formu"ndan yararlanılmıştır (T.C. Sağlık Bakanlığı, 2005). Altı bölüm ve toplam 20 maddeden oluşan bu formda; bireysel ve ailesel meme kanseri öyküsü, yaş, doğum yaşı, beden kitle yapısı ve menstrual özellikler dikkate alınarak meme kanseri riski puanlanmaktadır. Elde edilen puana göre 200 ve altı "düşük risk", 201–300 "orta risk", 301–400 "yüksek risk" ve 400 üzeri ise "en yüksek risk" düzeyinde değerlendirilmektedir.

Verilerin Değerlendirilmesi

Verilerin analizi IBM SPSS 27 paket programı ile gerçekleştirilmiştir. Sürekli değişkenler aritmetik ortalama ± standart sapma ile, kategorik veriler ise frekans ve yüzde (%) değerleriyle ifade edilmiştir. Anlamlılık düzeyi 0.05 üzerinden değerlendirilmiş ve kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puanların ±1 aralığında[21] olması puanların normal dağıldığını göstermektedir. Bu sonuca göre ölçekten alınan puanların analizi yapılırken parametrik testlerden yararlanılmıştır. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puanları tanıtıcı bilgiler ve meme kanseri tarama yöntemlerini kullanma durumları açısından karşılaştırmak için ikili gruplarda

bağımsız gruplar t-testi ve üç ve üzeri gruplarda tek yönlü ANOVA testi kullanılmıştır. Tek yönlü ANOVA testinde sonucu anlamlı çıkanlarda çoklu karşılaştırma yaparken, homojen dağılan verilerde Tukey ve homojen dağılmayan verilerde ise Games-Howell testi kullanılmıştır. Formdan alınan puanlar ile yaş arasındaki ilişkide Pearson momentler çarpım korelasyon testi kullanılmıştır.

Araştırmanın Etik Yönü: Trabzon Üniversitesi Sosyal ve Beşeri Bilimsel Araştırmalar Etik Kurulun'dan (18/03/2024 tarih ve E-81614018-050.04-2400014631 sayılı) yazılı onay alınmıştır. Araştırmaya katılan bireylerden yazılı onam alınmış ve çalışma Helsinki Bildirgesi kapsamında yürütülmüştür.

BULGULAR

Kadınlara ait tanıtıcı bilgilerin dağılımı Tablo 1'de verilmiştir.

Tablo 1. Kadınlara Ait Tanıtıcı Bilgilerin Dağılımı (N=407)

Tanıtıcı Bilgiler		**N**	**%**
Medeni Durum	Evli	361	88.7
	Bekar	46	11.3
Eğitim Durumu	Okuryazar	16	3.9
	İlköğretim	89	21.9
	Lise	176	43.2
	Ön Lisans	47	11.5
	Lisans	67	16.5
	Lisansüstü	12	2.9
Çalışma Durumu	Çalışıyor	184	45.2
	Çalışmıyor	223	54.8
Ailede Meme Kanseri Varlığı	Yok	265	65.1
	Hala, Teyze ya da Büyükanne	103	25.3
	Anne ya da Kız Kardeş	32	7.9
	Anne ve Kız Kardeş	5	1.2
	Anne ve İki Kız Kardeş	2	0.5
Çocuk Doğurma Yaşı	Çocuk Yok	59	14.5
	Otuz Yaş Öncesi İlk Doğum	301	74.0
	Otuz Yaş Sonrası İlk Doğum	47	11.5
Menstrual Yaş	11 Yaş ve Altı	105	25.8
	12-14 Yaş	261	64.1
	15 Yaş ve Üstü	41	10.1
Beden Yapısı	Zayıf	54	13.3
	Orta	257	63.1
	Şişman	96	23.6
Menopozda Hormon Kullanımı	Evet	39	9.6
	Hayır	145	35.6
	Menopoza Girmemiş	223	54.8
Tahmin Edilen Meme Kanseri Riski	Hiç Riski Yok	52	12.8
	Düşük Riskli	111	27.3
	Yüksek Riskli	27	6.6
	Bilmiyor	217	53.3
Risk Düzeyi	Düşük	312	76.7
	Orta	83	20.4
	Yüksek	12	2.9

	Min.	**Maks.**	**x̄**	**SS**
Yaş	31	85	48.45	10.09

Tablo 1 incelendiğinde kadınların yaş ortalaması 48.45±10.09 olup %88.7'si evlidır. %43.2'si lise mezunu, %54.8'nıni çalışmadığı, %65.1'inin ailesinde meme kanseri yokken, %25.3'ünün hala, teyze ya da büyükannesinde meme kanseri olduğu, %74'ünün otuz yaş öncesi ilk doğumunu yaptığı, %64.1'inin menstrual yaşı 12-14 yaş aralığında olduğu, %63.1'inin orta beden yapısında, %35.6'sının menopoz döneminde hormon tedavisi kullanmadığı belirlenmiştir. Tahmin edilen meme kanseri risk düzeylerini %27.3'ü düşük riskli, %53.3'ü ise meme kanseri riskini bilmemediğini ifade etmiştir. Çalışma sonucunda kadınların %76.7'sinin meme kanseri açısından düşük riskli, %20.4'ünün orta ve %2.9'unun ise yüksek riskli olduğu belirlenmiştir.

Kadınlara ait meme kanseri tarama yöntemlerini kullanma durumlarının dağılımı Tablo 2'de verilmiştir.

Tablo 2. Kadınlara Ait Meme Kanseri Tarama Yöntemlerini Kullanma Durumlarının Dağılımı (N=407)

Meme Kanseri Tarama Yöntemlerini Kullanma Durumları		**N**	**%**
Kendi Kendine Meme Muayenesini Duyma Durumu	Evet	366	89.9
	Hayır	41	10.1
Kendi Kendine Meme Muayenesi Yapma Sıklığı	Yok	104	25.6
	Sık Sık	63	15.5
	Ayda Bir	100	24.6
	Üç Ayda Bir	113	27.8
	Yılda Bir	27	6.6
Klinik Meme Muayenesini Duyma Durumu	Evet	345	84.8
	Hayır	62	15.2
Klinik Meme Muayenesini Yaptırma Durumu	Hayır	246	60.4
	Kontrol Amaçlı Yaptırmış	140	34.4
	Memede Sorun Nedeniyle Yaptırmış	21	5.2
Mamografi Çektirme Durumu	Hayır	230	56.5
	Evet	150	36.9
	Düzenli Çektiriyor	27	6.6
Meme Ultrasonu Çektirme Durumu	Hayır	296	72.7
	Evet	89	21.9
	Düzenli Çektiriyor	22	5.4

Tablo 2 incelendiğinde kadınların %89.9'u kendi kendine meme muayenesini duymuş olup, %27.8'i üç ayda bir KKMM yaparken %25.6'sı hiç yapmamaktadır. Kadın katılımcıların %84.8'i klinik meme muayenesini duymuş olup %34.4'ü kontrol amaçlı ve %5.2'si memede sorun nedeniyle yaptırmışken, %60.4'ü yaptırmamıştır. Kadın katılımcıların %36.9'u daha önce mamografi çektirmiş ve sadece %6.6'sı düzenli olarak mamografi çektiriyor. Katılımcıların %72.7'si hiç meme ultrasonu çektirmemişken %5.4'ü düzenli olarak meme ultrasonu çektirmektedir.

Araştırmada kullanılan Meme Kanseri Risk Değerlendirme Formu'ndan alınan puanlara ilişkin istatistiksel bilgiler Tablo 3'te verilmiştir.

Tablo 3. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan Aldıkları Puanlara İlişkin İstatistiksel Bilgiler (N=407)

Min.	**Maks.**	**x̄**	**SS**
60.00	375.00	172.09	53.07

Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puan ortalaması 172.09±53.07 olup puan ortalaması düşük risk (T.C. Sağlık Bakanlığı, 2005) kategorisindedir.

Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puan ortalamalarının tanıtıcı bilgilere göre karşılaştırılması Tablo 4'te verilmiştir.

Tablo 4. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan Aldıkları Puan Ortalamalarının Tanıtıcı Bilgilere Göre Karşılaştırılması (N=407)

Tanıtıcı Bilgiler		**N**	**x̄**	**SS**
Medeni Durum	Evli	361	173.68	53.74
	Bekar	46	159.67	46.08
	Test ve Anlamlılık	t=1.689[a], p=0.092		
Eğitim Durumu	1.Okuryazar	16	239.06	76.77
	2.İlköğretim	89	185.30	46.45
	3.Lise	176	168.18	47.94
	4.Ön Lisans	47	170.74	58.64
	5.Lisans	67	155.60	49.57
	6.Lisansüstü	12	139.58	44.18
	Test ve Anlamlılık	F=9.491[b], **p<0.001**		
	Anlamlı Fark	1>3-4-5-6, 2>5-6		
Çalışma Durumu	Çalışıyor	184	162.45	53.89
	Çalışmıyor	223	180.05	51.14
	Test ve Anlamlılık	t=-3.374[a], **p<0.001**		
Ailede Meme Kanseri Varlığı	1.Yok	265	146.08	35.57
	2.Hala, Teyze ya da Büyükanne	103	208.50	34.53
	3.Anne ya da Kız Kardeş	32	235.16	39.73
	4.Anne ve Kız Kardeş	5	331.00	60.15
	5.Anne ve İki Kız Kardeş	2	337.50	17.68
	Test ve Anlamlılık	F=120.759[b], **p<0.001**		
	Anlamlı Fark	1<2-3-4-5, 2<3-4-5, 3<4-5		
Çocuk Doğurma Yaşı	Çocuk Yok	59	165.76	47.34
	Otuz Yaş Öncesi İlk Doğum	301	170.59	53.45
	Otuz Yaş Sonrası İlk Doğum	47	189.68	54.90
	Test ve Anlamlılık	F=3.155[b], **p=0.044**		
	Anlamlı Fark	-		
Menstrual Yaş	1.11 Yaş ve Altı	105	202.90	56.63
	2.12-14 Yaş	261	162.63	46.17
	3.15 Yaş ve Üstü	41	153.41	54.39
	Test ve Anlamlılık	F=27.580[b], **p<0.001**		
	Anlamlı Fark	1>2-3		
Beden Yapısı	1.Zayıf	54	141.39	42.97
	2.Orta	257	164.74	47.43
	3.Şişman	96	209.06	53.65
	Test ve Anlamlılık	F=41.801[b], **p<0.001**		
	Anlamlı Fark	1<2-3, 2<3		
Menopozda Hormon Kullanımı	Evet	39	215.90	66.55
	Hayır	145	187.43	49.30
	Menopoza Girmemiş	223	154.46	44.86
	Test ve Anlamlılık	F=37.310[b], **p<0.001**		
	Anlamlı Fark	1>2-3, 2>3		

Tablo 4. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan Aldıkları Puan Ortalamalarının Tanıtıcı Bilgilere Göre Karşılaştırılması (N=407) Devamı

Tanıtıcı Bilgiler		N	x̄	SS
Tahmin Edilen Meme Kanseri Riski	1.Hiç Riski Yok	52	149.62	42.01
	2.Düşük Riskli	111	182.48	51.67
	3.Yüksek Riskli	27	202.41	68.66
	4.Bilmiyor	217	168.40	51.42
	Test ve Anlamlılık		F=8.232[b], **p<0.001**	
	Anlamlı Fark		1<2-3-4	
Risk Düzeyi	1.Düşük	312	149.91	33.92
	2.Orta	83	233.37	19.03
	3.Yüksek	12	325.00	30.15
	Test ve Anlamlılık		F=378.954[b], **p<0.001**	
	Anlamlı Fark		1<2-3, 2<3	

[a]Bağımsız gruplar t-testi, [b]Tek yönlü ANOVA testi

Tablo 4 incelendiğinde Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puan ortalamalarının eğitim durumu, çalışma durumu, ailede meme kanseri varlığı, menstrual yaş, beden yapısı, menopozda hormon kullanımı, tahmin edilen meme kanseri riski ve risk düzeyine göre anlamlı olarak farklılaştığı bulunmuştur ($p<0.001$). Buna göre okuryazar olanların Meme Kanseri Risk Değerlendirme Formu puan ortalaması ilköğretim mezunu hariç diğerlerinden ve ilköğretim mezunu olanların lisans ve lisansüstü mezunlarından daha yüksektir. Çalışmayanların Meme Kanseri Risk Değerlendirme Formu puan ortalaması çalışanlardan daha yüksektir. Ailede meme kanseri varlığı açısından Meme Kanseri Risk Değerlendirme Formu puan ortalamaları yüksekten düşüğe doğru anne ve iki kız kardeş ya da anne ve kız kardeş, anne ya da kız kardeş, hala, teyze ya da büyükanne ve yoktur. Menstrual yaşı 11 yaş ve altı olanların puan ortalaması diğerlerinden daha yüksektir. Beden yapısı açısından Meme Kanseri Risk Değerlendirme Formu puan ortalamaları yüksekten düşüğe doğru şişman, orta ve zayıftır. Menopozda hormon kullanımı açısından Meme Kanseri Risk Değerlendirme Formu puan ortalamaları yüksekten düşüğe doğru evet, hayır ve menopoza girmemiştir. Tahmin edilen meme kanseri riski olarak hiç riski olmayanların puan ortalaması diğerlerinden daha düşüktür. Risk düzeyi açısından Meme Kanseri Risk Değerlendirme Formu puan ortalamaları yüksekten düşüğe doğru azalmaktadır.

Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puan ortalamalarının meme kanseri tarama yöntemlerini kullanma durumlarına göre karşılaştırılması Tablo 5'te verilmiştir.

Tablo 5. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan Aldıkları Puan Ortalamalarının Meme Kanseri Tarama Yöntemlerini Kullanma Durumlarına Göre Karşılaştırılması (N=407)

Meme Kanseri Tarama Yöntemlerini Kullanma Durumları		**N**	**x̄**	**SS**
Kendi Kendine Meme Muayenesini Duyma Durumu	Evet	366	172.40	53.78
	Hayır	41	169.39	46.68
	Test ve Anlamlılık	t=0.344[a], p=0.731		
Kendi Kendine Meme Muayenesi Yapma Sıklığı	Yok	104	178.70	55.32
	Sık Sık	63	177.78	69.84
	Ayda Bir	100	170.90	51.36
	Üç Ayda Bir	113	164.71	41.35
	Yılda Bir	27	168.70	47.95
	Test ve Anlamlılık	F=1.173[b], p=0.322		
	Anlamlı Fark	-		
Klinik Meme Muayenesini Duyma Durumu	Evet	345	170.72	53.28
	Hayır	62	179.71	51.60
	Test ve Anlamlılık	t=-1.228[a], p=0.220		
Klinik Meme Muayenesini Yaptırma Durumu	Hayır	246	170.35	46.49
	Kontrol Amaçlı Yaptırmış	140	175.75	59.61
	Memede Sorun Nedeniyle Yaptırmış	21	168.10	76.48
	Test ve Anlamlılık	F=0.523[b], p=0.593		
	Anlamlı Fark	-		
Mamografi Çektirme Durumu	Hayır	230	164.70	51.30
	Evet	150	181.30	50.41
	Düzenli Çektiriyor	27	183.89	71.55
	Test ve Anlamlılık	F=5.262[b], **p=0.006**		
	Anlamlı Fark	Evet>Hayır		
Meme Ultrasonu Çektirme Durumu	Hayır	296	170.02	50.26
	Evet	89	179.66	56.42
	Düzenli Çektiriyor	22	169.32	72.87
	Test ve Anlamlılık	F=1.162[b], p=0.314		
	Anlamlı Fark	-		

[a]Bağımsız gruplar t-testi, [b]Tek yönlü ANOVA testi

Tablo 5 incelendiğinde Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puan ortalamalarının mamografi çektirme durumuna göre anlamlı olarak farklılaştığı bulunmuştur ($p<0.01$). Buna göre mamografi çektirenlerin puan ortalaması çektirmeyenlerden daha yüksektir.

Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan aldıkları puanlar ile yaş arasındaki ilişkinin sonuçları Tablo 6'da verilmiştir.

Tablo 6. Kadınların Meme Kanseri Risk Değerlendirme Formu'ndan Aldıkları Puanlar ile Yaş Arasındaki İlişki (N=407)

	Meme Kanseri Risk Değerlendirme Formu
Yaş	r=0.538, **p<0.001**

Yaş ile Meme Kanseri Risk Değerlendirme Formu puanları arasında orta düzeyde pozitif yönlü anlamlı bir ilişki vardır (r=0.538, p<0.001) (Tablo 6).

SONUÇ VE ÖNERİLER

Bu araştırma, Türkiye'nin kırsalında yaşayan kadınların büyük çoğunluğunun meme kanseri açısından düşük risk düzeyinde olduğunu ortaya koymuştur.. Ancak, tarama davranışları incelendiğinde kadınların önemli bir kısmının meme kanseri erken tanı yöntemlerini yeterli düzeyde uygulamadığı belirlenmiştir. Araştırmada, mamografi çektirme davranışı ile menopoza girme durumu, yaş, beden yapısı, menstrüel başlangıç yaşı, tahmin edilen meme kanseri riski ve hesaplanan risk puanı arasında istatistiksel olarak anlamlı ilişkiler bulunmuştur. Bu sonuçlar, meme kanseri tarama davranışlarının sadece bilgi düzeyine değil, aynı zamanda demografik ve biyolojik faktörlerle de ilişkili olduğunu göstermektedir.

Elde edilen bulgular, kırsal bölgelerde yaşayan kadınların meme kanseri konusunda farkındalıklarının artırılmasına ve düzenli tarama davranışlarının teşvik edilmesine yönelik sağlık eğitimlerinin ve tarama hizmetlerinin yaygınlaştırılması gerekliliğini ortaya koymaktadır. Özellikle risk düzeyi yüksek olan gruplara yönelik hedefli müdahalelerin planlanması, erken tanı oranlarını artırarak meme kanserine bağlı mortaliteyi azaltmada etkili olabilir. Özellikle menopoz sonrası dönemdeki kadınlara yönelik bilgilendirme çalışmaları yaygınlaştırılmalı, risk algısını artırıcı eğitim programları uygulanmalıdır. Toplum temelli tarama programları güçlendirilerek, meme kanseri erken tanısı için katılım oranları artırılmalıdır.

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WILL ARTIFICIAL INTELLIGENCE REPLACE PSYCHOTHERAPISTS?

ABSTRACT

The purpose of this paper is to look at some hypotheses related to the idea that artificial intelligence could replace various human professions. This is a constant fear nowadays, for the near future, as we have seen many ticket sellers and even supermarket jobs taken over by machines. At the same time, there is always need for human supervision of the machines. We have recently seen discussions related to the way in which artificial intelligence could replace psychologists, psychoanalystis and other professionals in the mental health field. While the artificial intelligence systems can store up large amounts of theoretical knowledge and information, search for them in databases and use them applying them to a certain situation, there is one important aspect AI lacks: the empathy of a therapist, according to the Romanian Association for the Promotion of Psychoanalysis (AROPA). Indeed, AI may simulate emotional contact, empathy, sympathy, understanding, try to establish contact and dialogue similarly to a human person, yet eventually it does not feel the experiences the same way as we do. Psychoanalytic therapy relies on the analysis of the unconscious, starting from the personal experience with it of the therapist. AI clearly cannot do that. AI cannot dream and analyze its own dreams, AI does not commit slips of the tongue and parapraxes. AI does not need to start making free association and does not go into training to psychoanalyse itself first and then be able to work with patients. This is a crucial difference between human beings and AI, which can make the replacement of therapists by AI, especially in the domain of psychoanalysis, impossible.

Keywords: Transference, Empathy, Unconscious, Free Associations, Emotions

1. INTRODUCTION

Will artificial intelligence replace us in our professional domain of activity? This is a question which reflects our current fears. Yet, as we can notice repeatedly, the question is mostly modificed to include another element, that of responsibility. For instance, if something goes wrong, then who is responsible for this? The answer references the human beings.

Professions such as those of teacher, translator, seller, customer service, may be considered replaceable by using applications which can do this job. Yet, interaction with a human being can be considered complex and more helpful regarding the customer's requests. Currently, the profession of therapist is also considered as replaceable by applications or by other instances of artificial intelligence. Chat GPT is currently gaining popularity, and our interactions with it based on dialogue can be considered as rising in complexity.

The issue of artificial intelligence and its replacing human beings in various professions is frequently discussed nowadays. However, AI for the time being, at least, remains a simple tool. It needs human supervision in many professions, especially medicine, where the risk is high and where human responsibility is a major issue. In addition, we can notice AI being used in the educational field, yet it is used once again as a tool for various exercises, and students, as well as teachers and researchers are advised against using AI in order for it to do their work. Research papers and assignments should definitely not done by AI in the name of human researchers and students. AI is currently being used for artistic purposes, yet there is still resistance and fear of replacing human artists, as well as warning against taking over AI work as our own.

In addition, the field of medicine consideres the use of AI as high-risk, which leads to the necessity of it being backed up by human supervision. The field of psychotherapy should consider risks along the same lines. In addition, fields such as those including, traditionally, the dimension of empathy, especially professions from the domains of psychology and psychoianalysis, or those domains related to human feelings, should consider having as a professional a human being, who also has a psyche and emotions. This can help the professional consider the emotions and psyche of their patients by analogy with their own. AI tools such as Chat GPT, while mimicking empathy and human-like conversation, cannot in fact experience genuine human feelings. For professions requiring professional supervision and formation, and which are related to feelings, and experience with their own analysis and understanding of their own psyche, this is a clear, as well as basic, limitation, of AI.

2. RESEARCH AND FINDINGS

According to Zhang & Wang (2024), AI systems began to be used as early as the 1980, when they were "aimed to replicate human psychological expertise, leading to advanced diagnostic and therapeutic tools across various psychological disciplines." One area where they are still considered to be used with success is cognitive behavioral therapy (CBT). Computerized programs based on CBT were around by the end of the 20th century, "which were designed to provide structured, evidence-based interventions for common mental health conditions" (Zhang & Wang, 2024).

The Romanian Association for the Promotion of Psychoanalysis (AROPA), in their article titled *Will AI replace the human psychoanalyst?* (Va inlocui AI psihanalistul uman?), posted by Ionut ((2025), on the blog of the association, refer to frequent discussions which are going on nowadays that this is going to happen if it has not already happened. The reason is due to the fact that AI has a higher IQ than the majority of human beings. However, AROPA staff members claim, repeatedly, in their discussions in their online community, that what matters most for analysis is empathy, in the analysis of a patient, then the capacity to dream a lot, to remember, and to analyse your dreams, as well as the ability to feel the unconscious, all of which are significant for being a good psychoanalyst (Ionut, 2025). All these abilities refer to the human analyst, and not the to AI analyst. For AROPA, knowledge of theory and case studies cannot help in the absence of the previously mentioned abilities. Freud (1912) did not use precisely the term empathy, yet he did refer to a certain attitude of the analyst towards the patient.

Spytska (2025) supports the opinion set for by AROPA, and by the article by Ionut (2025), aligning with the idea that empathy of human therapists is one main advantage over AI, as well as major difference: "One key problem is a lack of emotional depth and empathy, which are necessary components of human-based treatment but difficult to reproduce with AI. Human therapists may adapt their approach depending on real-time emotional indicators, providing personalised treatment that AI chatbots, which rely on programmed replies, fail to match."

Indeed, we could claim that AI, in the case of the profession of the psychoanalyst, does not have the dimension of the unconscious, it has no emotions, it cannot work with them, and it cannot be like us. However, our tendency remains to attribute human traits to objects, including AI, to personify them. We see AI as a dialogue partner, a friend, even a psychoanalyst. We converse with ChatGPT and it responds, and we tend to attribute to it the human capacity for understanding.

However, AI has a bias, which is, after all, a bias that belongs to us and is transmitted to it through the datasets that are part of its training. There have been such examples when AI analyzed job applicants' files for various companies. One of the biases may also be that it tells us exactly what we want to hear, encouraging us, even if artificially, just through language, because it can imitate someone's understanding, emotionally, and we project onto it the idea that it empathizes with us. The images of robot young girls making Asian men happy on Facebook could be seen as confirmation. Such relationships can be ideal because, in reality, we are living alongside our own fantasies.

While AI cannot replace psychoanalysts, psychotherapists, and psichologists, it can, however, be used as a tool, to enhance or replace elements of traditional therapy. This includes the use of AI-powered chatbots, digital companions, and AI-assisted tools for therapists, aiming to improve accessibility of treatment and to therapy services dor patients (Grodniewicz & Hohol, 2023), predicting treatment outcomes (Grodniewicz & Hohol, 2023), improved diagnosis for depression and schizophrenia (Grodniewicz & Hohol, 2023) and to streamline various tasks within mental health care. For instance, we can mention the use of chatbots and digital companions, which can be used by patients during the time they spend alone, without the therapists, to improve their mindset. In this case, AI can be used to help patients track their progress and offer them support and encouragement in-between their therapy sessions. Administrative tasks can also benefit from using AI as tools, such as, for therapists, taking notes, creating the schedule, for preparing their bills, so that they can focus

more on taking care of their patients. AI tools can identify, in research, as well as diagnosis, pattenrs, predict behaviours, or diagnose some mental disorders, yet such tools should be used with care by the therapists, and rely on their own understanding of the patient. Therapy, and especially psychoanalytic psychotherapy, should rely most of all on the analyst's understanding of the patient, since each patient is, after all, an individual with his or her own problems and his or her own way of understanding their problems, as well as life itself.

Most of all, AI can, however, be used in the training of workers in the domains of psychotherapy, or to provide Information for patients regarding information about their health issues, about what each psychotherapy method can offer them, as well as about where to find a therapist in their area.

However, the domain of psychotherapy, and, psychoanalysis, especially, relies heavily on the empathy of the therapist, It also relies on the theraopist's own experience with his or her own analysis and possible treatment. Especially in psychoanalysts, the confrontantion with the future therapists's own unconscious based on assisted analysis with a formative psychoanalyst is a crucial point in his or her professional formation as an analyst. The psychoanalyst relies on his or her own experience with working with the unconscious, such as dream analysis, slips of the tongue and parapraxes (Freud, 1915), which are errors of speech and action, such as forgetting to do something or misplacing an object, or self-analysis, relying on writing down free associations and connecting the elements in order to understand what preoccupies him or her at a certain moment.

Psychoanalysis, as a therapy method for neuroses (Freud, 1977), relies heavily on unconscious contents, and the way it can be uncovered. Dream interpretation is deeply personal, which makes AI algorhythms simple landmarks or searches for further directions which can become completely different. Psychoanalysis does not rely on fixed symbols for dreams (Freud, 2024). While there can be typical dreams, as Freud (2024) had mentioned and analysed some, e.g. flying, which can be dreams of pleasure and freedom, being nakes in public, which reflect anxiety and vulnerability, taking an examination, which can be related to fear of failure, or, on the contrary, reassurance that the dreamer can get through this, especially if it is an exam they had already passed in real life, losing teeth, which can be related to castration anxiety, and all its psychological implications on life as an adult, falling, which can be related to loss of control, or giving in to sexual desires and temptation, death, which could mean change or be linked to death wishes, in trying to deal with strenuous situations. However, for Fteud, even such common and typical dreams should be, first of all, analysed based on the personal menaings they could have for dreamers, first of all, and only afterwards, in case the dreamer has no personal free associations based on the elements of these dreams, should the typical dream interpretation be given.

If we consider the differences between a human analyst and AI, we can consider the fact that AI tends to establish patterns based on the information it gathers from various therapists, their patients and case analyses, which can only lead to generalizations based on common traits and tendencies when it comes to various cases of various patients. Psychology and psychiatry tend to establish patterns based on diagnoses, while in psychoanalysis there can be a wide range of individual variation of perception of various common life experiences and their meanings in dreams. The particular life context of a particular patient is always the priority in psychoanalytic psychotherapy, where there are no diagnoses like in psychiatry and psychology. Even in psychiatry and psychology, the cases of certain patients are, first of all, considered based on the situation of the respective individual, and no clear-cut patterns

are applied, in spite of the tendency to bring generalizations into discussion. Any diagnosis is psychology and psychiatry may not fit a patient in every detail, as some features of the diagnosis may not be met. This makes each patient be, after all, a particular, individual case which should be considered and understood as such.

The human interaction with the psychotherapist is crucial in psychotherapy. Psychoanalysis especially emphasizes transference (Freud, 1994), which is considered to be the main, driving force in the success of the psychoanalytic cure. The patient's feelings of love for the analyst allow the resistances and defenses to be dropped, and to open in front of the therapist. Trust is significant in psychoanalysis, just as it is in other psychotherapies. The interaction with the analyst can help facilitate the cure and allow the patient for honesty and confession. The patient feels the need to be understood and to relate to the therapist.

There is, nowadays, a large amount of information, as all psychotherapies are presented for teh general public. Popular psychology articles raise awareness of various emotional issues we can come across and solutions for their solving. In addition, self-help books and podcasts, or other video materials, including the personal experiences of users who have been patients in psyhotherapy can be a starting point on self-exploration. At the same time, all the available information is not enough. Contact with a professional is required in severe cases. In addition, a professional can have a different perspective on an individual's problems than him or herself, first of all since he or she is a detached observer, and second of all, since he or she has professional and personal experience of working with themselves, as well as with other patients. What is more, at some point in our lives, we may feel the need to discuss with someone and ask for opinions on the various psychological issues we can confront ourselves in various life stages. We are social beings, and this is also visible when we confront ourselves with psychological problems. At some point, talking to a family member or friend may not be enough, just as simply reading about psychoanalysis as a method of help cannot be.

A patient feels the need to be listened to and understood, which is what a psychoanalyst and other mental health professionals could provide. Psychotherapists need to be not only good, empathetic listeners. They also need to be able to help through the talking cure their patients and offer them insight into their issues. In addition, patients need, in psychotherapy, to take an active role in order to offer the information for psychotherapists about their personal life context, as well as to further understand themselves what is going on with them.

Self-analysis may be a solution, however, eventually, a discussion with a professional can bring further insight into our personal issues. AI can be helpful in self-analysis and offer some landmarks, since it can offer the information we may look for and provide some guidelines, yet it is not enough. As patients, we have emotions, we have an unconscious dimension, and so do psychoanalysts. AI completely lacks these dimensions of life and can only mimick them. Eventually, this can prove to be a significant limitation.

When we have written dialogues based on looking for advice, dream interpretation, free association interpretation, speech or action errors, we need to keep in mind that it is not a real human being, and that it cannot have the same feelings and experience of life and with the unconscious like a human psychotherapist. We also need to consider that, while we may project on ChatGPT our needs to emotionally connect with someone, and while we may even think about our therapist, during the times we are not during the sessions, it cannot replace the genuine real person for which we develop feelings of transference during the sessions. We may imagine a real person typing the answers to our questions, yet even the written

dialogue can be limited, due to lack of non-verbal clues to the interaction with the other person. Eventually, we may be aware that AI is just a machine, and that our dialogue with it may be limited not only by the sets of information and database content available to it, but also by the way in personalizes our content for based on previous interactions with us, causing it to become, to some extent, biased and restricted to previous written exchanges.

3. CONCLUSIONS

- AI can be used as a tool in self-analysis, similarly to self-help books, and gathering information about psychotherapy.
- AI lacks the distinctly human dimensions of the unconscious, emotions, confronting with various life stages and their accompanying psychological dilemmas and crises, empathy, need for emotional closeness. It can, however, be good at mimicking these in conversation.
- AI can provide possibilities to exercise and imagine hypotheses to work with oursleves as patients or to trains as therapists, yet it has its limitations.
- Personal and emotional contact, based on both verbal and non-verbal communication, is significant for good psychotherapeutic results. The patient's body language and intonation cannot be analysed by AI as a human psychotherapist can. Visual contact also lacks in our interactions with AI.

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INVESTIGATING THE DRIVERS OF GLOBAL HEALTH INEQUITIES: A MULTIDISCIPLINARY STUDY OF ACCESS, POLICY, AND SOCIAL DETERMINANTS

ABSTRACT

Inequities in global healthcare systems reflect deeply rooted imbalances shaped by a range of social, economic, and policy-related factors. This review offers a multidisciplinary examination of these disparities, combining perspectives from social sciences, public health, and global policy studies. It investigates how systemic barriers—such as poverty, limited education, marginalization, and geographic isolation—restrict access to essential healthcare services and influence overall health outcomes. The discussion emphasizes the role of social determinants in shaping individual and community health, while also evaluating the effectiveness of global and national health policies in addressing these concerns. By comparing diverse healthcare models and case studies from both resource-rich and resource-limited regions, the review illustrates how inequality manifests in different settings. Examples include variations in healthcare infrastructure, workforce distribution, and policy prioritization, which collectively impact the equity of health service delivery. The analysis suggests that addressing these disparities calls for more than technical or clinical solutions. Sustainable progress depends on inclusive policymaking, equitable resource distribution, and culturally sensitive interventions. Moreover, the integration of social science research into healthcare planning is essential for understanding the broader context in which medical systems operate. This review advocates for a shift toward a more holistic, justice-oriented approach to health system reform—one that recognizes the interplay between biology, society, and governance in shaping global health outcomes.

Keywords: Health Inequities, Global Health Systems, Social Determinants of Health, Healthcare Access, Health Policy

INTRODUCTION

In contemporary global health discourse, inequities—systematic differences in health status and access to care remain persistent despite technological and clinical advancements. These disparities reflect underlying social injustices and structural constraints that disproportionately affect marginalized populations across geographic and socioeconomic divides (Marmot, 2015). Far from being incidental, health inequities manifest as outcomes of complex interactions between individual circumstances and the broader socio-political context.

Understanding the roots of health inequities requires moving beyond clinical or biomedical explanations to examine how healthcare access, policy environments, and social determinants coalesce to shape health trajectories (Solar & Irwin, 2010). This review offers a critical synthesis of literature that unpacks these domains, presenting a multidisciplinary framework essential for comprehending and ultimately addressing global health inequities.

LITERATURE REVIEW

Healthcare Access:

Beyond Mere Availability Access to healthcare encompasses more than the mere presence of services; it requires affordability, cultural acceptability, and adequate quality (Levesque et al., 2013). Populations burdened by poverty, rural isolation, or discrimination often face compounded barriers that impede utilization, resulting in unmet health needs (Syed et al., 2013). In many low- and middle-income countries, infrastructural deficiencies and workforce shortages exacerbate these challenges (Kruk et al., 2018). Even in affluent settings, systemic discrimination and implicit bias can limit equitable care delivery (Williams & Mohammed, 2013).

Health Policy:

Equity Through Governance and Implementation Health policies are foundational to equitable health systems. While universal health coverage (UHC) offers a normative goal, its translation into equitable outcomes is uneven and complicated by political, economic, and social realities (Tichenor et al., 2020). Fragmented governance, insufficient funding, and lack of participatory policy-making often hinder efforts to close equity gaps (McKee & Stuckler, 2019). Effective policy frameworks integrate social determinants considerations, emphasize inclusivity, and embed accountability mechanisms to ensure marginalized voices influence health system design (Gilson et al., 2018).

Social Determinants of Health:

Structural Foundations of Inequity The social determinants of health articulate how socioeconomic and environmental conditions are the bedrock upon which health disparities are built (Marmot et al., 2008). Income inequality, educational access, housing quality, and environmental exposures significantly shape health risks and outcomes (Braveman & Gottlieb, 2014). Intersectionality deepens this understanding by illustrating how overlapping identities such as race, gender, and class compound disadvantage (Bauer, 2014). A growing body of evidence underscores the necessity of multisectoral policies that address these fundamental drivers in tandem with healthcare interventions (Solar & Irwin, 2010).

METHODOLOGY

This study follows a rigorous systematic review methodology to collate and synthesize multidisciplinary research focused on global health inequities published between 2010 and 2025. Guided by frameworks outlined in academic standards (Paris Güncel Kitap, 2024), the process entailed:

- Comprehensive database searches across PubMed, Scopus, Web of Science, and Google Scholar using combinations of terms such as “global health inequities,” “healthcare access,” “health policy,” and “social determinants of health.”
- Inclusion of peer-reviewed empirical studies, systematic reviews, and policy analyses addressing key drivers of health disparities at international and national scales.
- Exclusion of non-peer-reviewed material, clinical studies not addressing systemic drivers, and articles lacking methodological rigor.
- Inductive thematic synthesis of extracted data to elucidate emergent themes related to access barriers, policy influence, and social determinants.
- Strict adherence to APA citation to ensure academic integrity.

RESEARCH AND FINDINGS

Persistent Barriers to Equitable Healthcare:

The review reveals that multifaceted barriers financial, geographic, cultural continue to undermine access globally. Rural populations and economically disadvantaged groups confront the steepest obstacles (Kruk et al., 2018). Emerging digital health strategies, including telemedicine, show promise but risk widening inequities if infrastructural and literacy gaps remain unaddressed (Robbins et al., 2021).

Policy Frameworks: Progress and Challenges

While UHC initiatives have made strides, they frequently fall short of addressing marginalized groups’ needs due to fragmented policies, limited funding, and inadequate stakeholder engagement (Balabanova et al., 2013). Countries achieving notable equity improvements typically embed health policy within broader social protection systems and foster transparent governance with community participation (Tichenor et al., 2020).

The Centrality of Social Determinants:

Income inequality, educational deprivation, environmental hazards, and social exclusion are identified as persistent, systemic drivers of health inequities (Braveman & Gottlieb, 2014). Intersectionality research demonstrates the cumulative disadvantage experienced by individuals inhabiting multiple marginalized identities (Bauer, 2014). Comprehensive approaches integrating social welfare, education, housing, and environmental policies alongside health reforms are increasingly recognized as necessary to meaningfully reduce disparities (Solar & Irwin, 2010).

CONCLUSION

Global health inequities are entrenched in complex, interacting social, political, and economic systems. Isolated health sector interventions are insufficient without addressing the broader social determinants and embedding equity within policy and governance frameworks. To advance health equity, a paradigm shift toward integrative, multisectoral

policies that prioritize marginalized populations and foster community engagement is imperative. Future research should focus on longitudinal evaluations of such integrated interventions and the adaptation of equity frameworks across diverse cultural and political contexts.

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ROLE OF IGF2 IN FIBROTIC RESPONSES TO HEPATIC CYSTIC ECHINOCOCCOSIS IN CATTLE

ABSTRACT

Objective:
This study aimed to evaluate the expression of insulin-like growth factor 2 (IGF2) and collagen type 1 (COL1) in bovine livers affected by cystic echinococcosis (CE) and to investigate their roles in fibrotic remodeling. To our knowledge, this is the first study demonstrating the localization of IGF2 not only in host-derived structures but also within *Echinococcus granulosus*-derived tissues, suggesting a parasite-driven modulation of host fibrosis.

Materials and Methods:

Liver samples from 12 naturally infected and 6 healthy cattle were evaluated. Histological staining (Masson's Trichrome) and immunohistochemical analysis using antibodies against IGF2 and COL1 were performed. Immunopositivity was assessed semi-quantitatively (0–3), and group comparisons were made using the Mann-Whitney U test ($p<0.05$).

Results:
While healthy livers showed minimal or no immunoreactivity, the CE group exhibited a significant increase in IGF2 and COL1 expressions ($p=0.0018$ and $p=0.0013$, respectively). IGF2 was strongly positive in multinucleated giant cells, fibrotic capsules, and notably within the parasite's laminar layer. COL1 was predominantly expressed in pericystic fibrotic regions. Masson's Trichrome staining confirmed extensive collagen accumulation around cysts.

Conclusion:
These results suggest that IGF2 and COL1 are actively involved in the fibrotic process in hepatic CE. The localization of IGF2 in both host and parasite structures highlights a potentially novel host-parasite interaction mechanism, where *E. granulosus* may exploit host growth factors to enhance fibrotic encapsulation and immune evasion.

Keywords: Echinococcus granulosus, IGF2, Collagen Type 1, Fibrosis, Immunohistochemistry

Introduction

Hepatic fibrosis is a pathological process characterized by the excessive accumulation of extracellular matrix (ECM) components, particularly collagen, in response to chronic liver injury of various etiologies including viral infections, toxins, and parasitic diseases (Bataller & Brenner, 2005). In the healthy liver, total collagen content is relatively low. Type I collagen fibers are confined to delicate perivascular networks surrounding the portal tracts (portal triads) and central veins, while type III collagen (reticulin fibers) predominates in the sinusoidal spaces, forming an essential part of the liver's normal microarchitecture (Baycumendur et al., 2022). Type I and III collagens together constitute approximately 60% of the hepatic collagen pool and are key matrix components involved in the fibrotic process. During early stages of fibrosis, their synthesis increases, and in advanced stages such as cirrhosis, dense type I collagen bands disrupt the hepatic lobular architecture (Niu et al., 2019).

Among the various fibrogenic mediators, insulin-like growth factor 2 (IGF2) has emerged as a crucial regulator. Through its interaction with IGF-1 receptors (IGF-1R) and insulin receptors (IR-A), IGF2 activates multiple signaling pathways including PI3K/Akt and JNK/c-Jun, thereby promoting fibroblast proliferation, inhibiting apoptosis, and enhancing the synthesis of ECM proteins such as collagen and fibronectin. Additionally, IGF2 modulates the MMP/TIMP balance and can activate CaMKIIδ/calcineurin and TGF-β signaling to further drive fibrosis (Zhu et al., 2022). Elevated expression of IGF2 has been reported in various fibrotic disorders, including liver cirrhosis (Hindin et al., 2013), idiopathic pulmonary fibrosis (Hu et al., 2014), and hypertrophic scars/keloids (Garrett et al., 2019).

Importantly, recent studies suggest that fibrogenic growth factors such as IGF2 may also play a significant role in parasitic diseases involving chronic liver inflammation and fibrosis, including cystic echinococcosis (CE). CE, caused by *Echinococcus granulosus* sensu lato, is a globally prevalent zoonotic helminthosis that predominantly affects the liver (Brunetti et al., 2010). Formation of fibrotic capsules around hydatid cysts is a hallmark of the chronic phase of CE, functioning both to contain the parasite and to facilitate immune evasion (Polat et al., 2003). Despite the known fibrotic remodeling in CE, the role of IGF2 in this process remains poorly characterized (Forbes & Cooper, 2013).

Our previous study demonstrated significant oxidative stress and tissue damage in bovine livers naturally infected with *E. granulosus*, indicating profound disruption of the hepatic microenvironment (Anteplioğlu et al., 2024). Building upon these findings, the present study aims to investigate the expression of IGF2 and collagen type I (COL1) in bovine livers with CE and explore their association with fibrotic responses.

Materials and Methods

Sample Collection

Liver samples were collected from 12 cattle with macroscopic hepatic hydatid cysts and 6 healthy controls at the municipal abattoir in Tokat/Zile. The tissue specimens were fixed in 10% neutral-buffered formalin and processed routinely for paraffin embedding.

Histological and Immunohistochemical Analysis

Serial sections of 4–5 µm thickness were obtained from paraffin blocks. For the demonstration of connective tissue, Masson's Trichrome staining was performed. Lesional areas were evaluated histologically, and microphotographs were captured using an Olympus BX51 microscope.

Immunohistochemical analyses were carried out using the indirect streptavidin-biotin peroxidase method with a commercial detection kit. Following deparaffinization, antigen retrieval was performed by heating the sections in citrate buffer (pH 6.0) in a microwave oven for 20 minutes, followed by cooling to room temperature. Endogenous peroxidase activity was blocked by incubating the sections in 3% hydrogen peroxide (H_2O_2) for 20 minutes at room temperature.

After blocking nonspecific binding, sections were incubated overnight at 4°C with primary antibodies against collagen type I (COL1) and insulin-like growth factor 2 (IGF2). Subsequently, secondary antibody and streptavidin-peroxidase steps were applied, and immunoreactivity was visualized using aminoethyl carbazole (AEC) chromogen. Mayer's hematoxylin was used as the counterstain, and sections were mounted with aqueous mounting medium.

For each sample, five randomly selected fields at 20× magnification were photographed and scored semi-quantitatively for staining intensity as follows: 0 = negative, 1 = mild, 2 = moderate, and 3 = strong.

Evaluation and Statistical Analysis

Immunohistochemical scores were statistically analyzed using the Mann–Whitney U test in SPSS 25.0 software. A p-value of <0.05 was considered statistically significant.

Results

Macroscopic and Histopathological Findings

Macroscopic examination of the infected livers revealed multiple, well-defined hydatid cysts filled with clear fluid and surrounded by thick fibrous capsules (Figure 1A). The cysts varied in size and were frequently located subcapsularly or within the parenchyma.

Masson's Trichrome staining demonstrated prominent fibrous capsule formation characterized by dense collagen accumulation around the hydatid cysts. The fibrotic areas appeared as intense blue staining, particularly in the pericystic zones (Figure 1B), confirming advanced fibrotic remodeling. Notably, multinucleated giant cells were frequently observed adjacent to the laminated layer and within the fibrotic capsule, reflecting a chronic granulomatous inflammatory response associated with the parasite.

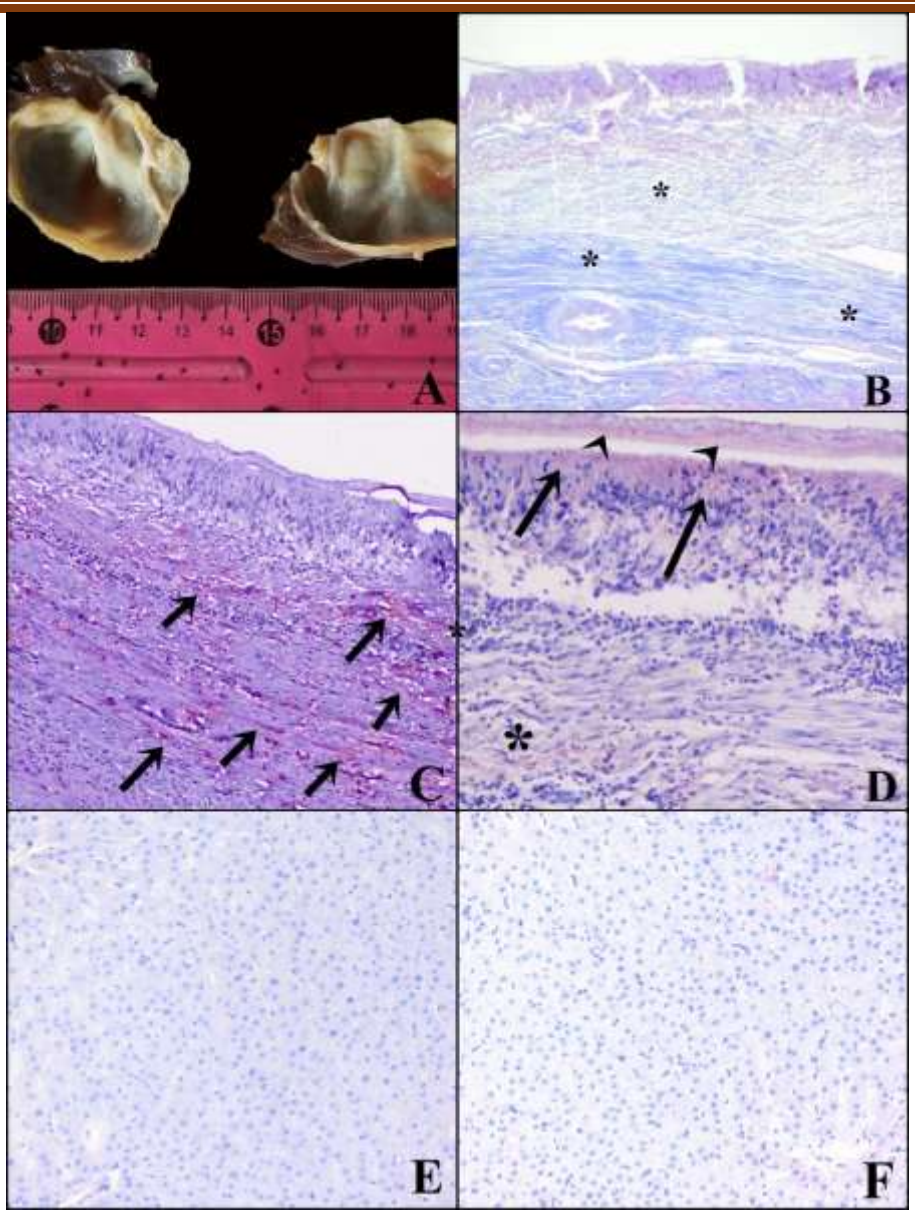


Figure 1. Macroscopic, histochemical, and immunohistochemical features of hepatic cystic echinococcosis in cattle. **(A)** Macroscopic view of two bovine livers harboring well-demarcated, fluid-filled hydatid cysts encapsulated by thick fibrous tissue. **(B)** Dense collagen deposition (blue) surrounding the cyst wall, indicating extensive pericystic fibrosis (asterisks). Masson's Trichrome staining, Magnification: 100X **(C)** Strong COL1 immunopositivity in the fibrotic capsule surrounding the cysts (arrows) in the infected liver. IHC. AEC chromogen with hematoxylin counterstain. Magnification: 200X **(D)** Intense IGF2 immunopositivity in inflammatory cells (arrows), the parasite-derived laminar layer (arrowheads), and the surrounding fibrotic tissue (*). IHC. AEC chromogen with hematoxylin counterstain. Magnification: 400X **(E)** COL1 expression was nearly absent in healthy liver, limited to occasional portal fibroblasts. IHC. AEC chromogen with hematoxylin counterstain. Magnification: 400X **(F)** Mild IGF2 immunoreactivity in hepatocytes of healthy liver tissue. IHC. AEC chromogen with hematoxylin counterstain. Magnification: 400X.

Immunohistochemical Findings

In the infected liver sections, COL1 immunoreactivity was markedly increased and primarily localized in the pericystic fibrotic capsules, appearing as strong cytoplasmic staining in fibroblasts and stromal cells (Figure 1C). IGF2 expression was also elevated in the infected group, predominantly observed in inflammatory cell populations within the fibrotic areas, and notably in the parasite's laminar layer (Figure 1D).

In contrast, the healthy liver tissues showed minimal to absent staining for both markers. COL1 was barely detectable in the portal areas (Figure 1E), while IGF2 expression was weak or completely absent in hepatocytes (Figure 1F).

Semi-quantitative scoring revealed a statistically significant increase in both IGF2 and COL1 expressions in the infected group compared to healthy controls (p=0.0018 and p=0.0013, respectively) (Table 1, Figure 2).

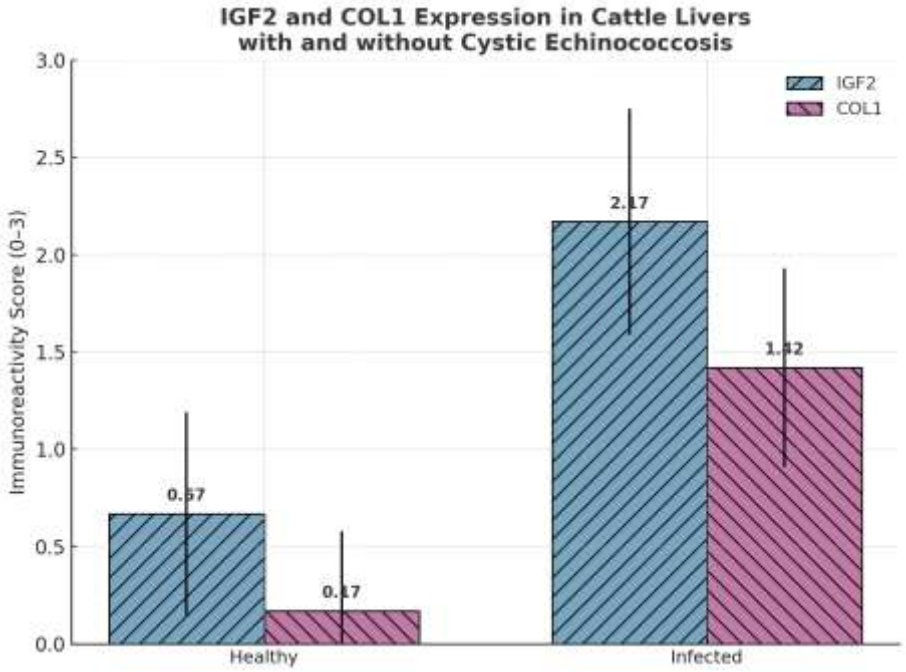


Figure 2. Semi-quantitative immunoreactivity scores for IGF2 and COL1 in healthy and infected bovine liver tissues.

Table 1. Semi-quantitative immunohistochemical scores (mean ± standard deviation) of IGF2 and COL1 expression in healthy and Echinococcus granulosus-infected bovine liver tissues.

Group	*n*	*IGF2 (Mean ± SD)*	*COL1 (Mean ± SD)*	*p (IGF2)*	*p (COL1)*
Healthy	6	0.67 ± 0.52	0.17 ± 0.41	0.0018	0.0013
Infected	12	2.17 ± 0.58	1.42 ± 0.51	—	—

Discussion

The fibrotic response in cystic echinococcosis (CE) can vary significantly among intermediate hosts. In cattle, hydatid cysts are often sterile and surrounded by a markedly thick fibrotic capsule, which is believed to impair parasite viability and lead to cyst degeneration or calcification over time (De Biase et al., 2023). This intense fibrotic reaction has been interpreted as a host defense mechanism that restricts parasite development. In contrast, in more permissive hosts such as sheep, the immune response tends to be more tolerogenic, allowing for larger, fertile cysts with thinner fibrotic walls (Hidalgo et al., 2019; Hidalgo et al., 2021). Therefore, in bovine CE, fibrosis—especially characterized by type I collagen deposition—may represent a critical barrier to cyst maturation.

Type I collagen (COL1) is both a product and a driver of fibrosis. Once fibrogenesis is initiated, activated fibroblasts (myofibroblasts) secrete large quantities of COL1 into the extracellular space, contributing to scar formation and disrupting normal tissue architecture, ultimately impairing organ function (Klingberg et al., 2013). In the present study, COL1 immunoreactivity was clearly demonstrated within the fibrotic capsule surrounding the cysts, confirming its pivotal role in fibrotic remodeling. Moreover, IGF2 immunopositivity was frequently co-localized in these areas, suggesting a possible interaction between collagen production and growth factor signaling in the fibrotic microenvironment.

Fibrosis during hydatid cyst development is generally regarded as part of the host's effort to isolate and neutralize the parasite. As the cyst expands, fibroblasts and mononuclear cells in the surrounding liver tissue are stimulated—particularly through fibrogenic cytokines such as TGF-β—to produce increasing amounts of collagen. TGF-β/Smad signaling pathways have been shown to play a central role in this process by upregulating COL1 expression in pericystic regions (Niu et al., 2019). Interestingly, Echinococcus granulosus appears capable of manipulating this fibrotic response. For example, it has been demonstrated that hydatid cyst fluid can suppress hepatic expression of miR-19, a microRNA that normally inhibits TGF-β receptor II. This suppression leads to excessive TGF-β signaling and exacerbates fibrosis (Zhang et al., 2016). In our study, IGF2 immunopositivity was not only evident in the inflammatory cells but also clearly present in the parasite-derived laminated layer, supporting the idea that the parasite may contribute to the modulation of host fibrogenesis.

Our findings confirm a significant upregulation of both IGF2 and COL1 in bovine livers with CE. IGF2 expression was especially notable in fibrotic zones, where it was observed in host fibroinflammatory cells and parasite structures. This dual localization is indicative of a complex host-parasite interaction in which IGF2 may act as a regulatory molecule promoting extracellular matrix deposition and tissue remodeling. Previous research has reported altered circulating levels of IGFs in human patients with hepatic CE. For instance, patients with liver-localized hydatid cysts were found to have significantly reduced serum levels of IGF-I and IGF-II compared to healthy controls (Nedic et al., 2003). However, to the best of our knowledge, the current study is the first to demonstrate IGF2 immunoreactivity within fibrotic hepatic tissues in naturally infected cattle.

Our previous work had demonstrated elevated oxidative stress markers and tissue injury in bovine hepatic CE (Anteplioğlu et al., 2024). Building upon these findings, we now provide evidence that growth factor activity, specifically IGF2, may be actively involved in driving the fibrotic remodeling process that contributes to cyst containment and chronicity. IGF2 has been widely studied in oncogenesis and fibrosis. In cancers such as hepatocellular carcinoma and colorectal and lung cancers, IGF2 overexpression supports tumor growth and survival

(Forbes & Cooper, 2013). Similarly, in chronic fibrotic diseases of the liver, lung, and kidney, IGF2 contributes to fibroblast proliferation and extracellular matrix deposition. Our current findings further support its critical role in fibrogenesis during CE.

The correlation between IGF2 expression and pericystic fibrotic regions reinforces the hypothesis that growth factors are not merely bystanders but may be co-opted by the parasite to maintain its niche within the host liver. Thus, IGF2 may serve as both a marker and a mediator of parasite-induced fibrosis.

Interestingly, the presence of IGF2 within the parasite's laminated layer may not be incidental but rather indicative of a parasite-driven strategy to manipulate the host tissue microenvironment. One plausible explanation is that increased IGF2 expression facilitates fibrotic capsule formation, which, while limiting parasite dissemination, paradoxically supports its long-term survival by establishing a stable, immunoprivileged niche. The dense collagen matrix may act as a physical barrier that restricts immune cell infiltration and antigen presentation, thereby aiding immune evasion. Additionally, fibrosis-associated tissue remodeling may enhance angiogenesis and alter local nutrient gradients, providing the parasite with sustained access to host-derived nutrients. Furthermore, IGF2-mediated signaling may downregulate pro-inflammatory pathways and modulate fibroblast-immune cell interactions, contributing to a more tolerogenic microenvironment. These speculative but biologically plausible mechanisms suggest that E. granulosus may actively promote IGF2 expression as part of a multifaceted survival strategy within hepatic tissue.

Conclusion

This study highlights the significant roles of IGF2 and COL1 in the fibrotic response to hepatic cystic echinococcosis in cattle. The detection of IGF2 within both host immune cells and parasite-derived structures suggests that *E. granulosus* may exploit host growth factor signaling to sustain fibrotic capsule formation, promoting its persistence within the liver. These findings point to the potential of IGF2 as a therapeutic target in parasitic liver fibrosis. Future studies should further explore the mechanistic role of IGF2 in host-parasite interactions and its utility as a biomarker or interventional molecule in echinococcosis-related fibrosis.

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TRIPLE PATHOLOGY: A RARE CASE OF INTERSECTION OF APLASTIC ANEMIA, CHRONIC HEPATITIS B AND ORAL LICHEN PLANUS

ABSTRACT

Purpose: This case report aims to present the clinical progression and histopathological findings of a 41-year-old female patient diagnosed with aplastic anemia, chronic hepatitis B, and oral lichen planus. The purpose is to explore the potential immunopathogenic links among these conditions and to emphasize the importance of interdisciplinary monitoring.

Material and Method: Clinical data were collected retrospectively from the patient's hospital records, including hematological parameters, virological and serological tests, liver and oral mucosal biopsies, and follow-up assessments from 2012 to 2024. Histological analyses were reviewed for diagnostic confirmation.

Findings: A bone marrow biopsy performed in 2012 revealed severe hypocellularity, erythroid predominance, and mild T-cell increase, consistent with aplastic anemia. Persistently positive HBsAg confirmed chronic hepatitis B, elevated HBV DNA (34,443 IU/mL), and liver biopsy showing moderate interface hepatitis and mild fibrosis (HAI 8/18, Ishak stage 1/6). In 2023, the patient developed painful papular lesions on the ventral tongue; a biopsy confirmed oral lichen planus with reactive atypia and ulceration. The patient had no active symptoms under antiviral treatment (Sebivo) and remained under regular hematological and hepatological surveillance.

Conclusion: This rare triad illustrates the interplay between chronic viral infection, immune dysregulation, and mucocutaneous pathology. Clinicians should be vigilant about systemic immune-related manifestations in patients with chronic hepatitis B. Long-term interdisciplinary follow-up is essential to monitor disease progression and manage complications effectively.

Keywords: Aplastic anemia, Chronic hepatitis B, Oral lichen planus, Immune-mediated disease

INTRODUCTION

Aplastic anemia is a rare but life-threatening hematologic disorder characterized by bone marrow failure and resultant pancytopenia, which manifests as fatigue, weakness, susceptibility to infections, and bleeding tendencies. Its incidence is estimated at 2 to 5 cases per million individuals annually[1]. The coexistence of aplastic anemia with chronic hepatitis B virus (HBV) infection and oral lichen planus (OLP) is exceptionally uncommon and has been documented only in isolated case reports[2].

Chronic hepatitis B is a widespread viral infection affecting over 250 million people globally. It is associated with significant hepatic morbidity, including cirrhosis and hepatocellular carcinoma, and may also present with systemic and extrahepatic manifestations[3]. In particular, HBV-related immune dysregulation has been implicated in the development of hematologic abnormalities, including aplastic anemia[4]. This relationship is hypothesized to stem from chronic antigenic stimulation and resultant immune-mediated marrow suppression.

OLP is a chronic, immune-mediated inflammatory condition of the oral mucosa, often regarded as a potentially premalignant disorder[5], (Figure 1). Although the etiology remains multifactorial, several studies suggest a potential link between OLP and viral infections, particularly HBV[2]. Geographic variation in the prevalence of HBV among OLP patients supports this association: for example, 6.71% of OLP patients in Iran[4] and 8.8% in Saudi Arabia were found to be HBsAg-positive[6], while studies from India and Syria have reported no significant correlation, indicating potential regional and genetic factors in pathogenesis[7].

The diagnosis of HBV in patients with OLP relies on serological testing, including HBsAg and HBV-DNA assessments. However, the absence of standardized screening protocols in some regions may contribute to underdiagnosis, and the clinical overlap in mucocutaneous symptoms between OLP and HBV-related manifestations can complicate the diagnostic process[2].

Although aplastic anemia, chronic hepatitis B, and oral lichen planus can each present independently, their concurrent appearance in a single patient suggests a possible shared immunopathogenic mechanism. The present case report describes a 41-year-old female diagnosed with all three conditions. This report aims to explore the clinical course, diagnostic complexities, and potential pathophysiological links among these entities, emphasizing the importance of comprehensive, multidisciplinary management in such complex clinical presentations.



Figure 1. Oral lichen planus in the oris cavity

CASE PRESENTATION

A 41-year-old female patient presented with a complex medical history that includes aplastic anemia, chronic HBV infection, and OLP.

The patient's clinical trajectory began in 2012 when she was evaluated as a potential hematopoietic stem cell donor for her brother, who had been diagnosed with aplastic anemia. During the evaluation, bone marrow biopsy (BMB) revealed a markedly hypocellular marrow, predominating erythroid lineage, mild T-cell proliferation, and dysplastic features in the granulocytic and erythroid series. The findings were consistent with a diagnosis of aplastic anemia. The patient had no significant hematologic symptoms at that time but was placed under regular hematologic monitoring.

In 2013, further laboratory workup revealed positive HBsAg, positive anti-HBe, negative HBeAg, and a high HBV DNA viral load (34,443 IU/mL), indicating chronic active hepatitis B. Liver biopsy performed the same year demonstrated moderate interface hepatitis, portal inflammation, focal necrosis, and mild fibrosis (Histological Activity Index: 8/18; Ishak Fibrosis Stage: 1/6). Immunohistochemical staining was positive for HBsAg, confirming the chronicity of the infection. She was initiated on Sebivo (telbivudine) therapy and remained clinically stable without hepatic decompensation.

In 2023, the patient reported the emergence of erythematous papular lesions on the ventral surface of the tongue. An oral mucosal biopsy confirmed the diagnosis of oral lichen planus, characterized by reactive atypia and ulceration. No signs of dysplasia or malignancy were

observed. The patient denied significant pain or systemic symptoms but noted mild local discomfort.

The patient remained under routine hepatology and hematology care throughout the follow-up period. She had no history of recent transfusions, immunosuppressive therapy, or other autoimmune diseases. Laboratory parameters showed mild cytopenias without progressive marrow failure. She did not report any recent infections or constitutional symptoms.

The coexistence of aplastic anemia, chronic HBV infection, and OLP in this patient underscores the potential interplay between viral infection and immune-mediated pathology. Her case illustrates the importance of multidisciplinary monitoring to manage overlapping systemic, hepatic, hematologic, and mucosal complications.

RESEARCH AND FINDINGS

This case presents a unique intersection of three distinct yet potentially interrelated conditions: aplastic anemia, chronic hepatitis B infection, and oral lichen planus. A retrospective review of the patient's clinical and histopathological data from 2012 to 2024 provides insight into these comorbidities' temporal and pathological development.

Hematologic Findings: The initial bone marrow biopsy, conducted in 2012 during a routine donor screening, revealed markedly hypocellular marrow with a relative erythroid predominance, mild T-lymphocytic proliferation, and evidence of dysmorphic changes in granulocytic and erythroid series. Plasma cell infiltration was low (1%), and no leukemic transformation or clonal hematologic malignancy was identified. These findings fulfilled the diagnostic criteria for aplastic anemia. Hematological indices remained relatively stable, with no significant progression in cytopenias or transfusion requirements.

Hepatic Findings: In 2013, the patient tested positive for hepatitis B surface antigen (HBsAg), with concurrent anti-HBe positivity and elevated HBV DNA levels (34,443 IU/mL). A liver biopsy confirmed the diagnosis of chronic hepatitis B, revealing moderate interface hepatitis, focal necrosis, and mild periportal fibrosis (Ishak stage 1/6, HAI 8/18). Immunohistochemical analysis showed HBsAg positivity in hepatocytes, consistent with ongoing viral activity. The patient was initiated on antiviral therapy (telbivudine), with biochemical and virologic responses monitored during follow-up. She exhibited no signs of cirrhosis or hepatic decompensation.

Oral Mucosal Findings: In early 2023, the patient reported the development of erythematous and ulcerated papular lesions on the ventral surface of the tongue. Histopathological evaluation of an oral mucosal biopsy demonstrated classic features of oral lichen planus, including band-like lymphocytic infiltration, basal cell degeneration, and saw-tooth rete ridges, accompanied by reactive atypia and localized ulceration. No evidence of epithelial dysplasia or malignancy was observed.

Interdisciplinary Interpretation: The co-occurrence of these three conditions raises the possibility of a shared immunopathological mechanism. Chronic HBV infection has been implicated in both hematologic and mucocutaneous immune dysregulation, and the development of aplastic anemia in HBV-positive patients is thought to be associated with immune-mediated suppression of hematopoiesis. Similarly, oral lichen planus is a T-cell-mediated autoimmune disorder that has been reported with higher frequency in patients with HBV, particularly in regions with endemic viral prevalence[8].

In this case, the temporal onset of aplastic anemia preceded the diagnosis of chronic hepatitis B and oral lichen planus, suggesting a potential latent immunological predisposition that may have been amplified by persistent viral antigenic stimulation. Despite the presence of three immune-mediated conditions, the long-term stability of hematologic and hepatic function highlights the value of consistent monitoring and integrated care across specialties.

DISCUSSION

Hepatitis-associated aplastic anemia (HAAA) is a rare condition characterized by the development of bone marrow failure following an episode of acute hepatitis. The clinical manifestations of HAAA include pancytopenia, a reduction in the number of red and white blood cells and platelets, leading to symptoms such as anemia, infections, and bleeding. The onset of aplastic anemia typically occurs within a few months after the hepatitis episode, and the condition is often severe and life-threatening if left untreated[9]. In terms of liver involvement, patients with HAAA often present with jaundice and liver injury, as indicated by elevated liver enzymes and bilirubin levels. However, the severity of the hepatitis does not correlate with the severity of aplastic anemia[9,10].

On the other hand, OLP is a chronic inflammatory condition that affects the mucous membranes inside the mouth. White, lacy patches, red, inflamed tissues, or open sores characterize it. These lesions can cause pain or burning, especially when eating spicy, hot, or acidic foods[10]. HAAA is a rare condition, accounting for approximately 1-5% of all aplastic anemia cases. It is more common in young males, and the onset of aplastic anemia typically occurs within a few months after an episode of acute hepatitis. The condition is often associated with seronegative hepatitis, and the exact viral etiology is frequently unknown[9-11]. Chronic hepatitis B is a significant public health problem worldwide, with a higher prevalence in certain regions. The association between chronic hepatitis B and aplastic anemia is not well-established. Still, there have been reports of aplastic anemia occurring in patients with chronic hepatitis B, suggesting a possible link between the two conditions[9,10].

OLP is a relatively common condition, with a prevalence of approximately 0.5-2% in the general population. It is more common in middle-aged individuals and is often associated with autoimmune conditions such as hepatitis C and thyroid disease. The exact etiology of OLP is not fully understood, but it is believed to involve immune-mediated mechanisms[10]. The pathophysiology of HAAA is believed to involve immune-mediated mechanisms, where an abnormal immune response to a viral trigger leads to the destruction of hematopoietic stem cells in the bone marrow. This immune dysregulation is thought to be responsible for the development of aplastic anemia following an episode of hepatitis. The immune response is characterized by the activation of T lymphocytes, which play a central role in destroying bone marrow cells[9].

In chronic hepatitis B, the immune response to the virus can lead to liver inflammation and damage. The exact mechanisms by which chronic hepatitis B may contribute to the development of aplastic anemia are not well understood. Still, the immune dysregulation associated with chronic hepatitis B may play a role in the development of aplastic anemia in some patients [9,12].

OLP is also believed to involve immune-mediated mechanisms, where an abnormal immune response leads to the inflammation and damage of mucous membranes. The condition is

often associated with autoimmune diseases, and immune dysregulation may contribute to developing OLP in some patients[13].

CONCLUSION

The intersection of aplastic anemia, chronic hepatitis B, and oral lichen planus is a complex area of research that involves immune-mediated mechanisms and significant clinical challenges. Treating these conditions requires a multidisciplinary approach, and further research is needed to understand the underlying pathophysiological mechanisms and develop more effective treatment strategies.

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THE ROLE OF INSPIRATORY MUSCLE TRAINING SUPPORTED BY MANUAL THERAPY IN IMPROVING POSTURE AND FUNCTIONAL MOBILITY IN NEUROMUSCULAR DISEASES

ABSTRACT

Objective: In neuromuscular diseases, respiratory muscles are affected. Respiratory problems become inevitable due to progressive intercostal and diaphragmatic muscle weakness. Many factors, such as the loss of functional muscle tissue, disuse of muscles, and cardiopulmonary involvement, also lead to a decrease in balance and functional mobility. In addition, postural changes related to progressive muscle involvement are observed. These postural changes cause rigidity of the chest wall, limiting its expansion. In the literature, it has been reported that respiratory muscle training is effective in neuromuscular diseases; however, excessive loading may increase muscle damage. For maximal effect, the optimal length-tension relationship in the respiratory muscles can be achieved through manual therapy, making respiratory muscle training more effective. In light of this information, we investigated the effect of inspiratory muscle training combined with manual therapy on functional mobility and posture in neuromuscular disease.

Materials and Methods: The study was conducted with 28 patients aged between 7-18 years who were being followed up with a diagnosis of neuromuscular disease and met the inclusion criteria. The patients were randomly divided into two groups with equal numbers. In the intervention group, inspiratory muscle training combined with manual therapy was added to the conventional physiotherapy program. Manual therapy techniques were applied three times a week, and respiratory muscle training was performed twice a day, five days a week, for a duration of six weeks. The control group received only the conventional physiotherapy program. Assessments were conducted before and after the treatment. Posture was evaluated using the Corbin Posture Scale, functional mobility was assessed with the Timed Up and Go (TUG) test, and balance was assessed by Berg Balance Test.

Results: In the intervention group, a statistically significant decrease was observed in the mean score of the Corbin Posture Scale after treatment ($p<0.001$). In the control group, an increase was observed in the mean score of the Corbin Posture Scale ($p>0.05$). In the TUG measurements, the mean completion time in the intervention group decreased from 27.79 seconds to 23.79 seconds ($p<0.001$). In the control group, a statistically insignificant increase

was observed ($p>0.05$). While the total Berg Balance Test score of the intervention group increased ($p<0,01$), the total score of the control group decreased ($p<0,05$).

Conclusion: It was observed that inspiratory muscle training combined with manual therapy was more effective and beneficial for posture, balance and functional mobility compared to the conventional method in neuromuscular diseases. This approach may contribute to the development of different therapeutic strategies by physiotherapists in rehabilitation and to the enhancement of treatment effectiveness.

Keywords: Neuromuscular Disease, Inspiratory muscle training, Manual therapy, Posture, Functional Mobility

NÖROMUSKÜLER HASTALIKLARDA POSTÜR VE FONKSİYONEL MOBİLİTE GELİŞTİRİLMESİNDE MANUEL TERAPİ İLE DESTEKLENEN İNSPİRATUAR KAS EĞİTİMİNİN ROLÜ

ÖZET

Amaç: Nöromusküler hastalıklarda solunum kasları etkilenmektedir. İlerleyici interkostal ve diyafragmatik kas zayıflığı nedeniyle solunum problemleri kaçınılmaz hale gelir. Fonksiyonel kas dokusu kaybı, kasların kullanılmaması ve kardiyopulmoner tutulum gibi birçok faktör, denge ve fonksiyonel mobilitede azalmaya da yol açar. Ayrıca, ilerleyici kas tutulumu ile ilişkili postüral değişiklikler gözlenmektedir. Bu postüral değişiklikler göğüs duvarında rijiditeye neden olarak ekspansiyonunu sınırlar. Literatürde, solunum kas eğitiminin nöromusküler hastalıklarda etkili olduğu bildirilmiştir; ancak, aşırı yüklenme kas hasarını artırabilir. Maksimum etki için, solunum kaslarında optimal uzunluk-gerilim ilişkisi manuel terapi yoluyla sağlanarak solunum kas eğitiminin daha etkili hale gelmesi mümkün olabilir. Bu bilgiler doğrultusunda, nöromusküler hastalıklarda manuel terapi ile kombine edilen inspiratuvar kas eğitiminin fonksiyonel mobilite ve postür üzerindeki etkisini araştırdık**.**

Gereç ve Yöntem: Çalışma, nöromusküler hastalık tanısı ile takip edilen ve dahil edilme kriterlerini karşılayan 7-18 yaş arası 28 hasta ile yürütüldü. Hastalar rastgele ve eşit sayıda iki gruba ayrıldı. Çalışma grubunda, konvansiyonel fizyoterapi programına ek olarak manuel terapi ile kombine inspiratuvar kas eğitimi uygulandı. Manuel terapi teknikleri haftada üç kez, solunum kas eğitimi ise haftada beş gün, günde iki kez olmak üzere altı hafta boyunca uygulandı. Kontrol grubuna yalnızca konvansiyonel fizyoterapi programı verildi. Değerlendirmeler tedavi öncesi ve sonrası yapıldı. Postür, Corbin Postür Ölçeği ile; fonksiyonel mobilite, Timed Up and Go (TUG) testi ile; denge ise Berg Denge Ölçeği ile değerlendirildi.

Bulgular: Müdahale grubunda, tedavi sonrasında Corbin Postür Ölçeği ortalama skorunda istatistiksel olarak anlamlı bir azalma gözlendi ($p<0.001$). Kontrol grubunda ise ortalama skor artış gösterdi ($p>0.05$). TUG ölçümlerinde, müdahale grubunun ortalama tamamlanma süresi 27.79 saniyeden 23.79 saniyeye düştü ($p<0.001$). Kontrol grubunda istatistiksel olarak anlamlı olmayan bir artış gözlendi ($p>0.05$). Müdahale grubunun toplam Berg Denge Ölçeği puanı artarken ($p<0,01$), kontrol grubunun toplam puanı azaldı ($p<0,05$).

Sonuç: Nöromüsküler hastalıklarda, manuel terapi ile kombine edilen inspiratuvar kas eğitiminin, postür, denge ve fonksiyonel mobilite açısından konvansiyonel yönteme kıyasla daha etkili ve faydalı olduğu gözlemlenmiştir. Bu yaklaşım, fizyoterapistlerin rehabilitasyonda farklı tedavi stratejileri geliştirmelerine ve tedavi etkinliğinin artırılmasına katkı sağlayabilir**.**

Anahtar Kelimeler: Nöromusküler Hastalık, Inspiratuvar Kas Eğitimi, Manuel Terapi, Postür, Fonksiyonel Mobilite

GİRİŞ

Nöromusküler hastalıklar kaslarda görülen ilerleyici kuvvet kaybı ve atrofi ile karakterize kalıtsal veya sonradan gelişen bir hastalık grubudur. Ön boynuz motor hücrelerinde, nöromusküler kavşakta, periferik sinirlerde veya kastaki anormallikler neden olmaktadır (1).İlerleyici kas kuvveti kaybı ve solunum fonksiyonlarının bozulması kas hastalıklarında en sık görülen semptomlardır (2,3). Hastalığın prognozunu etkileyen diğer semptomlar ise postüral deformiteler, ağrı, aktivite limitasyonları, yorgunluk, egzersiz kapasitesinde azalmaya kadar geniş bir yelpazeyi kapsar (4). Tam iyileşmeyi sağlayan tedavi yöntemi henüz yoktur. Başlangıç yaşı da hastalığın ilerleyişinde önemli bir faktör olmakla birlikte nöromusküler hastalıklarda solunum yetmezliği solunum bakımındaki gelişmelerden önce başlıca morbidite ve mortalite nedeniydi (5,6). Son yıllarda kaydedilen koruyucu ve destekleyici solunumsal müdahalelerdeki gelişmelere rağmen nöromusküler hastalıkların çoğunda solunum komplikasyonları gelişmesi önlenememektedir (7).

Nöromusküler hastalıklar solunum kaslarında kuvvet kaybına neden oldukları için solunum problemlerine yol açmaktadır (8). Hastalığın ilerleyen dönemlerinde solunum problemleri ile ilişkili fonksiyon kaybı meydana gelmektedir (9). İnspiratuar kaslarda gelişen güç kaybı ve tendon, ligamentlerdeki sertlik sonucu göğüs duvarı ve akciğer kompliyansında azalma gelişebilmektedir (10). Bu hastalarda solunum kas kuvvetindeki kayıp, göğüs duvarı ve akciğer kompliyansındaki azalmaya, hiperkapninin ve hipokseminin de eklenmesiyle solunum iş yükü artmaktadır (11). Hastalarda progresif kas tutulumuna bağlı olarak postür değişiklikleri de görülmektedir. Bununla birlikte ilerleyen evrelerde göğüs kafesinin ve omurganın ligaman ve tendonlarında gelişen sertlik ve skolyoza bağlı olarak göğüs duvarı kompliyansı azalır. Bu postural değişiklikler göğüs duvarında rijiditeye yol açarak ekspansiyonunu limitlemektedir (12,13). Göğüs duvarının mobilitesinin arttırılması solunum kasları için gerekli olan optimal uzunluğun elde edilmesine ve daha fazla kuvvet ortaya çıkarılmasına yardımcı olacaktır (14). Solunum kas eğitimi sadece dispne gibi akciğer sonuçlarını iyileştirmede değil, aynı zamanda solunum fonksiyonel kapasiteyi ve egzersiz toleransını artırmadır. Ek olarak, çalışmalar solunum kas eğitiminin sağlıklı bireyler, kronik obstrüktif akciğer hastalığı (KOAH) ve inmede diyaframın bel omurlarına bağlanması nedeniyle üst ekstremite hareketleri sırasında mekanik stabilizasyon sağladığı ve karın içi basıncını artırarak bel omurgasını stabilize ederek dengeyi iyileştirdiği gösterilmiştir. Birçok çalışmadan elde edilen sonuçlar, KOAH, yaşlı yetişkinler ve inmede gövde stabilitesi ile dengede artışlar olduğunu göstermektedir (15-18). Aynı zamanda hastanın denge ve hareketlilik yönlerini de geliştirerek genel sağlıklarını iyileştirir.

Solunum kas eğitiminin dispne, akciğer fonksiyonu, inspiratuar kas gücü ve yaşam kalitesi üzerindeki etkilerini değerlendirmek için çok sayıda sistematik inceleme ve meta-analiz yürütülmüştür. Ancak solunum kas eğitiminin işlevsel hareketliliği ve dengeyi hangi hasta grubunda ne ölçüde iyileştirdiği henüz tam olarak belirlenmemiştir (19). Literatürde nöromusküler hastalıklarda solunum kas eğitiminin önemli ve etkili olduğu bildirilmiştir. Ancak egzersiz sırasında fazla yükleme kas harabiyetini arttırabildiği de yapılan çalışmalarda bildirilmektedir (20). Bu nedenle aşırı yüklenme olmadan maksimal etkiyi oluşturabilmek için solunum kaslarında optimal uzunluk-gerilim ilişkisini manuel terapi yaklaşımı ile sağlayıp solunum kas eğitimini daha etkili hale getirebilir. Literatüre baktığımızda nöromusküler hastalıklarda solunum kas eğitiminin fonksiyonel mobilite, denge ve postür üzerine etkisini değerlendiren bir çalışmaya rastlanmamıştır. Biz de bu bilgiler ışığında çalışmamızda nöromusküler hastalıklarda manuel terapi ile birlikte yapılan

inspiratuar kas eğitiminin postür, dinamik denge ve fonksiyonel mobilite üzerine etkisini araştırmayı amaçladık.

YÖNTEM

Prospektif, randomize, kontrollü, çift kör bir çalışma gerçekleştirildi. Çalışmanın etik kurul onayı İstinye Üniversitesi İnsan Araştırmaları Etik Kurulu tarafından verildi. Helsinki Bildirgesi, İyi Klinik Uygulamaları kılavuzuna uygun olarak yürütüldü. Araştırmaya katılacak tüm hastalardan çalışmayla ilgili bilgilendirilmiş ve aydınlatılmış onam formu alındı. Randomizasyon, web tabanlı bir bilgisayar programı tarafından oluşturulan bir randomizasyon tablosu kullanılarak yapıldı. Katılımcılar 1:1 oranında çalışma ve kontrol grubuna atandı. Hastaların değerlendirmesi ve müdahaleleri farklı bir araştırmacı tarafından gerçekleştirildi.

Çalışma nöromusküler hastalık tanısı almış, dahil edilme kriterlerini sağlayan hastalar ile gerçekleştirildi. Çalışmanın örneklem büyüklüğü hesaplanırken Power (G-Power) analizi kullanıldı. İki taraflı bir güven aralığı ile bir örneklem boyutu hesaplandı. Örneklem büyüklüğünü belirlemek için çift yönlü hipotez kurulduğunda, %80 güç ve 0.05 tip1 hata, orta düzey etki büyüklüğü (effect size=0.40) ile gruplar arasındaki farkı tespit edebilmek için çalışmaya her bir grupta kontrol grubu (14 kişi) ve çalışma grubunda (14 kişi) olmak üzere toplam 28 kişinin dahil edilmesi gerektiği bulundu. Çalışma grubuna konvansiyonel fizyoterapi yöntemlerine ek olarak manuel terapi ile birlikte inspiratuar solunum kas eğitimi uygulandı. Kontrol grubuna ise konvansiyonel fizyoterapi yöntemleri uygulandı.

Araştırmaya dahil olma kriterleri 7-18 yaş aralığında olmak, nöromusküler hastalık tanısı almış olmak, gönüllü olmak, koopere olmak, işitme güçlüğü ve görme kaybının olmaması, ambule olmak; araştırmaya hariç olma kriterleri ise solunum yolu enfeksiyonunun olması, ciddi kardiyak probleme sahip olması, toraks çevresinde fraktür olması şeklinde belirlendi.

Sonuç Ölçümleri

Çalışmaya dahil edilen tüm hastaların demografik, klinik ve kişisel özellikleri kaydedildi. Hastaların özgeçmiş ve soygeçmiş bilgileri, egzersiz alışkanlığı, eşlik eden hastalıkları, kullanılan ilaçlar, oksijen desteği alıp almadığı kaydedildi. Solunum semptomların varlığı sorgulanıp kaydedildi. Çalışmadaki tüm değerlendirmeler ATS kriterlerine uygun olarak gerçekleştirilmiştir

Postür değerlendirilmesi: Corbin Postür Ölçeği kullanıldı. Postüral anomalinin puanlanması (0:yok, 1:hafif, 2:orta, 3:şiddetli) olarak yapıldı. Lateral ve posteriorden bakılarak değerlendirilen postüral puanlar toplanıp (0-2: mükemmel, 3-4: çok iyi, 5-7: iyi, 8-11: orta, 12≥ kötü) kaydedildi (21).

Zamanlı kalk ve yürü testi (TUG): Dinamik dengenin ve fonksiyonel mobilitenin ölçülmesinde kullanıldı. Testin yapılabilmesi için 3 metre işaretlenmiş alan, sandalye ve kronometre kullanıldı. Bireylerin komutla birlikte kalkarak yürüme alanının sonuna kadar gidip geri dönmesi istendi. Kalk komutuyla birlikte kronometre başlatılarak oturana kadar geçen süre kaydedildi (22).

Berg Denge Ölçeği: Dengenin değerlendirmesi için kullanılan bir skaladır. Ölçümün uygulanmasında cetvel, kronometre, sandalye ve basamak kullanıldı. Ölçek 14 maddeden

oluşmaktadır. Her bir madde 0-4 arası puanlanmaktadır. Dört puan görevin bağımsız olarak gerçekleştiğini ifade etmektedir. 0-20 puan arası dengenin bozuk olduğunu, 21-40 dengenin kabul edilebilir olduğunu, 41-56 dengenin iyi olduğunu göstermektedir (23).

Tedavi Programı

Manuel tedavi yaklaşımı ve inspiratuar kas eğitimi yalnızca çalışma grubuna uygulanırken, her iki gruba da konvansiyonel fizyoterapi programı uygulandı. Manuel terapi yaklaşımı olarak suboksipital gevşetme, rib raising, diafragma miyofasiyal gevşetme, anterior thoracic miyofasiyal ve sternum gevşetme, anterior servikal miyofasiyal gevşetme, costal ligament gevşetme, lenf pump, skalenlere, pektoral kaslara, latissimus dorsi ve serratus anteriora kas enerji teknikleri uygulandı. Miyofasiyal gevşetme (realise) tekniklerinin her biri 1-3 dakika uygulandı. Mobilizasyon her bir eklemde 30 sn ve 5 tekrarlı yapıldı. Manuel terapi protokolü seansı 20-25 dakika sürdü. Manuel terapi protokolü, haftada 3 gün 6 hafta boyunca toplam 18 seans uygulandı.

Solunum kas eğitimi maksimum inspiratuar basıncın %30'unda eşik yükleme tekniği ile Threshold IMT (Inspiratuar Muscle Trainer) solunum egzersiz cihazı kullanılarak 6 hafta boyunca günde 2 kez 15'er dakika, (toplam günlük 30 dk.), haftada 5 gün şeklinde solunum kas egzersiz eğitimi yapıldı. Her hafta yeni maksimum inspiratuar basıncı ölçülerek yeni değere göre solunum egzersiz cihazı direnci ayarlandı ve iş yükü artışı sağlandı.

İstatistiksel Analiz

İstatistiksel analizler SPSS 22 kullanılarak yapıldı. Değişkenlerin normal dağılıma uygunluğu analitik yöntemler (Kolmogorov-Smirnov/Shapiro-Wilk testler) kullanılarak incelendi. Tanımlayıcı analizler normal dağılan değişkenler için ortalama ve standart sapma, normal dağılmayan değişkenler için ortanca ve çeyrekler arası aralık kullanılarak verildi. Çalışmave kontrol grubunun ölçümle belirlenen değerlerinin karşılaştırılmasında iki ortalama arasındaki farkın önemlilik testi (T test), eğer veriler normal dağılıma uygun değil ise Mann Whitney U testi kullanıldı. Değişkenlerden normal dağılım kriterlerini sağlayanlarda zamanla meydana gelen değişim için ise Wilcoxon testi ve Paired Sample T testi ile yapıldı. İstatistiksel anlamlılık için toplam tip-1 hata düzeyi %5 olarak belirlendi.

BULGULAR

Çalışma grubu (n:14) ve kontrol grubu (n:14) olmak üzere çalışmaya 28 kişi dahil edilmiştir Çalışma ve kontrol grubu arasında yaş,boy, BMİ, kilo, cinsiyet, eğitim durumu, ek hastalık, yardımcı cihaz kullanımı, ailede kas hastalığında istatistiksel olarak anlamlı bir fark olmadığı ($p>0,05$) demografik özellikler açısından benzerlik sağlandığı ve gruplar arası homojenitenin olduğu Tablo 1.-2.'de gösterilmiştir.

Berg Denge Ölçeği toplam skoru çalışma grubunda tedavi öncesi 30,71'den tedavi sonrası 32,36 ya yükselmiş, istatistiksel olarak anlamlı bir fark olduğu ($p<0,01$) belirlenmiştir. Kontrol grubunda ise tedavi önces 28,36 'dan tedavi sonrası 27,64'e istatistiksel olarak anlamlı olan bir azalma tespit edilmiştir ($p<0,05$) (Tablo 3). Corbin postür skoru çalışma grubunda tedavi öncesi 25,00 iken tedavi sonrası 22,64'e düşmüş, istatistiksel olarak anlamlı bir azalma olduğu ($p<0,01$) belirlenmiştir. Kontrol grubunda ise 22,14'den 23,57'ye istatistiksel olarak anlamlı olmayan bir artış görülmüştür ($p>0,05$) (Tablo 3). TUG skoru ise çalışma grubunda tedavi öncesi 27,79'den tedavi sonrası 23,79'a düşmüş olup istatistiksel

olarak anlamlı bir fark olduğu ($p<0,01$) belirlenmiştir. Kontrol grubunda ise 28,43'den 29,64'e istatistiksel olarak anlamlı olmayan bir artış görülmüştür ($p>0,05$) (Tablo 3).

TARTIŞMA

Nöromusküler kas hastalıkları ilerleyici kuvvet kaybı ve kas atrofisi ile karakterize heterojen bir hastalık grubudur (24,25). Hastalığa bağlı olarak inspiratuar ve ekspiratuar solunum kaslarında tutulum gerçekleşir ve solunum fonksiyonları bozulur. Ek olarak ilerleyen evrelerde ligaman ve tendonlarda gelişen sertliğe bağlı olarak göğüs duvarı kompliyansı azalır. Fizyolojik yanıt olarak gelişen solunum sayısı artışı ile hipoventilasyon gelişir (26). Günümüzdeki tedavi yaklaşımları ile semptomlar ortadan kaldırılamamaktadır. Tedavi yaklaşımlarında temel amaç hastanın fonksiyonelliğini korumak ve hastalığın semptomlarını azaltmaktır. Bu nedenle koruyucu ve destekleyici yaklaşımların hastaların yaşam kalitesi ve ambulasyon süreleri açısından önemi büyüktür. Yapılan çalışmalarda, nöromusküler kas hastalarında inspiratuar kas eğitiminin tedaviye yardımcı olarak kullanıldığı görülmektedir (27). Manuel terapi ise eklem hareketliliğini artırmakta, kas ile fasyanın uzunluk gerilim ilişkisini düzenlemektedir. Solunum mekaniğinde etkili olan eklemlerin hareketliliğinin artması solunum kapasitesini artırmaktadır. Literatür incelendiğinde nöromusküler kas hastalıklarında solunum kas kuvveti eğitiminin ve manuel terapinin etkinliğini inceleyen bir çalışmaya rastlanmamıştır. Manuel terapi ile birlikte inspiratuar kas eğitiminin postür, fonksiyonel mobilite ve denge üzerindeki etkisini araştırmayı amaçlayan çalışmamız sonucunda manuel terapi ile birlikte inspiratuar kas eğitiminin postür, denge ve fonksiyonel mobilite değerlendirmelerinde olumlu etkileri olduğu görüldü. Literatürde KOAH hastaları üzerinde yapılan bir çalışmada solunum kas eğitimi pulmoner rehabilitasyon protokolüne kıyasla denge ve yürüyüş performansını önemli ölçüde olumlu etkilediğini göstermiştir (28). İnme hastalarında konvansiyonel rehabilitasyon tedavisi ile birlikte uygulanan solunum kas eğitiminin gövde kontrolü, denge yeteneği ve günlük yaşam aktiviteleri üzerine etkisini araştıran bir çalışmada, solunum kas eğitiminin, solunum kas gücünü, gövde kontrolünü, denge fonksiyonunu iyileştirdiği kanıtlandı (29). Yine başka bir çalışmada inmeli hastalarda solunum kas eğitiminin solunum fonksiyonu, denge ve günlük yaşam aktiviteleri üzerindeki etkileri değerlendirilmiştir. Solunum kas eğitiminin inmeli hastalarda solunum fonksiyonlarını, dengeyi ve günlük yaşam aktivitelerini iyileştirdiği gösterilmiştir (30). İnmeli hastalarda solunum kas eğitiminin denge ve yürüme yeteneği üzerine etkileri ile ilgili yapılan bir derlemede ise inme sonrası hastalarda solunum fonksiyonunu ve yürüme yeteneğini iyileştirmede etkili olduğu, dengede ise anlamlı bir değişim görülmediği sonucuna ulaşmışlardır (31). Destek ve bakıma ihtiyaç duyan yaşlılarda solunum kası gücü ile statik denge arasındaki ilişki değerlendirilmiş ve maksimal inspiratuar basıncın tek ayak üzerinde durma süresi ile anlamlı şekilde ilişkili olduğu gösterilmiştir (32).

Serebral palsi tanılı bireylerde inspiratuar kas eğitiminin etkilerini inceleyen çalışmaya SP'li 25 çocuk dahil edilmiştir. 6 hafta süresince maksimal inspiratuar basıncın %30'unda solunum kas eğitimi uygulanmıştır (14). Benzer yaş grubu ve örneklem büyüklüğünde olan çalışmamızda maksimum inspiratuar basıncın %30'unda eşik yükleme tekniği ile Threshold cihazı kullanılarak 6 hafta boyunca günde 2 kez 15'er dakika, haftada 5 gün eğitim yapılmıştır. Her hafta yeni maksimum inspiratuar basıncı ölçülerek yeni değere göre solunum egzersiz cihazı direnci ayarlandı. Keles ve arkadaşlarının yaptıkları çalışmada inspiratuar kas eğitiminin gövde kontrolü, solunum kas gücü ve yaşam kalitesi üzerinde olumlu etkilerinin olduğu bildirilmiştir. İnspirasyonda diyafram ve parasternal interkostal

kaslar gövde stabilizasyonu gibi bir dizi kasılmalarda yer almaktadır (33,34). Literatürde alt ve üst ekstremitelerin fleksiyonu ve gövde ekstansiyonundan önce diyaframın kasılarak gövde stabilizasyonunu sağlamada önemli olduğunu bildiren çalışmalar mevcuttur (35). Serebral palsili bireyler üzerinde yapılan başka bir çalışmada manuel diyafram germe tekniğinin solunum fonksiyonu üzerine etkinliği randomize kontrollü olarak incelemişlerdir. Standart fizyoterapinin yanı sıra altı hafta boyunca haftada üç gün ardışık olmayan günlerde manuel diyafram germe tekniğinin uygulandığı çalışmada araştırmacılar manuel diyafram germe tekniğinin diyafram hareketliliğini, alt karın ve göğüs duvarı genişlemesini önemli ölçüde iyileştirebileceğini bildirmişlerdir (36).

Nöromusküler kas hastalarında gövde kaslarının yanı sıra gövde kontrolünde önemli görevi olan solunum kasları da zayıfladığından egzersiz kapasitesi düşmekte ve günlük yaşam aktivitelerini yerine getirmede zorluklar ortaya çıkmaktadır. Önceki çalışmalarda, solunum kası aktivasyonunun bozulmasının, normal denge ve hareketlilik için gerekli olan gövde stabilitesinin azalmasına yol açabileceği belirtilmiştir. Nöromusküler hastalarda solunum kaslarının olumsuz etkilendiği bilinmesine rağmen literatürde rehabilitasyon programlarının daha çok fiziksel ve fonksiyonel iyileşmeye odaklandığı görülmektedir. Solunum kas eğitiminin sağlıklı yaşlı yetişkinlerde duruş stabilitesi ve denge üzerindeki etkisi gösterilmiştir (37).Solunum kas eğitimi üzerine yapılan çalışmalar çoğunlukla egzersiz kapasitesi üzerine yürütülmüştür ve gövde kontrolü ve denge üzerindeki etkileri üzerine yapılan çalışmalar genellikle inmeli hastalarda sınırlıdır. İnmeli hastalarda inspiratuar kas eğitiminin solunum fonksiyonu, solunum kas kuvveti, fonksiyonel mobilite, denge ve fonksiyonel kapasite üzerine etkilerini inceleyen çalışmada bizim çalışmamızda olduğu gibi TUG ve Berg Denge Ölçeği kullanılmıştır. Çalışma grubunda Berg Denge Ölçeği ve TUG değerlendirmelerinde istatistiksel olarak anlamlı iyileşmeler görülürken, sadece nörogelişimsel tedavi programının uygulandığı kontrol grubunda yalnızca denge düzeyinde iyileşme görülmüştür (38). Başka bir çalışmada inmeli hastalarda solunum kas eğitiminin, denge üzerindeki etkileri çalışmamıza benzer şekilde Berg Denge Ölçeği ile değerlendirilmiş ve çalışma grubunda denge iyileşmiştir (30). Bizim çalışmamızda ise çalışma grubunda Berg Denge Ölçeği toplam skoru tedavi öncesi 30,71'den tedavi sonrası 32,36 ya yükselmiş, istatistiksel olarak anlamlı bir fark olduğu belirlenmiştir. Kontrol grubunda ise 28,36 'dan 27,64'e istatistiksel olarak anlamlı olan bir azalma tespit edilmiştir ($p<0,05$). Denge ile ilgili sorunlar, yürürken sabitliği ve güvenliği etkileyebilir. Pediatrik nöromüsküler hastalıkta yürüme ve fonksiyonel ambulasyonun incelendiği bir derlemede TUG iki çalışmada fiziksel engelli çocuklarda yürüyüşle ilgili dengenin değerlendirilmesinde geçerli, güvenilir ve duyarlı bir ölçüm yöntemi olarak rapor edilmiştir (39). Sağlıklı yaşlı yetişkinlerin dengesi üzerinde inspiratuvar kas eğitiminin etkilerini değerlendiren çalışmada hareketlilik ve fonksiyonem mobilitelerinin değerlendirilmesinde çalışmamızda olduğu gibi TUG kullanılmıştır (16). Çalışmamızın TUG ölçümlerinde ise araştırma grubunun ortalama tamamlama süreleri tedavi öncesinde 27,79 sn, tedavi sonrasında 23,79 sn olarak kaydedilmiştir. Kontrol grubunun ölçümlerinde ise tedavi öncesi ortalama skor 28,43 sn, tedavi sonrası ortalama skor 29,64 sn olarak kaydedildi. Her iki grubunda TUG skorları yüksek, fonksiyonel mobiliteleri düşüktü, düşme riskleri yüksekti. Araştırma grubunda TUG skorunda olumlu yönde gelişme görüldü ve fonksiyonel mobilitesinde gelişme olduğu belirlendi. Duchenne müsküler distrofisinde (DMD) gövde değerlendirmesinin önemini araştıran kesitsel bir çalışmada 50 DMD hastası üzerinde çalışılmıştır (40). Hastaların çoğunda (%72) bir çeşit spinal deformite vardı. Çalışmamızda postürün değerlendirilmesinde de Corbin postür ölçeği kullanıldı. Araştırma grubunun tedavi öncesi ortalama skoru ortalaması 25,00, tedavi sonrası 22,64 olarak kaydedildi. Kontrol grubunun ise tedavi öncesi ortalama skoru 22,14, tedavi sonrası ortalama skoru 23,57olarak kaydedildi.

Her iki gruptaki olgular da kötü postür skorlarına sahipti. Ama çalışma grubunda istatisitksel olarak anlamlı bir iyileşme görülmüştür.

Sonuç olarak, nöromusküler hastalıklarda, manuel terapi ile kombine edilen inspiratuvar kas eğitiminin, postür, denge ve fonksiyonel mobilite açısından konvansiyonel yönteme kıyasla daha etkili ve faydalı olduğu gözlemlenmiştir. Bu yaklaşım, fizyoterapistlerin bakış açılarını değiştirerek, rehabilitasyonda farklı tedavi stratejileri geliştirmelerine ve tedavi etkinliğinin artırılmasına katkı sağlayabilir**.**

Tablo 1-2. Hastaların Demografik ve Klinik Özelliklerinin Karşılaştırılması
Tablo 1.

Değişken	Çalışma Grubu	Kontrol Grubu	t	p
Yaş	12,21±3,02	10,00±2,80	2,012	0,055
Boy(cm)	126,64±19,12	121,71±16,66	0,727	0,474
Kilo(kg)	41,29±5,44	40,21±6,18	0,487	0,630
BMI(kg/m2)	26,52±5,08	27,63±4,32	-0,623	0,539
Hastalık başlangıç yaşı	5,07±1,59	4,21±1,12	-	0,179

t; Gruplar arası önemlilik testi (T-testi), Mann Whitney U Testi, *; p<0,05, **p<0,01, SD; Standart Sapma, BMI; Vücut Kitle İndeksi

Tablo 2.

Değişken		Çalışma Grubu	Kontrol Grubu	p
		n (%)	n (%)	
Eğitim Durumu	Okul Öncesi	0 (0)	2 (14,3)	0,103
	İlkokul	5 (35,7)	6 (42,9)	
	Ortaokul	5 (35,7)	6 (42,9)	
	Lise	4(28,6)	0 (0)	
Cinsiyet	Kadın	7 (50)	7 (50)	1,000
	Erkek	7 (50)	7 (50)	
Dominant Taraf	Sağ	14 (100)	13(92,9)	0,309
	Sol	0 (0)	1(7,1)	
Ek Hastalık	Var	1 (7,1)	1(7,1)	1,000
	Yok	13 (92,9)	13 (92,9)	
Ailede Kas Hastalığı	Var	11(78,6)	3(21,4)	1,000
	Yok	11(78,6)	3(21,4)	
Yardımcı Cihaz	Var	2(14,3)	12(85,7)	1,000
	Yok	2(14,3)	12(85,7)	

t; Gruplar arası önemlilik testi (T-testi),*; p<0,05, **p<0,01.

Tablo 3. Çalışma ve kontrol gruplarının tedavi öncesi ve sonrası Berg Denge Testi, Corbin Postür, TUG toplam skorlarının rup içi karşılaştırılması

Değişken		Dönem	Ortalama±SS	p
Berg Denge Toplam Skor	Çalışma Grubu	Tedavi Öncesi	30,71±3,38	**0,007
		Tedavi Sonrası	32,36±4,11	
	Kontrol Grubu	Tedavi Öncesi	28,36±3,03	*0,020
		Tedavi Sonrası	27,64±3,34	
Corbin Postür Toplam Skor	Çalışma Grubu	Tedavi Öncesi	25,00±1,11	**0,001
		Tedavi Sonrası	22,64±1,34	
	Kontrol Grubu	Tedavi Öncesi	22,14±6,56	0,522
		Tedavi Sonrası	23,57±2,47	
TUG	Çalışma Grubu	Tedavi Öncesi	27,79±3,47	**0,001
		Tedavi Sonrası	23,79±2,49	
	Kontrol Grubu	Tedavi Öncesi	28,43±3,90	0,253
		Tedavi Sonrası	29,64±5,24	

Wilcoxon Testi, SS; Standart Sapma, **p<0,01, *p<0,05, TUG; Zamanlı kalk ve yürü testi

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CASE REPORT: DIAGNOSIS OF AORTIC ANEURYSM IN A PATIENT ADMITTING WITH LEFT SIDE PAIN

VAKA SUNUMU: SOL YAN AĞRISI İLE BAŞVURAN HASTADA AORT ANEVRİZMASI TANISI

ÖZET

Aort diseksiyonu, aortun iç tabakasının yırtılmasıyla kanın damar katmanları arasına girerek sahte bir lümen oluşturduğu, acil müdahale gerektiren hayati bir durumdur. Aort duvarı üç katmandan (intima, media, adventisya) oluşur ve diseksiyon genellikle intima yırtığıyla başlar. Diseksiyonlar Stanford sınıflamasına göre Tip A (çıkan aort) ve Tip B (inen aort) olarak ayrılır. Tip A cerrahi, Tip B ise medikal tedaviyle yönetilir.

Başlıca risk faktörleri arasında hipertansiyon, bağ dokusu hastalıkları (Marfan sendromu), ateroskleroz, travma ve ileri yaş yer alır. Klinik belirtiler arasında ani, şiddetli göğüs, sırt veya karın ağrısı, bayılma, nabız farkı ve felç bulguları sayılabilir. Tanı genellikle BT anjiyografi ile konur. Tedavi aciliyet gerektirir; Tip A diseksiyonlar cerrahi ile, Tip B diseksiyonlar ise genellikle ilaçla tedavi edilir.

Sunulan olguda, 65 yaşındaki erkek hasta sol yan ağrısı ile başvurmuş, yapılan BT'de infrarenal aortta 83 mm çapında anevrizma ve trombüsler tespit edilmiştir. Bu bulgular rüptür açısından yüksek risk oluşturduğundan hasta acil vasküler cerrahiye yönlendirilmiştir. Büyük çaplı anevrizmaların erken tespiti ve uygun yönetimi hayat kurtarıcıdır.

Anahtar kelimeler: aort diseksiyonu, karın ağrısı, acil servis

Aort Diseksiyonu

Aort diseksiyonu, aortun intima tabakasının yırtılması sonucu oluşan, hayatı tehdit eden ciddi bir damar hastalığıdır. Bu durumda kan, aort duvarının katmanları arasına girerek onları birbirinden ayırır (diseke eder). Bu durum, aort duvarında sahte bir kanal (false lumen) oluşmasına ve kan akışının bozulmasına neden olur. Aort diseksiyonu nadir görülmekle birlikte çok ciddi sonuçlara yol açabilir. Erken tanı ve acil müdahale, yaşam şansını önemli ölçüde artırır.

Aortun Anatomisi ve Diseksiyonun Mekanizması

Aort duvarı üç ana katmandan oluşur:

- İntima (iç tabaka)
- Media (orta kas tabakası)
- Adventisya (dış bağ dokusu tabakası)

Diseksiyon, genellikle iç tabakanın (intima) yırtılması ile başlar. Yüksek basınçla akan kan, bu yırtıktan orta tabakaya girer ve damar duvarını katmanlarına ayırarak ilerler. Diseksiyon boyunca ilerleyen bu sahte kanal, ana damar dallarını tıkayabilir ya da aort duvarının tamamen yırtılmasına (rüptür) yol açarak ölüme neden olabilir.

Sınıflandırma

Aort diseksiyonları genellikle Stanford veya DeBakey sınıflamalarına göre gruplandırılır:

Stanford Sınıflaması:

Tip A: Asenden aortayı tutar. En tehlikeli formdur. Genellikle acil cerrahi gerekir.

Tip B: Desenden aortayı tutar. Genellikle ilaçla tedavi edilir, ancak komplikasyon gelişirse cerrahi müdahale gerekebilir.

DeBakey Sınıflaması:

Tip I: Diseksiyon asenden aortta başlar, tüm aort boyunca ilerler.

Tip II: Sadece asenden aortu kapsar.

Tip III: Sadece desenden aortta görülür.

Nedenleri ve Risk Faktörleri

Aort diseksiyonunun en önemli risk faktörü kontrolsüz hipertansiyondur. Diğer nedenler şunlardır:

- Marfan sendromu, Ehlers-Danlos sendromu gibi bağ dokusu hastalıkları
- Ateroskleroz
- Aort kapak hastalıkları
- Kistik medial dejenerasyon

- Travmalar (örneğin yüksekten düşme, trafik kazası)
- Gebelik (özellikle 3. trimester)
- Aort cerrahisi veya anjiyografi sonrası iatrojenik hasar
- İleri yaş
- Erkek cinsiyet
- Sigara kullanımı

Belirtiler

Aort diseksiyonunun belirtileri ani ve şiddetlidir. En sık görülen belirti:

- Göğüste, sırtta veya karında ani başlayan yırtılır tarzda çok şiddetli ağrı. Bu ağrı bazen omuzlara, boyna veya bacaklara yayılabilir.
- Diğer belirtiler:
    - Bayılma
    - Nefes darlığı
    - Nabız farkı (kollarda veya bacaklarda)
    - Kan basıncında asimetri
    - Stroke belirtileri
    - Kalp seslerinde değişiklik
    - Soğuk terleme, anksiete, ajitasyon
    - Diseksiyon seviyesine bağlı olarak renal iskemi sonucu yan ağrısı, alt ekstremite dolaşımının bozulmasına bağlı olarak alt ekstremite ağrısı, mezenter arter iskemisine bağlı olarak iskemik karın ağrısı görülebilir.

Tanı Yöntemleri

Aort diseksiyonu şüphesi acil durumdur ve hızlı tanı konulması gerekir. Kullanılan görüntüleme yöntemleri:

- Bilgisayarlı Tomografi (BT) Anjiyografi: En sık kullanılan ve hızlı sonuç veren yöntemdir.
- Transözofageal Ekokardiyografi (TEE): Özellikle ameliyat öncesi hızlı değerlendirme için faydalıdır.
- Manyetik Rezonans Anjiyografi (MRA): Detaylı görüntü sağlar ancak acil vakalar için zaman alıcı olabilir.
- Düz röntgen: Dolaylı bulgular (mediasten genişlemesi) gösterebilir ama tanı için yeterli değildir.

Tedavi

Tedavi yaklaşımı, diseksiyonun tipine göre değişir:

Tip A (Stanford):

- Genellikle acil cerrahi gerekir.
- Ameliyatla yırtılan aort bölgesi çıkarılır ve yerine greft yerleştirilir.
- Ameliyat gecikirse ölüm riski saatte %1 artar.

Tip B:

- İlk olarak kan basıncını kontrol altına alma amaçlanır.
- Beta blokerler gibi antihipertansif ilaçlarla tansiyon düşürülür.
- Komplikasyon varsa (organ iskemisi, rüptür, ağrı kontrolsüzlüğü), cerrahi veya endovasküler stentleme yapılır.

Prognoz ve Takip

Erken müdahale edilmezse aort diseksiyonu ilk 24 saatte ölüm oranı %20-30'a kadar çıkar. 48 saatten sonra bu oran daha da artar. Tip A diseksiyonlarında ölüm oranı çok daha yüksektir. Başarıyla tedavi edilen hastalar, yaşam boyu kan basıncı kontrolü altında tutulmalı ve düzenli görüntüleme ile takip edilmelidir.

Sonuç

Aort diseksiyonu, ani başlangıçlı, çok ciddi ve potansiyel olarak ölümcül bir damar hastalığıdır. Bilinçli bir toplum, erken tanı ve uygun tıbbi müdahale sayesinde hayatta kalma oranı artırılabilir. Özellikle hipertansiyonu olan bireylerin düzenli kontrollerini yaptırmaları, bu hastalıktan korunmada kritik önem taşır.

Olgu

65 yaşında erkek hasta, acil servise sol yan ağrısı şikayeti ile başvurdu. Hastanın anamnezinde ani başlayan, giderek artan karakterde sol yan ağrısı olduğu öğrenildi.

Fizik Muayene

Muayenede batında hassasiyet, rebound ve defans mevcuttu. Ayrıca sol kostovertebral açı üzerinde belirgin hassasiyet saptandı.

Laboratuvar ve Görüntüleme Bulguları

Batın ultrasonografisinde ürogenital sistemde patolojik bulguya rastlanmadı. Laboratuvar incelemelerinde üre 71 mg/dL, kreatinin 1.5 mg/dL olarak ölçüldü. Diğer biyokimyasal parametrelerde anlamlı bir patoloji izlenmedi.

Bilgisayarlı batın tomografisinde, aortta infrarenal seviyede en geniş yerinde çapı 83 mm'ye ulaşan anevrizmatik genişleme izlendi. Anevrizmanın bulunduğu segmentte, en kalın yerinde 24 mm'ye ulaşan periferik trombüsler mevcuttu.

Değerlendirme ve Sonuç

Sol yan ağrısı ile başvuran hastada yapılan değerlendirmeler sonucunda, infrarenal aort anevrizması tanısı konulmuştur. Anevrizmanın boyutu ve trombüs varlığı nedeniyle hastanın acil olarak vasküler cerrahiye yönlendirilmesi planlandı. Bu tür büyük çaplı anevrizmaların rüptür riski yüksek olduğundan erken müdahale hayat kurtarıcıdır.

Tartışma

Abdominal aort anevrizmalarının semptomatik hale gelmeden önce tespiti, ciddi komplikasyonların önlenmesinde kritik öneme sahiptir. Özellikle 5.5 cm üzeri çaplara ulaştığında rüptür riski artmakta ve acil cerrahi endikasyonu oluşmaktadır. Yapılan çalışmalarda, 7 cm'nin üzerindeki anevrizmaların yıllık rüptür riski %30'a kadar çıkmaktadır (Brewster et al., 2003). Bu olguda 83 mm gibi ciddi bir çap ölçülmüş olup, periferik trombüs oluşumu da rüptür riski açısından dikkat çekicidir.

Ayrıca, acil servise yan ağrısı ile başvuran hastalarda genellikle renal veya muskuloskeletal nedenler ön planda düşünülse de, özellikle ileri yaş erkek hastalarda aort anevrizması da mutlaka ayırıcı tanıda göz önünde bulundurulmalıdır. BT anjiyografi bu açıdan altın standart görüntüleme yöntemidir ve hastanın yönetimini doğrudan etkiler.

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A CASE OF LEPTOSPIROSIS WITH FULMINANT COURSE IN THE EMERGENCY DEPARTMENT: CASE REPORT

ACİL SERVİSTE FULMİNAN SEYİRLİ BİR LEPTOSPİROZ VAKASI: OLGU SUNUMU

ÖZET:

Leptospiroz, Leptospira cinsi spiral şeklindeki bakterilerin neden olduğu zoonotik bir enfeksiyon hastalığıdır. Dünya genelinde özellikle tropikal ve subtropikal bölgelerde yaygın olan bu hastalık, son yıllarda iklim değişiklikleri, sel felaketleri ve artan şehirleşme gibi çevresel faktörlerle birlikte daha sık görülmeye başlamıştır. İnsanlara genellikle enfekte hayvanların idrarıyla kontamine olmuş su veya toprakla temas yoluyla bulaşır. Özellikle kemirgenler, hastalığın başlıca rezervuarları arasında yer alır. Leptospiroz vakaları, meslek gruplarına göre de değişkenlik gösterebilir; çiftçiler, kanalizasyon işçileri, veterinerler ve kampçılar risk altında olan gruplar arasında sayılabilir.

Giriş:

Leptospiroz ve Weil Hastalığı

Leptospiroz, Leptospira adı verilen spiral şekilli bakterilerin neden olduğu zoonotik bir enfeksiyon hastalığıdır. Dünya genelinde yaygın olan bu hastalık, özellikle tropikal ve subtropikal bölgelerde, nemli ve sıcak iklimlerde daha sık görülür. Hastalık, kirli su veya toprakla doğrudan temas sonucu bulaşabilir. Enfekte hayvanların (özellikle fare, sıçan gibi kemirgenler) idrarlarıyla kontamine olmuş su kaynakları en yaygın bulaşma yoludur.

Leptospiroz, insanlara genellikle deri yoluyla — özellikle açık yaralar veya çatlaklar varsa — ya da göz, burun ve ağız mukozaları üzerinden geçer. Tarım işçileri, kanalizasyon çalışanları, veterinerler, çiftçiler ve açık su kaynaklarında çalışan veya yüzen bireyler risk grubundadır. Ayrıca doğal afetler (sel gibi) sırasında leptospiroz salgınları görülebilir, çünkü bu durumlarda kanalizasyon sistemleri bozulur ve kontamine sular geniş alanlara yayılır.

Belirtiler ve Klinik Seyir

Leptospiroz enfeksiyonu genellikle iki fazda gelişir:

1. Akut faz (leptospiremik faz): Enfeksiyonun ilk 4-7 günü boyunca bakteri kana yayılır. Bu dönemde yüksek ateş, baş ağrısı, kas ağrısı (özellikle baldır kaslarında), titreme, bulantı, kusma ve gözlerde kızarıklık görülür. Bu belirtiler, gribal enfeksiyonlarla karıştırılabilir.
2. İmmün faz: İlk belirtiler kaybolduktan sonra geçici bir iyilik hali olabilir. Ardından hastalığın ikinci evresi olan immün faz başlar. Bu dönemde leptospiralar beyin omurilik sıvısı, gözler ve böbrek gibi organlara yerleşebilir. Menenjit, böbrek yetmezliği, karaciğer hasarı ve kanamalı komplikasyonlar gelişebilir.

Weil Hastalığı (Ağır Leptospiroz)

Leptospirozun en şiddetli formu Weil hastalığı olarak adlandırılır. Bu form, daha çok karaciğer, böbrek ve damar sistemlerini tutar.

Aşağıdaki ciddi belirtilerle karakterizedir:

- Sarılık (karaciğer yetmezliğine bağlı)
- Akut böbrek yetmezliği
- Kanama bozuklukları (özellikle burun ve diş eti kanamaları, idrarda veya dışkıda kan)
- Miyokardit
- Akciğer kanamaları ve solunum sıkıntısı

Weil hastalığı, hastanede tedavi gerektiren ciddi ve yaşamı tehdit eden bir durumdur. Tedavi edilmediği takdirde ölüm oranı %5 ila %15 arasında değişebilir.

Tanı ve Tedavi

Leptospirozun tanısı klinik belirtilerle birlikte laboratuvar testlerine dayanır. Kan testleri, idrar testleri ve beyin omurilik sıvısı analizleri ile tanı konulabilir. Leptospiraların doğrudan

mikroskobik gözlemi veya kültürü nadiren kullanılır; genellikle serolojik testler (örneğin MAT testi - Mikro Aglütinasyon Testi) veya PCR yöntemleri tanıda daha yaygındır.

Tedavide, erken dönemde başlanan antibiyotikler hastalığın süresini ve şiddetini azaltabilir. En sık kullanılan antibiyotikler arasında doksisiklin, penisilin ve ampisilin yer alır. Ağır vakalarda damar içi sıvı tedavisi, diyaliz, oksijen desteği ve yoğun bakım tedavisi gerekebilir.

Korunma Yolları

Leptospirozdan korunmak için aşağıdaki önlemler önemlidir:

Kirli su ve toprakla temastan kaçınılmalı.

- Açık yaralar suya temas ettirilmemeli, su geçirmez giysiler giyilmeli.
- Tarım ve inşaat gibi riskli sektörlerde koruyucu önlemler alınmalı.
- Enfekte hayvanlarla temas sınırlandırılmalı.
- Fare ve sıçan kontrolü sağlanmalı.
- Riskli bölgelere giden kişiler için profilaktik antibiyotik uygulanabilir.

Sonuç

Leptospiroz, basit bir grip benzeri hastalık gibi başlayabilir, ancak tedavi edilmezse ciddi organ hasarına ve hatta ölüme yol açabilir. Özellikle Weil hastalığı formu, acil müdahale gerektiren bir klinik tabloya dönüşebilir. Bu nedenle erken tanı, uygun tedavi ve etkili koruma önlemleri halk sağlığı açısından son derece önemlidir.

Olgu Sunumu:

Yirmi yaşında erkek hasta, acil servise bir haftadır devam eden halsizlik, bulantı, kusma ve ateş şikayetleri ile başvurdu. Özgeçmişinde bilinen kronik hastalık öyküsü bulunmamaktaydı. Fizik muayenesinde vital bulgular stabil olmakla birlikte, skleralarda belirgin ikter saptandı. Laboratuvar tetkiklerinde lökositoz (WBC: 17 x10³/µL), ciddi trombositopeni (PLT: 38.6 x10³/µL), belirgin azotemi (Üre: 217 mg/dL, Kreatinin: 8 mg/dL), hiperbilirubinemi (Total Bilirubin: 8.9 mg/dL, Direkt: 4.8 mg/dL, İndirekt: 4.14 mg/dL), transaminaz yüksekliği (ALT: 179 U/L, AST: 247 U/L), LDH: 768 U/L ve CRP: 15 mg/L olarak tespit edildi. Batın ultrasonografisinde hepatomegali ve splenomegali saptandı.

Takip sürecinde hastada ani gelişen solunum sıkıntısı ve hipoksemi görüldü. Radyolojik ve klinik değerlendirmeyle intraalveoler hemoraji düşünüldü. %100 oksijen desteğine rağmen oksijen satürasyonu %60'ın altına düştü. Kan gazı değerlendirmesinde progresif asidoz saptandı. Yoğun destek tedavilerine rağmen, hastanın genel durumu hızla bozuldu ve başvurusunun ikinci gününde kardiyopulmoner arrest gelişti. Tüm müdahalelere rağmen hasta eksitus oldu.

Sonuç:

Bu vaka, leptospirozun genç ve altta yatan hastalığı olmayan bireylerde dahi fulminan seyredebildiğini göstermektedir. Erken tanı, destek tedavisi ve uygun antibiyotik tedavisi ile

mortalite azaltılabilirken, hastalığın hızlı progresyonu nedeniyle acil servis hekimlerinin leptospiroz ayırıcı tanısını akılda tutmaları büyük önem taşımaktadır.

Tartışma:

Leptospiroz, özellikle gelişmekte olan ülkelerde ve tropikal iklime sahip bölgelerde önemli bir halk sağlığı sorunu olmaya devam etmektedir. Enfekte hayvanların idrarıyla kontamine olmuş su veya toprakla temas sonucu bulaşan hastalık, genellikle asemptomatik ya da hafif seyretmekle birlikte bazı olgularda ağır, hatta ölümcül komplikasyonlarla ilerleyebilir. Sunulan vakada görülen sarılık, renal yetmezlik, trombositopeni ve pulmoner hemoraji tablosu, leptospirozun en şiddetli formu olan Weil hastalığı ile uyumludur.

Literatürde bildirilen bazı çalışmalarda, özellikle böbrek yetmezliği ve solunum sistemi tutulumu olan hastalarda mortalitenin %50'ye kadar çıkabildiği belirtilmektedir. Intraalveoler hemoraji, leptospirozun nadir fakat en ölümcül komplikasyonlarından biridir ve tanısı çoğunlukla gecikir (Dolhnikoff et al., 2007). Çalışmalar, bu klinik tablonun erken tanısı ve yoğun destek tedavisinin uygulanmasının prognozu ciddi şekilde etkilediğini göstermektedir (Levett, 2001).

Bu vakada dikkat çeken bir diğer bulgu, hipoksemiye rağmen %100 oksijen tedavisine yanıt alınamamasıydı. Bu durum, diffüz alveoler hasarın bir göstergesi olup, leptospirozun solunum sistemine olan invaziv etkisini ortaya koymaktadır. Benzer vakalarda immün plazma değişimi, kortikosteroid tedavisi ve erken ventilatör desteğinin olumlu sonuçlar sağlayabileceği bazı yayınlarda vurgulanmıştır (Dolhnikoff et al., 2007; Daher et al., 2010).

Bu nedenle, özellikle nonspesifik başlangıç semptomları olan hastalarda, epidemiyolojik öykü ve laboratuvar bulguları göz önüne alınarak leptospiroz tanısının erken düşünülmesi önemlidir. Acil servis hekimlerinin bu nadir fakat ölümcül tabloya karşı duyarlı olmaları, erken tanı ve tedavi açısından hayat kurtarıcı olabilir.

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INVESTIGATION OF MIR125A EXPRESSION LEVEL IN CHRONIC OBSTRUCTIVE LUNG DISEASE

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is a common lung disease characterized by airway inflammation, with high morbidity and mortality, and an increasing frequency with age. MicroRNAs (miRNAs) are small, non-coding RNA molecules that regulate gene expression after transcription. Increasing evidence of the regulatory roles of miRNAs in COPD pathogenesis reveals that these molecules hold a critical place in understanding the molecular mechanisms of the disease. Studies show that miR-125a-5p is generally expressed at low levels in COPD patients, and this is associated with increased inflammation and disease severity. It has been reported that miR-125a-5p plays a crucial regulatory role in COPD-related pathological processes, such as the aging of lung epithelial cells and the activation of immune cells, through the regulation of oxidative stress and inflammatory responses induced by cigarette smoke. The aim of this study is to determine the expression level of the MIR125A gene in a group of patients diagnosed with COPD.

Materials and Methods: In this study, the expression level of MIR125A-5p in 53 COPD patients (16 Stable COPD, 37 Acute COPD) and 52 healthy controls was determined by real-time polymerase chain reaction (RT-PCR) method. miRNA expression data were calculated with log2−delta delta CT ($2^{-\Delta\Delta Ct}$). Statistical significance of miRNA expression was evaluated with one-way ANOVA test.

Results: The expression level of MIR125A-5p was found to be statistically different between patients and controls (p=0.012, respectively).

Conclusion: As a result, it was determined that the expression level of MIR125A-5p in circulation was lower in COPD patients in this study, suggesting that MIR125A may be effective in the pathogenesis of COPD.

Keywords: Chronic Obstructive Pulmonary Disease, Inflammation, MIR125A, RT-PCR

KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞINDA MIR125A'NIN İFADE DÜZEYİNİN ARAŞTIRILMASI

ÖZET

Giriş: Kronik obstrüktif akciğer hastalığı (KOAH), solunum yolu inflamasyonları ile karakterize edilen, yüksek morbidite ve mortaliteye sahip ve sıklığı yaşla artan, yaygın bir akciğer hastalığıdır. MikroRNA'lar (miRNA'lar), transkripsiyon sonrası gen ekspresyonunu düzenleyen küçük, kodlamayan RNA molekülleridir. KOAH patogenezinde miRNA'ların düzenleyici rollerine dair artan kanıtlar, bu moleküllerin hastalığın moleküler mekanizmalarının anlaşılmasında kritik bir yer tuttuğunu ortaya koymaktadır. Çalışmalar, miR-125a-5p'nin KOAH hastalarında genellikle düşük ifade düzeyi gösterdiğini ve bu durumun artan inflamasyon ve hastalık şiddeti ile ilişkili olduğunu göstermektedir. miR-125a-5p'nin sigara dumanı tarafından tetiklenen oksidatif stres ve inflamatuar yanıtları düzenleyerek, akciğer epitel hücrelerinin yaşlanması ve bağışıklık hücrelerinin aktivasyonu gibi KOAH ile ilişkili patolojik süreçlerde kritik bir düzenleyici rol oynadığı bildirilmiştir. Bu çalışmanın amacı, KOAH tanısı alan hasta grubunda MIR125A geninin ifade düzeyini belirlemektir.

Materyal ve Metod: Bu çalışmada, 53 KOAH Hastası (16 Stabil KOAH, 37 Akut KOAH) ve 52 sağlıklı kontrolde MIR125A-5p ifade düzeyi real time-polimeraz zincir reaksiyonu (RT-PCR) metodu ile belirlendi. miRNA'nın ifade verileri log2−delta delta CT ($2^{-\Delta\Delta Ct}$) ile hesaplandı. miRNA ifadesinin istatistiksel önemi one-way ANOVA testi ile değerlendirildi.

Bulgular: MIR125A-5p'nin ifade düzeyinin hasta ve kontroller arasında istatistiksel olarak farklı olduğu görüldü (sırasıyla p=0.012).

Sonuç: Bu çalışmada dolaşımdaki MIR125A-5p'nın ifade düzeyinin KOAH hastalarında daha düşük olduğu saptandı ki bu durum MIR125A'nın KOAH hastalığının patogenezinde etkili olabileceğini düşündürmektedir.

Anahtar Kelimeler: Kronik Obstrüktif Akciğer Hastalığı, MIR125A, RT-PCR

1. GİRİŞ

miRNA, transkripsiyon sonrası gen ekspresyonunu düzenleyen küçük, kodlamayan RNA moleküllerdir (Qiao et al., 2023). miRNA'lar genellikle hücreye veya organa özgü mRNA ekspresyonunu düzenlerler. Bu nedenle, stres direnci, hücresel proliferasyon, apoptoz, hücresel farklılaşma ve hastalık oluşumu ve ilerlemesi gibi birçok biyolojik sürece katılabilirler (Zhu et al., 2020). miRNA'ların birçok biyolojik sıvıda oldukça kararlı bir şekilde bulunduğu tespit edilmiştir; bu nedenle, özellikle dolaşımdaki miRNA'lar, potansiyel biyobelirteç adayları olarak kabul edilmektedir (Burke et al., 2022).

miR-125a-5p, hücre çoğalması, farklılaşması ve apoptozunun düzenlenmesinde rol oynayan önemli bir miRNA'dır. Bu miRNA, hücresel süreçlerin düzenlenmesinde geniş bir etkiye sahip olup kanser, kardiyovasküler hastalıklar ve sinir sistemi bozuklukları gibi ciddi sağlık sorunlarıyla ilişkilendirilmiştir (Y. Wang et al., 2021). Kanser hücrelerinde hücresel proliferasyonu ve metastazı düzenlerken, aynı zamanda hücresel farklılaşma ve apoptoz gibi süreçleri de etkiler (Q. Wang et al., 2024). miR-125a-5p, kanser hücrelerinin büyümesini ve metastazını engelleyerek tümör baskılayıcı bir rol oynamaktadır. Bu miRNA, hücre ölümünü ve çoğalmasını kontrol ederek kanserin ilerlemesini önler (Chen et al., 2015). Örneğin, servikal kanseri olan hastalarda miR-125a-5p'nin kontrol grubuna göre daha düşük seviyelerde olduğu ve STAT3 ekspresyonunu inhibe ederek kanser ilerlemesini önemli ölçüde baskıladığı bildirilmiştir (Fan et al.,2015).

Sigara dumanı ve diğer çevresel faktörler, KOAH için başlıca risk etmenleri arasında yer alır ve oksidatif stres ile inflamasyonu tetikleyen mekanizmalar aracılığıyla hastalık gelişimine katkıda bulunur. Bu süreçte bazı miRNA'lar, risk faktörlerinin neden olduğu moleküler değişiklikleri düzenleyerek patolojik mekanizmalara dahil olur. miR-125a-5p'nin, özellikle sigaraya bağlı gelişen KOAH ve amfizem vakalarında, akciğer epitelyal hücrelerinin yaşlanma sürecinde önemli bir rol oynadığı gösterilmiştir. Sigara dumanına maruz kalan bireylerde miR-125a-5p'nin ifade düzeyinin arttığı; bu artışın hücresel yaşlanmayı ve yaşlanmaya bağlı salgı fenotipini (SASP) tetiklediği ortaya konmuştur (Wu et al., 2022). Alveoler makrofajların ve diğer bağışıklık hücrelerinin aşırı aktivasyonu, KOAH'ın patogenezinde kritik bir rol oynamaktadır. Bu hücresel yanıtlar, hastalığın ilerlemesine ve hava yolu inflamasyonuna katkı sağlar. KOAH'ta immün yanıtın dengelenmesi için miR-125a-5p'nin, makrofaj polarizasyonu ve diğer bağışıklık yanıtlarını düzenleyerek bu süreci değiştirebileceği bildirilmektedir (Lee et al., 2016).

Bu nedenle, bu çalışmanın birincil amacı, KOAH hastalarında miR-125a-5p'nin gen ekspresyon düzeylerini inceleyerek, bu miRNA'nın hastalığın tanı ve takibinde potansiyel bir biyobelirteç olarak kullanılıp kullanılamayacağını belirlemektir.

2. MATERYAL VE METOD

2.1. Çalışma Grubu

Bu çalışmaya, Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Göğüs Hastalıkları polikliniğine başvuran ve atakta olmayan 16 Stabil KOAH hastası ile Göğüs Hastalıkları servisine atak nedeni ile yatırılan 37 Akut KOAH hastası olmak üzere toplam 53 KOAH hastası dahil edildi. Kontrol grubu ise 52 bireyden oluşmaktaydı. Hasta ve kontrol grubundaki bireylerden çalışmamıza dahil edildiklerine dair izinleri alındı. Bu çalışma için, Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar

Etik Kurulu'nun 23.06.2022 tarihli toplantısında 22-KAEK-145 kayıt numarası ile onay alındı.

2.2. Çalışma Materyalinin Hazırlanması ve Real-Time Polimeraz Zincir Reaksiyonu

5 ml kan örneği EDTA'lı tüplerine alınmış ve 3000 rpm'de 10 dakika santrifüj edilmiştir. Santrifüjlemeden sonra elde edilen plazma örnekleri, mikrosantrifüj tüplerine aktarılarak -80°C'de muhafaza edilmiştir. Bu plazma örneklerinden miRNA'lar, SanPrep Kolonlu microRNA Mini-Preps Kiti (Biobasic) kullanılarak saflaştırılmıştır. cDNA eldesi, Single miRNA qPCR Assay kitinin (Atlas Biotechnologies, Türkiye) içinde bulunan cDNA sentez karışımı kullanılarak yapılmıştır. Plazmadaki MIR125A ifade düzeyini ölçmek için real-time polimeraz zincir reaksiyonu (RT-PCR) uygulanmıştır. Hesaplamalarda hedef genin ve normalizasyon için kullanılan referans genin (Rnu-6) Ct değerleri kullanılmıştır.

2.3. İstatistiksel Değerlendirme

miRNA ifade verilerini değerlendirmek için log2-delta delta CT ($2^{-\Delta\Delta Ct}$) analizi yapılmıştır. miRNA ifadesinin istatistiksel önemini belirlemek için one-way ANOVA testi kullanılmıştır. Tüm p değerleri iki kuyrukludur ve 0,05'ten küçük p değerleri, istatistiksel olarak anlamlı kabul edilmiştir.

3. BULGULAR

Bu çalışmada, KOAH hastalığı ile MIR125A-5p'nin ifade düzeyi arasındaki ilişkinin araştırılması amacıyla KOAH tanısı konulan 53 hasta ve herhangi bir akciğer hastalığı veya kronik bir hastalığı olmayan sağlıklı 52 kontrol incelendi. Hastaların yaş ortalaması 70.02±9.289, kontrollerin yaş ortalaması ise 66.56±10.185'di. Hastaların 10'u (%18.9) kadın, 43'ü (%81.1) erkek; kontrollerin ise 4'ü (%7.7) kadın, 48'i (%92.3) erkek idi. Hasta ve kontrollerin yaş ve cinsiyetleri birbiri ile uyumlu idi (sırasıyla p=0.072 ve p=0.150) (Tablo 1). 53 KOAH hastasının 16'sı Stabil (%30.2), 37'si Akut KOAH (%69.8) hastası idi.

MIR125A-5p'nin ekspresyon düzeyinin kontrol ve hasta gruplarındaki dağılımları incelenerek bunlara ait p değerleri ve tanımlayıcı istatistikler hesaplandı. MIR125A-5p'nin ifade düzeyinin hasta ve kontroller arasında istatistiksel olarak anlamlı bir fark gösterdiği saptandı (sırasıyla p=0.012) (Tablo 2). Kontrollere kıyasla KOAH hastalarında MIR125A'nın ifade düzeyi düşüktü.

Tablo 1. KOAH hastaları ve Kontrollerde MIR125A-5p'nin ifade düzeyleri

miRNA	Grup	N	İfade Düzeyleri ($2^{-\Delta\Delta Ct}$)	p değeri
MIR125A-5p	KOAH Hastaları	53	5.57±13.238	**0.012**
	Kontroller	52	26.44±58.021	

Tablo 2. Akut KOAH, Stabil KOAH ve Kontrol grubunda MIR125A-5p geninin ifade düzeyleri

Grup	N	İfade Düzeyi ($2^{-\Delta\Delta Ct}$)	P değeri		
			Akut KOAH'a karşın Stabil KOAH	Akut KOAH'a karşın Kontrol	Stabil KOAH'a karşın Kontrol
Akut KOAH	37	4.52±8.062	0.959	**0.045**	0.280
Stabil KOAH	16	8.01±21.036			
Kontrol	52	26.44±58.021			

4. TARTIŞMA

Sigara dumanı ve diğer çevresel faktörler, KOAH için başlıca risk etmenleri arasında yer alır ve oksidatif stres ile inflamasyonu tetikleyen mekanizmalar aracılığıyla hastalık gelişimine katkıda bulunur. Bu süreçte bazı miRNA'lar, risk faktörlerinin neden olduğu moleküler değişiklikleri düzenleyerek patolojik mekanizmalara dahil olur. miR-125a-5p'nin, özellikle sigara kaynaklı KOAH ve amfizemde, akciğer epitelyal hücrelerinin yaşlanması sürecinde önemli bir rol oynadığı gösterilmiştir. Sigara dumanına maruz kalan bireylerde, miR-125a-5p seviyelerinin arttığı, bunun da hücre yaşlanmasını ve yaşlanmaya bağlı salgı fenotipini (SASP) tetiklediği bulunmuştur (Wu et al., 2022). Alveoler makrofajların ve diğer bağışıklık hücrelerinin aşırı aktivasyonu, KOAH'ın patogenezinde kritik bir rol oynamaktadır. Bu hücresel yanıtlar, hastalığın ilerlemesine ve hava yolu inflamasyonuna katkı sağlar. KOAH'ta immün yanıtın dengelenmesi için miR-125a-5p'nin, makrofaj polarizasyonu ve diğer bağışıklık yanıtlarını düzenleyerek bu süreci değiştirebileceği bildirilmektedir (Lee et al., 2016).

Yapılan literatür taraması sonucunda miR125A-5p'nin ifade düzeyi ile KOAH arasındaki ilişkiyi araştıran sadece bir çalışmaya rastlanmıştır. Wu ve arkadaşları tarafından yapılan çalışmada, miR-125a-5p'nin KOAH hastalarının akciğer dokularında yüksek düzeyde ifade edildiği ve ayrıca Sp1 transkripsiyon faktörü aracılığıyla Sirtuin 1 (SIRT1) ve Hipoksi ile indüklenebilir faktör-1α (HIF-1α), sinyal yolaklarını düzenleyerek hücresel yaşlanmayı ve hastalık patogenezini etkilediği gösterilmiştir. Bu bulgular, MIR-125a-5p'nin KOAH sürecinde daha aktif bir rol oynayabileceğini ve hastalığın patogenezine katkıda bulunabileceğini göstermektedir (Wu et al., 2022). Bizim yaptığımız çalışmada ise, KOAH'lı hastaların serumunda miR125A-5p'nin ifade düzeyinin düşük olduğu görülmüştür. Bu durum, akciğer dokusunda ve serumda miR125A-5p'nin ekspresyon düzeyinde bir fark oluşabileceğini düşündürmektedir.

Yakın tarihte yapılan bir çalışmada, pankreas kanseri dokularında, plazma örneklerinde ve hücre hatlarında MIR-125a-5p seviyelerinin düşük olduğu belirlenmiştir. Bu düşük ekspresyonun, STAT3'ü baskılayarak otofaji ve apoptoz süreçlerini aktive ettiği bildirilmiştir (Pan et al., 2024). Başka bir çalışmada ise, sağlıklı bireylere göre Alzheimer Hastalığı olan bireylerde serumdaki MIR-125a-5p'nin ifade düzeyinin düşük olduğu görülmüştür. Bu durum, Alzheimer hastalığındaki sinaptik fonksiyonlar ve nöroenflamasyon

gibi patolojik süreçler üzerinde etkili olabileceğini göstermiştir (de Lourdes Signorini-Souza et al., 2024).

Sonuç olarak, bu çalışmada dolaşımdaki MIR125A-5p'nin ifade düzeyinin hasta ve kontroller arasında istatistiksel olarak farklı olduğu görüldü, bu durum KOAH hastalığının patogenezinde etkili olabileceğini düşündürmektedir. Bu çalışmanın, MIR125A-5p'nin ifade düzeyinin, KOAH hastalığı ve diğer birçok hastalıkta yapılacak çalışmalar için bir temel oluşturacağı kanaatindeyiz.

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INVESTIGATION OF MIR22 IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD), characterized by respiratory tract inflammation, is a lung disease with increasing frequency with age and high morbidity and mortality. MicroRNAs (miRNAs) are small non-coding RNAs with a length of 18 to 22 nucleotides and regulate gene expression at the posttranscriptional level. Many dysregulated miRNAs have been shown to play a role in various biological pathways like inflammation, cancer, airway epithelial differentiation and lung development. Therefore, the aim of this study was to investigate whether the plasma expression level of MIR22, whose dysregulation has been associated with asthma and emphysema, can be used as a parameter in the diagnosis and follow-up of COPD.

Materials and Methods: A total of 58 male individuals, 33 COPD patients and 25 healthy controls, were included in this study. Real-time polymerase chain reaction (RT-PCR) was used to analyze the expression level of MIR22-3p. Log2−delta delta CT ($2^{-\Delta\Delta Ct}$) analysis was used to calculate miRNA expression data. Statistical significance of miRNA expression was evaluated with one-way ANOVA test.

Results: There was no significant difference in the expression level of MIR22-3p between COPD patients and healthy controls ($p>0.05$). When COPD patients were grouped as stable COPD and acute COPD, there was no change in the expression level of MIR22 between different groups ($p>0.05$).

Conclusion: In this study, it was observed that there was no relationship between plasma MIR22-3p expression level and COPD. Repeating the study by increasing the number of samples will provide a clearer understanding of the relationship between MIR22 and COPD.

Keywords: Chronic obstructive pulmonary disease, MIR22, RT-PCR

KRONİK OBSTRÜKTİF AKCİĞER HASTALIĞINDA MIR22'NİN ARAŞTIRILMASI

ÖZET

Giriş: Solunum yolu inflamasyonları ile karakterize edilen Kronik obstrüktif akciğer hastalığı (KOAH), yaşla birlikte sıklığı artan ve yüksek morbidite ve mortaliteye sahip bir akciğer hastalığıdır. MikroRNA'lar (miRNA'lar), 18 ila 22 nükleotid uzunluğunda küçük kodlamayan RNA'lardır ve posttranskripsiyonel düzeyde gen ifadesini düzenlerler. Birçok düzensiz miRNA'nın, iltihaplanma, kanser, hava yolu epitel farklılaşması ve akciğer gelişimi ile çeşitli biyolojik yolaklarda görev aldığı ortaya konmuştur. Bu nedenle, bu çalışmanın amacı, düzensizliği astım ve amfizem ile ilişkilendirilmiş olan MIR22'nin plazmadaki ifade düzeyinin, KOAH hastalığının tanı ve takibinde bir parametre olarak kullanılıp kullanılamayacağını araştırmaktır.

Materyal ve Metod: Bu çalışmaya 33 KOAH hastası ve 25 sağlıklı kontrol olmak üzere toplam 58 erkek birey dahil edilmiştir. MIR22-3p'nin ifade düzeyini analiz etmek için gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) kullanılmıştır. miRNA ifade verilerini hesaplamak için Log2−delta delta CT ($2^{-\Delta\Delta Ct}$) analizinden faydalanılmıştır. miRNA ifadesinin istatistiksel önemini one-way ANOVA testi ile değerlendirilmiştir.

Bulgular: KOAH hastaları ile sağlıklı kontroller arasında, MIR22-3p'nin ifade düzeyi açısından anlamlı bir fark bulunmamıştır ($p>0.05$). KOAH hastalarını, stabil KOAH ve akut KOAH olarak gruplandırıldığında, MIR22'nin ifade düzeyi açısından, farklı gruplar arasında da bir değişikliğe rastlanmamıştır ($p>0.05$).

Sonuç: Bu çalışmada, plazma MIR22-3p ifade düzeyi ile KOAH arasında bir ilişki olmadığı görülmüştür. Örnek sayısının arttırılarak çalışmanın tekrarlanması MIR22 ile KOAH arasındaki ilişkinin daha net bir şekilde anlaşılmasını sağlayacaktır.

Anahtar Kelimeler: Kronik obstrüktif akciğer hastalığı, MIR22, RT-PCR

1. GİRİŞ

Solunum yolu inflamasyonları ile karakterize edilen Kronik obstrüktif akciğer hastalığı (KOAH), yaşla birlikte sıklığı artan ve yüksek morbidite ve mortaliteye sahip bir akciğer hastalığıdır (Onishi, 2017). Hastalık, devam eden ekspiratuar hava akımı kısıtlılığı ve sürekli inflamasyon yanıtıyla karakterizedir (Bagdonas ve ark., 2015). KOAH, dünyada hastalıklardan ölümlerde dördüncü sırada yer alır ve yılda 126.000 ölüme neden olmaktadır (Schwartz, 2012).

mikroRNA'lar (miRNA'lar), 19 ila 25 nükleotid uzunluğunda, küçük kodlamayan RNA'lardır ve posttranskripsiyonel düzeyde gen ifadesini düzenlerler (Green ve ark., 2021). Birçok düzensiz miRNA'nın, iltihaplanma, kanser, hava yolu epitel farklılaşması ve akciğer gelişimi gibi çeşitli biyolojik yolaklarda görev aldığı bildirilmiştir (Pelaia ve ark., 2006). miRNA'lar, endojen doğası nedeniyle hem terapötik bir hedef hem de biyobelirteç olarak çalışarak, hastalık riskini azaltma yeteneğine sahiptir. Son zamanlarda yapılan çalışmalar, MIR22'nin, organizmaların bağışıklık kaskatında aktif roller oynadığını ve düzensizliğinin birer akciğer hastalığı olan astım ve amfizem dahil olmak üzere farklı inflamatuvar hastalıklarla ilişkili olduğunu ortaya koymuştur (Lu ve ark., 2015; Ming ve ark., 2016).

Bu nedenle, bu çalışmanın amacı, MIR22'nin plazmadaki ifade düzeyinin, KOAH hastalığının tanı ve takibinde bir parametre olarak kullanılıp kullanılamayacağını araştırmaktır.

2. MATERYAL VE METOD

2.1. Çalışma Grubu

Bu çalışmaya Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Göğüs Hastalıkları Polikliniğine başvuran 33 KOAH hastası (13 stabil KOAH, 20 Akut KOAH) ve 25 sağlıklı kontrol olmak üzere toplam 58 erkek birey dahil edilmiştir. Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Müdahale Olmayan Bilimsel Araştırmalar Etik Kurulu, 08.04.2025 tarihli toplantısında 25-MOBAEK-117 kayıt numarasıyla bu çalışmaya onay vermiştir.

2.2. Çalışma Materyalinin Hazırlanması ve Real-Time Polimeraz Zincir Reaksiyonu

5 ml kan örneği EDTA'lı tüplerine alınmış ve 3000 rpm'de 10 dakika santrifüj edilmiştir.

Santrifüjlemeden sonra elde edilen plazma örnekleri, mikrosantrifüj tüplerine aktarılarak -80°C'de muhafaza edilmiştir. Bu plazma örneklerinden miRNA'lar, SanPrep Kolonlu microRNA Mini-Preps Kiti (Biobasic) kullanılarak saflaştırılmıştır. cDNA eldesi, Single miRNA qPCR Assay kitinin (Atlas Biotechnologies, Türkiye) içinde bulunan cDNA sentez karışımı kullanılarak yapılmıştır. Plazmadaki MIR22 ifade düzeyini ölçmek için real-time polimeraz zincir reaksiyonu (RT-PCR) uygulanmıştır. Hesaplamalarda hedef genin ve normalizasyon için kullanılan referans genin (Rnu-6) Ct değerleri kullanılmıştır.

2.3. İstatistiksel Analiz

miRNA ifade verilerini değerlendirmek için log2-delta delta CT ($2^{-\Delta\Delta Ct}$) analizi yapılmıştır. miRNA ifadesinin istatistiksel önemini belirlemek için one-way ANOVA testi

kullanılmıştır. Tüm p değerleri iki kuyrukludur ve 0,05'ten küçük p değerleri, istatistiksel olarak anlamlı kabul edilmiştir.

3. BULGULAR

KOAH hastaları ile sağlıklı kontroller arasında, MIR22-3p'nin ifade düzeyi açısından anlamlı bir fark bulunmamıştır (Tablo 1) ($p>0.05$). KOAH hastaları, stabil KOAH ve akut KOAH olarak gruplandırıldığında, MIR22'nin ifade düzeyi açısından, farklı gruplar arasında da bir değişikliğe rastlanmamıştır (Tablo 2) ($p>0.05$).

Tablo 1. KOAH hastaları ve Kontrollerde MIR22-3p'nin ifade düzeyleri

miRNA	**Grup**	**N**	**İfade düzeyi ($2^{-\Delta\Delta Ct}$)**	**p değeri**
MIR22-3p	KOAH hastası	33	2.24±2.456	0.144
	Kontrol	25	4.58±8.663	

Tablo 2. Akut KOAH, Stabil KOAH ve Kontrol grubunda MIR22-3p geninin ifade düzeyleri

miRNA	**Grup**	**N**	**İfade düzeyil ($2^{-\Delta\Delta Ct}$)**	**p değeri**
MIR22-3p	Akut KOAH	20	2.18±1.910	0.347
	Stabil KOAH	13	2.33±3.208	
	Kontrol	25	4.58±8.663	

4. TARTIŞMA

Plazma dahil çeşitli vücut sıvılarında ve hücre dışı boşluklarda hücresiz formlarda bulunabilen miRNA'lar, moleküler belirteç kategorisi oluşturma potansiyeline sahiptir (Png ve ark., 2011; Zhou ve ark., 2012). Çok sayıda çalışma, MIR22'nin metabolizma, hematopoez, hücre bölünmesi, büyüme, yapışma, senesans, apoptozis, anjiyogenez, fibrogenez, doku homeostazisi, doku yeniden şekillenmesi ve inflamasyon dahil olmak üzere çeşitli patofizyolojik işlevlerde hayati bir rolü olduğunu göstermektedir (Jovicic ve ark., 2013; Gu ve ark., 2017). MIR22'nin, organizmaların bağışıklık kaskatında aktif roller oynadığı ve düzensizliğinin astım ve amfizem dahil olmak üzere farklı inflamatuvar hastalıklarla ilişkili olduğu ortaya konulmuştur (Lu ve ark., 2015; Ming ve ark., 2016). In vitro çalışmalar, amfizemli sigara içenlerin akciğer antijeni sunan hücrelerinde, amfizemsiz kontrol deneklerinin aksine MIR22'nin yukarı regülasyonunu göstermiştir (Lu ve ark., 2015). Yakın tarihli bir çalışmada, serum MIR22-3p ifade düzeyinin, sigara içen KOAH hastalarına kıyasla, biokütle dumanına maruz kalan KOAH hastalarında aşağı düzenlenmiş olduğu ortaya konulmuştur (Velasco-Torres ve ark., 2019).

Sonuç olarak, bu çalışmada, plazma MIR22-3p ifade düzeyi ile KOAH arasında bir ilişki olmadığı görülmüştür. Örnek sayısının arttırılarak çalışmanın tekrarlanması, MIR22 ile KOAH arasındaki ilişkinin daha net bir şekilde anlaşılmasını sağlayacaktır.

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ADVANCES IN THE TREATMENT OF CLEFT LIP AND PALATE USING LOW-FREQUENCY VIBRATION DEVICES

ABSTRACT

This study comprehensively addresses recent advancements in the use of low-frequency vibration devices in the treatment of cleft lip and palate. Cleft lip and palate are among the most serious congenital anomalies, causing both aesthetic and functional problems that adversely affect individuals' abilities in feeding, speech, respiration, and social communication. While traditional treatment approaches primarily rely on surgical repair, the preoperative and postoperative use of innovative technologies such as low-frequency vibration devices and nasoalveolar molding (NAM) has significantly increased in recent years. Low-frequency vibration devices enhance microcirculation, support wound healing, reduce inflammation, and accelerate tissue remodeling processes, thereby improving surgical success rates.

This article thoroughly discusses the biological mechanisms of low-frequency vibration devices, clinical usage protocols, and the clinical outcomes reported in the literature. Moreover, the advantages and limitations associated with their use are evaluated. NAM therapy, initiated shortly after birth, is an orthopedic intervention aimed at optimizing the position of the nasal cartilage and alveolar segments. NAM applications reduce the need for surgical intervention, lower the risk of postoperative complications, and improve aesthetic outcomes.

The study also emphasizes the importance of multidisciplinary treatment approaches, highlighting that coordinated teamwork among specialists such as plastic surgeons, orthodontists, pediatricians, and speech-language therapists significantly enhances long-term clinical success. Parental education, active participation in the treatment process, and adherence to device usage protocols play a critical role in treatment outcomes. In conclusion, low-frequency vibration devices and NAM applications support surgical interventions in the treatment of cleft lip and palate, enhance patients' quality of life, and optimize the overall treatment process. It is anticipated that the impact of biotechnological innovations and personalized treatment protocols in this field will continue to grow in the future.

Keywords: Cleft lip, cleft palate, vibration therapy, NAM, wound healing, pediatric surgery.

DUDAK VE DAMAK YARIKLARININ DÜŞÜK TİTREŞİMLİ CİHAZ KULLANARAK TEDAVİSİNDE GELİŞMELER

ÖZET

Bu çalışma, dudak ve damak yarıklarının tedavisinde düşük titreşimli cihazların kullanımına yönelik güncel gelişmeleri kapsamlı bir şekilde ele almaktadır. Dudak ve damak yarıkları hem estetik hem de fonksiyonel problemlere yol açarak bireylerin beslenme, konuşma, solunum ve sosyal iletişim becerilerini olumsuz etkileyen ciddi doğumsal anomaliler arasında yer almaktadır. Geleneksel tedavi yaklaşımları temel olarak cerrahi onarımı esas alırken, son yıllarda düşük frekanslı vibrasyon cihazları ve nazoalveolar molding (NAM) gibi yenilikçi teknolojilerin cerrahi öncesi ve sonrası süreçlerde kullanımı giderek artmaktadır. Düşük titreşimli cihazlar, mikro dolaşımı artırarak yara iyileşmesini desteklemekte, inflamasyonu azaltmakta ve doku remodeling süreçlerini hızlandırarak cerrahi başarı oranlarını yükseltmektedir.

Makale, düşük titreşimli cihazların biyolojik mekanizmalarını, klinik kullanım protokollerini ve literatürde bildirilen klinik sonuçları ayrıntılı olarak tartışmaktadır. Ayrıca, bu cihazların kullanımına ilişkin avantajlar ve karşılaşılan sınırlılıklar değerlendirilmektedir. NAM tedavisi ise doğumdan kısa süre sonra başlanan, burun kartilajı ve alveoler segmentlerin optimal pozisyona getirilmesini amaçlayan ortopedik bir müdahaledir. NAM uygulamaları, cerrahi müdahale ihtiyacını azaltmakta, postoperatif komplikasyon riskini düşürmekte ve estetik sonuçları iyileştirmektedir.

Çalışmada ayrıca, multidisipliner tedavi yaklaşımlarının önemi vurgulanmakta; plastik cerrahlar, ortodontistler, pediatristler, dil ve konuşma terapistleri gibi uzmanlardan oluşan ekiplerin koordineli çalışmasının, uzun dönemli klinik başarıyı artırdığı belirtilmektedir. Ailelerin bilgilendirilmesi, tedavi sürecine aktif katılımı ve cihaz kullanımındaki uyumu, tedavi sonuçları üzerinde belirleyici etkiye sahiptir. Sonuç olarak, düşük titreşimli cihazlar ve NAM uygulamaları, dudak ve damak yarığı tedavisinde cerrahi girişimlere destek sağlayarak hastaların yaşam kalitesini artırmakta ve tedavi sürecini optimize etmektedir. Gelecekte, biyoteknolojik yeniliklerin ve bireyselleştirilmiş tedavi protokollerinin bu alandaki etkisinin daha da artacağı öngörülmektedir.

Anahtar Kelimeler: Dudak yarığı, damak yarığı, vibrasyon terapisi, NAM, yara iyileşmesi, çocuk cerrahisi.

1.INTRODUCTION

Cleft lip and palate are complex congenital anomalies that arise due to disruptions in the fusion of facial structures during the 4th to 12th weeks of embryological development ***(Mossey et al., 2009).*** These clefts are not merely anatomical defects; they are also the source of significant functional and psychosocial problems. Individuals with cleft lip and palate often experience difficulties in feeding, speech and articulation disorders, hearing loss (particularly due to middle ear infections), and prominent facial deformities ***(Shkoukani, Chen, & Vong, 2013***). All these complications can adversely affect an individual's social integration, psychological well-being, and overall quality of life.

Traditional treatment approaches primarily rely on surgical interventions. Lip repair is generally performed within the first 3 to 6 months after birth, while palate repair is scheduled between 9 and 18 months of age. However, surgical interventions do not always yield satisfactory results, and secondary corrective surgeries may often be required ***(Semb & Shaw, 2010).*** Therefore, the development of adjunctive treatment methods to support surgical outcomes has become increasingly important.

In recent years, innovative approaches such as low-frequency vibration therapy and nasoalveolar molding (NAM) have made significant contributions to cleft treatment. Low-frequency vibration devices are utilized to accelerate wound healing, reduce inflammation, and support tissue remodeling processes ***(Chan et al., 2013).*** NAM, on the other hand, enhances the anatomical alignment of the alveolar segments and nasal cartilage during the preoperative period, thereby improving surgical success and aesthetic outcomes ***(Grayson et al., 1999).***

This study provides a comprehensive examination of the biological effects, clinical outcomes, advantages, and limitations of using low-frequency vibration devices and NAM applications in the treatment of cleft lip and palate. It also emphasizes the importance of multidisciplinary treatment teams and parental involvement. It is evident that modern treatment protocols contribute significantly to improving surgical outcomes and enhancing patients' quality of life.

2. Definition and Epidemiology of Cleft Lip and Palate

Cleft lip and palate are defined as openings that occur due to failures in the fusion of facial structures along the midline during embryological development. According to anatomical classification, clefts may be limited to the lip (cheiloschisis), to the palate (palatoschisis), or involve both the lip and palate ***(cheilopalatoschisis) (Mossey et al., 2009).*** Cleft lips are often observed on one or both sides of the upper lip, whereas cleft palates can affect the hard and/or soft palate. These anomalies result in significant aesthetic and functional consequences, leading to difficulties in feeding, speech, hearing, and facial expression.

Epidemiological data reveal that cleft lip and palate occur in approximately 1 out of every 700 live births worldwide ***(World Health Organization [WHO], 2002).*** However, prevalence rates vary depending on factors such as ethnicity, gender, geographic region, and socioeconomic status. For example, in Asian populations, cleft lip and palate are observed in approximately 1 in 500 births, whereas the prevalence is significantly lower among

African populations ***(Stanier & Moore, 2004).*** Among individuals of European descent, the prevalence is estimated at approximately 1 in 1000 births.

The distribution and type of clefts also differ according to demographic characteristics. Left-sided cleft lips are reported in approximately 70% of unilateral cases, while bilateral cleft lips are less common but tend to be more severe ***(Dixon, Marazita, Beaty, & Murray, 2011).*** Isolated cleft palates have been reported to occur more frequently among female infants. Additionally, a gender-based distribution has been observed, with cleft lip occurring more often in males and cleft palate more frequently in females. These variations have direct implications for both clinical management and public health planning. In regions with higher prevalence rates, strengthening early diagnosis and intervention strategies is critically important for reducing the risk of complications.

3. Etiology of Cleft Lip and Palate

The formation of cleft lip and palate involves a complex interaction between genetic and environmental factors. Modern genetic studies have demonstrated that these anomalies follow a polygenic-multifactorial inheritance model ***(Dixon, Marazita, Beaty, & Murray, 2011).*** Among the genetic factors, mutations in critical genes such as IRF6, MSX1, and PVRL1 are particularly notable. For instance, mutations in the IRF6 gene are identified as a major cause of syndromic cleft lip and palate, particularly in conditions such as Van der Woude syndrome ***(Rahimov et al., 2008).*** Mutations in the MSX1 gene are also associated with cleft formation, often accompanied by anomalies in tooth development.

Environmental factors significantly contribute to the risk as well. Maternal smoking during pregnancy reduces fetal oxygen transport, disrupts cellular growth, and increases the risk of cleft formation. Meta-analyses have shown that maternal smoking elevates the risk of clefts by approximately 1.3 times ***(Little et al., 2004).*** Similarly, alcohol consumption during pregnancy has been linked to midline facial developmental abnormalities.

Folate deficiency represents a prominent risk factor in cleft development. During embryogenesis, folic acid is critical for DNA synthesis and cellular proliferation. A deficiency in folic acid can impair the normal fusion of craniofacial tissues, leading to the formation of clefts ***(Wilcox et al., 2007).*** Indeed, reports from certain populations have indicated a reduction in cleft incidence following the implementation of widespread folic acid supplementation programs.

Additionally, exposure to various teratogens has been associated with an increased risk of cleft lip and palate. Agents such as antiepileptic drugs (e.g., phenytoin) and high doses of vitamin A have been shown to cause morphogenetic disruptions in facial structures during embryonic development ***(Mitchell et al., 2003).*** Other external factors, including radiation, viral infections, and environmental toxins, have also been implicated as risk factors.

In conclusion, the formation of cleft lip and palate results from the interplay between genetic predisposition and environmental exposures. This understanding necessitates a multidisciplinary approach for both reducing risk factors and developing effective early diagnosis strategies.

4. Traditional Treatment Methods

The foundation of traditional approaches to the treatment of cleft lip and palate is surgical intervention. Surgical treatment aims to correct both aesthetic appearance and functional deficiencies. The type and severity of the cleft, as well as the patient's age, play a decisive role in the timing and scope of the surgical procedures to be performed. In addition to surgery, supportive orthodontic treatments, speech therapy, and nutritional management have become integral parts of the treatment process. However, focusing solely on surgical intervention is not sufficient; achieving optimal outcomes requires a multidisciplinary approach. Surgical treatment particularly targets correcting facial asymmetry, reconstructing the normal anatomical structure of the nose and oral cavity, and supporting the individual's psychosocial development. Recent advancements in surgical techniques have contributed to a decrease in complication rates and improvements in aesthetic outcomes.

4.1 Surgical Interventions

Cleft lip and palate are repaired through surgical interventions planned shortly after birth. Repair of cleft lips is generally performed on infants aged between 3 and 6 months, a period considered optimal due to sufficient growth and tolerance for anesthesia. Palatal repairs, on the other hand, are carried out between 9 and 18 months of age to support the functional development of speech ***(Semb & Shaw, 2010)***. Among the most commonly employed techniques for lip repair are the Millard rotation-advancement flap procedure and the Tennison-Randall triangular flap method. These techniques aim to restore the functional integrity of the lip muscles while minimizing scar formation. Maintaining nasal aesthetics is also a critical factor for successful lip surgery, as cleft lips are often accompanied by nasal deformities ***(Cutting et al., 2003).***

For palate repair surgeries, the primary goal is to separate the oral and nasal cavities, thereby enabling normal feeding, speech, and hearing functions. One of the most frequently used techniques is the Furlow double-opposing Z-plasty, which aims to realign the muscles of the palate and create a functional soft palate ***(Furlow, 1986).*** This technique has proven particularly effective in reducing the risk of velopharyngeal insufficiency. Although surgical interventions successfully achieve anatomical closure of the cleft, optimal results are not always attainable with a single procedure. In many cases, secondary surgeries are required. These secondary interventions often include nasal aesthetic corrections, alveolar bone grafting, or velopharyngeal correction surgeries aimed at improving speech function ***(Sadove & van Aalst, 2005).***

Factors influencing the success of surgical treatment include the type and severity of the cleft, the timing of surgery, the surgeon’s experience, and the overall health status of the patient. In recent years, preoperative orthopedic preparations, such as the use of nasoalveolar molding (NAM) devices, have further improved surgical outcomes ***(Grayson et al., 1999).*** In conclusion, the surgical treatment of cleft lip and palate is a complex process, and success rates are significantly enhanced when supported by a multidisciplinary approach.

4.2 Multidisciplinary Approaches

The treatment of complex craniofacial anomalies such as cleft lip and palate extends beyond surgical intervention and necessitates a collaborative multidisciplinary effort. Modern

treatment protocols emphasize a multidisciplinary approach to achieve the best aesthetic, functional, and psychosocial outcomes throughout an individual's development from birth to adulthood ***(American Cleft Palate-Craniofacial Association [ACPA], 2017).***

These multidisciplinary teams typically include plastic surgeons, pediatric surgeons, orthodontists, audiologists, speech-language therapists, psychologists, social workers, and nutritionists. Each specialist plays a critical role in the treatment process. For instance, while plastic surgeons are responsible for anatomical repairs, orthodontists support the proper development of the alveolar ridges, and speech-language therapists work on the prevention and rehabilitation of speech disorders. Audiologists play an important role in diagnosing middle ear diseases, which are frequently encountered in individuals with cleft palate, and in implementing interventions to prevent hearing loss ***(Shaw & Semb, 2010).***

The treatment process begins immediately after birth. During the neonatal period, feeding difficulties are managed through the use of palatal obturators. In later stages, orthodontic treatment, alveolar bone grafting, and secondary nasal-lip aesthetic surgeries may become necessary. Early initiation of speech-language therapy is recommended to monitor and support speech development ***(Hardin-Jones & Jones, 2005).***

Parental education and support also form a fundamental component of the multidisciplinary approach. Families must be informed at every stage of the treatment process, provided with psychosocial support, and encouraged to actively participate in the care of their child. Long-term follow-up and periodic evaluations are essential for optimizing facial development, aesthetic outcomes, speech performance, and psychological adjustment.

In conclusion, the multidisciplinary team approach in the treatment of individuals with cleft lip and palate not only facilitates physical repair but also enhances overall quality of life and social integration. This approach necessitates individualized treatment planning and the integration of expertise from various specialties throughout the continuum of care.

5. Use of Palatal Obturators

Palatal obturators are prosthetic devices developed to support essential functions such as feeding and speech in infants with cleft lip and palate. These obturators temporarily separate the oral and nasal cavities, allowing for the proper regulation of sucking and swallowing processes ***(Marshalla, 2015).*** Feeding difficulties are among the most commonly encountered problems in infants with cleft palate. The use of obturators not only facilitates feeding before surgical intervention but also promotes healthier development of intraoral anatomical structures. Furthermore, obturators assist surgeons in better flap planning during surgical procedures by providing a more organized anatomical foundation ***(Habel, Sell, & Mars, 1996).***

5.1 Types of Feeding Obturators

Feeding obturators, developed to facilitate the feeding process in infants with cleft lip and palate, help coordinate sucking, swallowing, and breathing by anatomically separating the oral and nasal cavities. These devices can be applied immediately after birth and provide crucial functional support until surgical intervention is possible ***(Brunet et al., 2016).*** Modern obturators are typically made from hard acrylic resin-based materials. However, to

enhance user comfort, modified designs with soft coatings such as silicone have also been developed. These designs offer better adaptation to the delicate oral mucosa and reduce the risk of irritation.
In recent years, with the widespread use of 3D printing technology in the medical field, it has become possible to produce obturators fully customized to the patient's specific anatomical characteristics ***(Almoraissi, 2018).***

Feeding obturators produced via 3D printing are designed based on digital scanning data and are rapidly manufactured using biocompatible polymers. This method reduces measurement errors compared to traditional techniques and allows for the device to be delivered to the patient in a much shorter timeframe. The average production time is approximately 45 minutes, providing a significant advantage, especially in neonatal care units where time is critical. In some cases, particularly for infants with large clefts, extraoral support devices may also be used. These devices increase the stability of the obturator within the mouth, allowing for easier feeding. Additionally, obturators made from flexible and lightweight materials such as ethylene-vinyl acetate (EVA) are preferred for neonates with sensitive oral tissues.

Feeding obturators can be classified based on their design and material properties. The table below summarizes the commonly used types of feeding obturators along with their advantages and disadvantages.

Table 1. Types and Features of Feeding Obturators.

Type	**Material**	**Advantages**	**Disadvantages**
Traditional Acrylic Obturator	Hard acrylic resin	Durable, long-lasting, easy to sterilize	May be difficult to adapt, risk of irritation
Soft-Coated Obturator	Acrylic base + silicone	Comfortable to use, better adaptation to oral tissue	May require frequent replacement, less durable
3D Printed Obturator	PLA (Polylactic Acid) or biocompatible resin	Fast and patient-specific production, better fit	High production cost, requires specialized equipment
Flexible EVA Obturator	Ethylene-vinyl acetate (EVA)	Lightweight, flexible, economical	Not suitable for long-term use, risk of deformation

In modern clinical practice, the appropriate type of obturator must be selected based on the nature of the cleft, the sensitivity of the oral tissues, and the family's caregiving conditions. For instance, rigid acrylic obturators with extraoral support are preferred for infants with wide clefts, whereas soft-coated or EVA-based flexible obturators offer a more practical option for cases with minor palatal openings.

For effective use of feeding obturators, regular clinical follow-ups are essential. As the infant grows, the anatomical structure changes, necessitating frequent adjustments to maintain proper fit. Otherwise, the device may fail to provide adequate feeding support and could cause pressure sores on the oral mucosa ***(Brunet et al., 2016; Almoraissi, 2018).***

Maintaining the hygiene of feeding obturators is also critically important to minimize infection risks. Families must be educated on daily cleaning protocols and encouraged to strictly adhere to them. It should be noted that devices with silicone coatings or flexible materials are more susceptible to bacterial growth in moist environments over prolonged periods. In the future, advancements in biomaterial technologies are expected to lead to the development of more durable, antibacterial-coated, and self-sterilizing obturators. Additionally, the integration of 3D printing and AI-assisted scanning systems is anticipated to further accelerate the treatment process and enhance its effectiveness. In conclusion, the proper selection and use of feeding obturators are indispensable for supporting the healthy development of infants with cleft lip and palate during the pre-surgical period. Multidisciplinary team coordination and parental education are key elements in ensuring the success of this process.



Figure 1. Shows Palatal Obturators.

6. Use of Low-Frequency Vibration Devices (Vibration Therapy)

Low-frequency vibration devices stimulate muscle contractions and increase blood flow by generating micro-vibrations. Although vibration therapy (VT) has been used for many years in orthopedic rehabilitation, it has recently been applied in the treatment of cleft lip and palate to support wound healing ***(Cardinale & Bosco, 2003).***



Figure 2. Low-Frequency Vibration Devices

6.1 Physiological Effects of Vibration

Vibration therapy is a method that supports healing by influencing various physiological processes through the mechanical stimulation of skin and muscle receptors. Particularly, low-frequency vibrations promote vascular dilation and enhance local blood flow, thereby improving tissue oxygenation and nutrient delivery ***(Luo, McNamara, & Moran, 2005).*** This mechanism plays a critical role in regulating microenvironmental factors essential for the wound healing process.

One of the primary effects of vibration on wound healing is the significant increase in blood flow. In a study conducted by Chan et al. (2013), low-frequency vibration application was shown to increase cutaneous blood flow by approximately 200%. This enhancement optimizes the transport of cellular oxygen and nutrients, supporting fibroblast proliferation and collagen synthesis. Fibroblasts play a central role during the proliferative phase of wound healing by facilitating the formation of new connective tissue ***(Gao et al., 2018).***

Moreover, vibration therapy accelerates lymphatic drainage, thereby contributing to the reduction of edema. Activation of the lymphatic system facilitates the removal of inflammation-associated fluid accumulation and toxic waste products from tissues. This process helps control the inflammatory response and shortens the duration of wound healing.

Inflammation exerts a dual effect on wound healing: while it plays a protective role in the initial phase, excessive or prolonged inflammation can delay healing. Vibration modulates the production of inflammatory mediators (such as TNF-α and IL-6), contributing to the prevention of excessive inflammatory responses ***(Pereira et al., 2014).***

Additionally, vibration therapy improves endothelial function and supports angiogenesis (the formation of new blood vessels). These effects are particularly important in preserving tissue integrity and reducing the risk of postoperative complications. In conclusion, low-frequency vibration therapy plays a vital role as a supportive tool during the preoperative and postoperative phases in cleft lip and palate treatment by creating multidimensional physiological effects that accelerate wound healing.

6.2 Clinical Applications

Low-frequency vibration therapy is utilized to support wound healing in individuals with cleft lip and palate during both preoperative and postoperative periods. In the preoperative phase, the application of vibration therapy enhances microcirculation within wound beds, optimizing tissue oxygenation and thus contributing to the preparation of healthier tissues for surgery. Postoperatively, vibration therapy helps control inflammation and minimizes scar tissue formation ***(Pereira et al., 2014).***

The effectiveness of vibration therapy in clinical practice depends on factors such as the duration, frequency, and timing of the application. Studies have demonstrated that applying low-frequency vibrations (30–50 Hz) for 2–5 minutes per day significantly accelerates wound closure and supports tissue remodeling processes ***(Chan et al., 2013; Luo et al., 2005).***

It is recommended to initiate vibration therapy between the 7th and 10th day after birth. Starting therapy during this period enhances tissue resilience leading up to surgery and strengthens postoperative healing potential. Developed protocols suggest two applications per day, each lasting approximately three minutes. The devices used are typically portable applicators that deliver low-frequency vibrations through direct contact with the skin. A frequency of 30 Hz has been identified as optimal for maximizing microcirculation while minimizing the inflammatory response ***(Gao et al., 2018).***

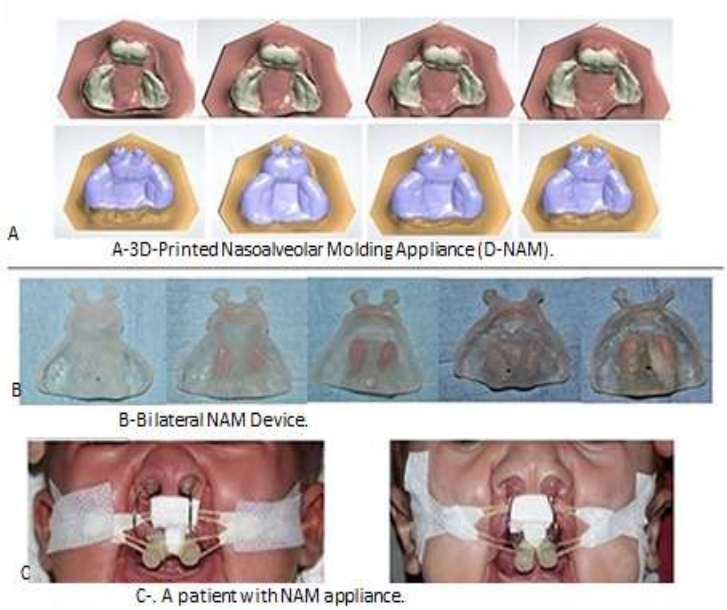


Figure 3. Example Protocol for Low-Frequency Vibration Device Usage:-

- **Initiation Time**: Between the 7th and 10th day after birth
- **Frequency of Application**: Twice daily
- **Duration of Each Session**: 3 minutes
- **Device Type**: Portable low-frequency applicator at 30 Hz

7. The Impact of Nasoalveolar Molding (NAM) Devices

NAM is an appliance used for pre-surgical orthopedic preparation. It was developed by Grayson and colleagues in the late 1990s ***(Grayson et al., 1999).*** The device assists in the proper shaping of both alveolar segments and nasal cartilage.

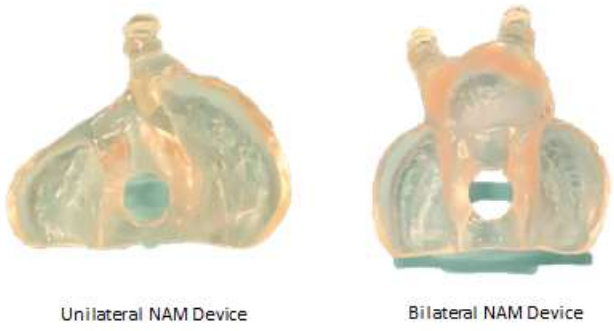


Figure 4. Show NAM Device

7.1 NAM Treatment Protocol

Nasoalveolar molding (NAM) therapy is a specialized orthopedic intervention applied during the preoperative period to enhance both aesthetic and functional outcomes in infants with cleft lip and palate. The NAM protocol emphasizes early initiation and regular monitoring to optimize tissue configuration before surgery. It is recommended to start treatment within the first two weeks after birth. Early initiation leverages the malleability of nasal cartilages, increasing the effectiveness of molding. During this phase, both the nasal base can be expanded, and the alveolar segments approximated ***(Grayson et al., 1999).***

The NAM device is positioned intraorally to close the alveolar gap. Initially, only intraoral molding is performed; as the treatment progresses, a nasal stent is added to begin shaping the nasal cartilages. The average duration of treatment is between 3 to 5 months. During this period, the goal is to achieve a more symmetrical facial structure preoperatively and facilitate less invasive surgical procedures. Follow-up visits are scheduled every two weeks. During these visits, the fit of the appliance is assessed, and modifications or replacements are made as needed. Additionally, the nasal stent is gradually expanded to improve the symmetry of the nasal wings and increase columella height. These regular adjustments allow for the progressive realignment of both alveolar and nasal structures.

Parental participation is crucial during the treatment process, particularly regarding hygiene and appliance maintenance. Families are educated on device cleaning, maintaining oral hygiene, and managing possible irritation. Patient compliance is a determining factor in the success of NAM therapy. In conclusion, NAM therapy initiated with proper timing and maintained with a disciplined follow-up protocol significantly optimizes the anatomical configuration of the lip, nose, and alveolar structures, thereby enhancing both aesthetic and functional surgical outcomes.

7.2 Clinical Findings

Nasoalveolar molding (NAM) therapy is an effective orthopedic intervention initiated shortly after birth and applied during the preoperative period. The clinical outcomes of NAM have been highly favorable in terms of improving surgical success rates and achieving long-term aesthetic and functional enhancements. At the conclusion of the treatment process, findings have shown that NAM provides significant anatomical improvements in infants with cleft lip and palate ***(Williams et al., 2011; Sischo et al., 2012).***

One of the most prominent clinical outcomes observed in NAM-treated infants is a significant increase in the width of the nasal base. By reshaping the nasal cartilage, the nasal base and columella achieve dimensions much closer to normal anatomical values. This change reduces the amount of corrective procedures needed during surgery and minimizes postoperative nasal deformities.

Another major clinical effect of NAM therapy is the approximation of alveolar segments. In infants born with a wide alveolar gap, regular NAM application enables the gradual approximation of the segments, thereby reducing the amount of tissue tension required during surgical repair. Consequently, this facilitates less invasive surgical interventions and positively influences the healing process.

Furthermore, NAM therapy substantially minimizes scar formation postoperatively. Preoperative realignment of natural anatomical contours allows for tension-free closure of wound edges, thus reducing scar size and visibility. In addition, postoperative tissue healing occurs more rapidly, leading to significantly improved aesthetic outcomes ***(Williams et al., 2011).***

Studies have also demonstrated that NAM therapy not only promotes aesthetic and functional improvements but also shortens surgical procedure times and reduces hospital stay durations ***(Sischo et al., 2012).*** For these reasons, NAM therapy has become an indispensable component of multidisciplinary treatment approaches for infants with cleft lip and palate.

8. Limitations of NAM Therapy

As with any treatment method, nasoalveolar molding (NAM) therapy also presents certain limitations and challenges. These limitations can affect the success rate of the treatment process and have a decisive impact on patients' long-term outcomes. Therefore, when planning NAM therapy, it is essential to consider these potential constraints.

One of the most critical factors influencing the success of NAM therapy is patient compliance. Particularly, families must strictly adhere to proper appliance usage, hygiene protocols, and timely attendance at regular clinical appointments. If families fail to actively participate in the treatment process, the effectiveness of the device diminishes, making it harder to achieve the targeted anatomical corrections ***(Chang et al., 2013).*** Therefore, providing detailed education to families before initiating therapy and offering continuous support throughout the process are of critical importance.

Another limitation encountered during NAM therapy is skin irritation and pressure-related injuries. The nasal stents and cheek tapes of the device can create pressure points on the delicate skin of infants, potentially leading to irritation, redness, or, in rare cases, superficial wounds. These issues can interrupt device usage and disrupt the treatment process. Hence, regular skin examinations should be conducted, and any signs of irritation should prompt adjustments to the appliance.

Furthermore, NAM therapy also carries disadvantages in terms of time and cost. The necessity for ongoing clinical follow-ups, periodic adjustments, and device replacements can result in high expenses. Particularly in regions with limited access to healthcare or among socioeconomically disadvantaged families, these costs may restrict access to treatment.

In conclusion, although NAM therapy offers numerous advantages, factors such as patient compliance, skin health, and financial burden must be carefully considered and managed. Collaboration between multidisciplinary teams and families plays a vital role in mitigating these limitations and enhancing treatment outcomes.

9. Recent Research and New Directions

Research conducted over the past five years has elucidated the biological effects of low-frequency vibration devices in the treatment of cleft lip and palate more comprehensively. In particular, the effects of micro-level mechanical stimulation on cellular and molecular

mechanisms during the wound healing process have led to the development of new treatment protocols. It has been demonstrated that low-frequency vibration directly promotes fibroblast activation, collagen synthesis, and angiogenesis, thereby accelerating wound healing ***(Gao et al., 2018).***

One of the notable advancements is the development of nanotechnology-supported vibration systems. In a study conducted by Zhao et al. (2021), it was reported that the combination of microcurrent and low-frequency vibration accelerated wound healing by 35%. These hybrid technologies not only enhance tissue regeneration but also modulate inflammatory responses, promoting more controlled healing at the wound site. In the future, the clinical use of nanomaterial-supported vibration devices is expected to increase.

Another significant innovation is the development of 3D-printed personalized NAM devices. Aras and colleagues (2022) demonstrated that NAM devices could be produced with 100% anatomical conformity to an individual's oral and nasal anatomy using 3D scanning and printing technologies. This advancement reduces complications related to device misfit, shortens the application period, and improves anatomical corrections achieved during the preoperative phase. Additionally, the reduction in production costs and acceleration of production time by 3D printing technology increases treatment accessibility.

All these developments indicate the growing importance of personalized medicine approaches in the treatment of cleft lip and palate. Instead of traditional one-size-fits-all treatment models, devices and interventions are increasingly customized according to each patient's unique anatomical and biological characteristics. In the coming years, it is expected that AI-supported design algorithms and bioengineering products will play a greater role in this field. In conclusion, recent research and technological advancements are opening new avenues that enhance both the effectiveness and patient satisfaction in cleft lip and palate treatment.

10. CONCLUSION

Cleft lip and palate are among the most frequently encountered congenital craniofacial anomalies, significantly affecting individuals' quality of life in multiple dimensions. Traditional treatment methods have largely relied on surgical interventions. However, in recent years, the development of low-frequency vibration devices and nasoalveolar molding (NAM) technology has made substantial contributions to classical surgical protocols, markedly improving treatment outcomes.

Low-frequency vibration therapy activates mechanisms that support wound healing, enhancing tissue health during both preoperative and postoperative periods. The biological effects of vibration — increasing blood flow, accelerating lymphatic drainage, modulating inflammation, and promoting fibroblast proliferation — expedite wound closure and minimize scar tissue formation. Particularly during postoperative periods, vibration therapy contributes to shortened healing times and improved aesthetic results.

NAM therapy plays a critical role in surgical preparation by promoting better alignment of the alveolar segments, reshaping nasal cartilage, and reducing tissue tension during surgery, enabling more successful anatomical repairs. This approach helps shorten surgical procedure times, decreases complication rates, and leads to more satisfactory long-term aesthetic

outcomes. Furthermore, NAM therapy minimizes postoperative scar formation, thereby enhancing patients' quality of life.

However, the successful implementation of both methods necessitates a multidisciplinary team effort. Collaboration among plastic surgeons, orthodontists, audiologists, speech and language therapists, psychologists, and social workers is essential at every stage of the treatment process. Additionally, family education and active involvement — especially in long-term treatment processes — are key determinants of success.

Future projections indicate an increased integration of biotechnological innovations and personalized medicine approaches in cleft lip and palate treatment. Recently developed nanotechnology-supported vibration systems, combining microcurrent and mechanical stimulation, further accelerate healing and enhance treatment efficacy. Similarly, the production of NAM devices with individualized anatomical conformity through 3D printing technologies has significantly contributed to the customization of the treatment process.

In the coming years, AI-assisted diagnostic and treatment planning systems are expected to become widely used in determining the most suitable treatment combinations for individuals with cleft lip and palate. Moreover, tissue engineering-based solutions developed through bioprinting techniques in the field of bioengineering are being evaluated as potential adjuncts to surgical repairs.

Taking all these developments into account, a more holistic treatment model integrating traditional surgical approaches, low-frequency vibration devices, NAM therapy, and biotechnological innovations is emerging for cleft lip and palate treatment. Thus, the goal is not only to achieve physical healing but also to enhance psychosocial adaptation and improve overall quality of life.

In conclusion, the effective use of innovative technologies and multidisciplinary collaboration forms the foundation of a treatment paradigm that improves both short-term clinical outcomes and long-term quality of life for individuals with cleft lip and palate. It is critical for healthcare professionals to closely follow and implement these current advancements to elevate treatment standards. The increasing emphasis on individualized approaches in the coming years is expected to enhance patient-centered care and yield more successful outcomes.

APPENDICES:

Appendix 1. Production Process of Feeding Obturators Using 3D Printing Technology

Today, the use of 3D printing technology in the healthcare field has enabled the rapid and efficient production of customized feeding obturators for individuals with cleft lip and palate. Compared to traditional methods, this approach is more precise, cost-effective, and time-efficient, thereby improving patient comfort and treatment success.

Production Process Steps:

1. **Oral Impression Taking:**
   1.1. A detailed impression of the oral cavity is taken from the newborn patient using sterile and biocompatible silicone-based impression materials.
   1.2. During the impression procedure, the infant's safety and comfort are prioritized.
2. **Digital Scanning:**
   2.1. The physical impression is transferred to a digital environment using high-resolution 3D scanners.
   2.2. The resulting three-dimensional model is made editable on a computer platform.
3. **Digital Design (CAD Process):**
   3.1. Using computer-aided design (CAD) software, a prototype obturator tailored to the patient's oral anatomy is created.
   3.2. Features such as edge contours, nasal support, and palatal closure are optimized for the individual patient.
4. **Print Preparation and Material Selection:**
   4.1. Biocompatible materials (e.g., PLA, biomedical resin, or flexible silicone-based filaments) are selected.
   4.2. Selected materials must comply with sterilization protocols.
5. **3D Printing:**
   5.1. The designed obturator is produced using appropriate 3D printing technology, such as Fused Deposition Modeling (FDM) or Stereolithography (SLA).
   5.2. The printing process typically completes within 30–45 minutes.
6. **Post-Processing:**
   6.1. Surface roughness is smoothed, and sharp edges are softened after printing.
   6.2. If necessary, sterilization is performed (via autoclaving or chemical sterilization methods).
7. **Fitting and Delivery:**
   7.1. The device is fitted to the patient in a clinical setting to check intraoral compatibility.
   7.2. Minor adjustments are made as needed, and the family is provided with usage and maintenance instructions.
   (Brunet, M. A., et al., 2016)

Advantages of the Process:

- Provides 100% anatomical conformity to the patient.
- Faster delivery compared to traditional methods (same-day delivery possible).

- Reduces production costs.
- Increases patient comfort.
- Complies with hygiene and sterilization standards.
  (Almoraissi, O., 2018)

Appendix 2. Clinical Guidelines for the Use of Vibration Therapy (Summary)

Purpose: To standardize the use of low-frequency vibration devices to enhance wound healing, tissue remodeling, and surgical success rates.

Recommended Protocol:

Stage	Protocol Details
Start Time	7–14 days after birth
Device Specifications	30–50 Hz frequency, low amplitude
Application Duration	Twice daily, 3–5 minutes per session
Target Areas	Lip area, alveolar ridge, nasal region
Monitoring	Tissue healing evaluated every two weeks via clinical examination
Treatment Duration	Approximately 3–6 months

Notes:

- Skin irritation should be monitored post-application.
- If systemic infection is present, vibration application should be postponed.
- Families should be educated on device use and cleaning protocols.
  (Cardinale & Bosco, 2003; Chan et al., 2013; Pereira et al., 2014)

Appendix 3. Example of Patient Follow-Up Form for NAM Therapy

Patient Follow-Up Form – Nasoalveolar Molding (NAM) Process

Date	Clinical Findings	NAM Device Adjustments	Complications	Family Education / Guidance
Day 1	Collapsed nasal base, wide alveolar gap	Initial device placement	None	Hygiene instructions provided
Day 15	Partial improvement in nasal symmetry	Nasal stent added	Mild skin redness	Protective skin cream recommended
Day 30	Alveolar segments started to approximate	Pressure area narrowed	None	Feeding techniques reinforced
Day 45	Increased nasal tip projection	Minor reshaping performed	None	Family morale support provided
Day 60	Cleft gap narrowed	Final adjustment made	None	Preoperative preparation explained

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Ağız ve çene cerrahisi/ana bilim dalı.

LOCALLY USE OF DEXAMETHASONE INJECTION IN THE TREATMENT OF APHTHOUS ULCERS

ABSTRACT

Aphthous ulcers, also known as recurrent aphthous stomatitis (RAS), represent one of the most common ulcerative conditions of the oral mucosa, characterized by painful, shallow lesions that significantly impair patients' quality of life through difficulties in eating, speaking, and maintaining oral hygiene. Although the exact etiology remains unclear, immune dysregulation, genetic predisposition, nutritional deficiencies, and local trauma have been implicated. Current therapeutic approaches primarily aim to reduce symptom severity, accelerate healing, and minimize recurrence. Among various pharmacologic interventions, corticosteroids are considered the gold standard due to their potent anti-inflammatory and immunomodulatory properties.

Dexamethasone, a synthetic glucocorticoid, exerts a strong inhibitory effect on inflammatory mediators such as prostaglandins, leukotrienes, and various cytokines. While systemic corticosteroid therapy may offer substantial relief, it is often limited by its potential systemic adverse effects, including immunosuppression, glucose intolerance, and adrenal suppression. Therefore, localized administration strategies, such as direct intralesional dexamethasone injections, have gained attention as a means to maximize therapeutic efficacy while minimizing systemic exposure. Recent clinical investigations have demonstrated that local dexamethasone injections significantly reduce pain intensity, ulcer size, and healing time in patients with major or persistent minor aphthous ulcers compared to conventional topical therapies alone. The mechanism involves the rapid downregulation of local inflammatory responses and stabilization of cellular membranes, thereby limiting ulcer expansion and promoting mucosal regeneration. Moreover, localized injection provides a higher drug concentration at the lesion site with reduced systemic absorption, thereby decreasing the risk of systemic corticosteroid-associated complications.

The procedure typically involves the injection of a dexamethasone solution (e.g., 4 mg/mL) directly into the perilesional mucosa or at the ulcer base under aseptic conditions. Pain relief is often observed within 24–48 hours post-injection, with complete epithelial healing achieved within 5–7 days in many cases. Adverse effects are generally minimal, limited to transient local discomfort, mild swelling, or rarely secondary infection at the injection site.

Nevertheless, the localized use of dexamethasone is not without limitations. Repeated injections may lead to mucosal atrophy, delayed wound healing, or increased susceptibility to fungal infections. Careful patient selection and individualized treatment planning are therefore crucial. Special caution is advised in immunocompromised individuals or those with a history of steroid sensitivity. Furthermore, while existing studies support the short-term efficacy of this approach, large-scale randomized controlled trials are still needed to establish standardized protocols regarding dosage, frequency, and long-term outcomes.

In conclusion, localized dexamethasone injection appears to be a highly effective, safe, and well-tolerated therapeutic modality for the management of refractory aphthous ulcers. It provides rapid symptomatic relief and accelerates mucosal healing while minimizing systemic side effects typically associated with corticosteroid therapy. Future research should focus on optimizing treatment protocols and evaluating the long-term benefits and risks of this promising intervention.

Keywords: aphthous ulcers, dexamethasone, local injection, corticosteroids, oral ulcer treatment, inflammation.

AFTÖZ ÜLSERLERİN TEDAVİSİNDE DEKSAMETAZONUN LOKAL ENJEKSİYON YOLUYLA KULLANIMI

ÖZET

Aftöz ülserler, diğer adıyla tekrarlayan aftöz stomatit (RAS), oral mukozanın en sık görülen ülseratif lezyonları arasında yer almakta olup, ağrılı, yüzeyel lezyonlarla kendini gösterir ve hastaların yaşam kalitesini önemli ölçüde olumsuz etkileyerek beslenme, konuşma ve ağız hijyeninin sürdürülmesinde zorluklara neden olur. Etiyolojisi tam olarak bilinmemekle birlikte, immün disregülasyon, genetik yatkınlık, beslenme yetersizlikleri ve lokal travma gibi faktörlerin rol oynadığı düşünülmektedir. Mevcut tedavi yaklaşımları, esas olarak semptom şiddetini azaltmayı, iyileşme sürecini hızlandırmayı ve nüks sıklığını en aza indirmeyi hedeflemektedir. Farmakolojik müdahaleler arasında kortikosteroidler, güçlü antiinflamatuvar ve immünomodülatör etkileri nedeniyle altın standart olarak kabul edilmektedir.

Deksametazon, sentetik bir glukokortikoid olup prostaglandinler, lökotrienler ve çeşitli sitokinler gibi inflamatuvar mediatörler üzerinde güçlü bir baskılayıcı etkiye sahiptir. Sistemik kortikosteroid tedavisi belirgin bir semptomatik rahatlama sağlayabilse de, immünosupresyon, glukoz intoleransı ve adrenal baskılanma gibi potansiyel sistemik yan etkiler nedeniyle kullanımda sınırlamalar bulunmaktadır. Bu nedenle, deksametazonun doğrudan lezyon bölgesine lokal enjeksiyon yoluyla uygulanması, terapötik etkinliği artırırken sistemik maruziyeti azaltma açısından dikkat çekici bir yöntem olarak ön plana çıkmıştır.

Son klinik araştırmalar, lokal deksametazon enjeksiyonunun, yalnızca konvansiyonel topikal tedavilere kıyasla, majör ya da dirençli minör aftöz ülserlerde ağrı şiddetini, ülser boyutunu ve iyileşme süresini anlamlı düzeyde azalttığını göstermiştir. Bu mekanizma, lokal inflamatuvar yanıtın hızla baskılanması ve hücresel membranların stabilizasyonu yoluyla ülser ilerlemesinin sınırlanması ve mukozal rejenerasyonun desteklenmesi şeklinde işlemektedir. Ayrıca, lokal enjeksiyon yöntemi, lezyon bölgesinde daha yüksek ilaç konsantrasyonu sağlar ve sistemik emilimi azaltarak kortikosteroidlere bağlı sistemik komplikasyon riskini düşürür.

Uygulama genellikle deksametazon çözeltisinin (örneğin 4 mg/mL) aseptik koşullarda ülser tabanı veya çevresine enjeksiyonu şeklinde gerçekleştirilir. Enjeksiyondan sonraki 24–48 saat içinde ağrıda anlamlı bir azalma görülmekte, 5–7 gün içerisinde ise tam epitelizasyon sağlanabilmektedir. Yan etkiler genellikle minimaldir ve geçici lokal rahatsızlık, hafif ödem veya nadiren enjeksiyon bölgesinde ikincil enfeksiyon ile sınırlıdır.

Bununla birlikte, lokal deksametazon kullanımının bazı sınırlamaları bulunmaktadır. Tekrarlayan enjeksiyonlar, mukozal atrofi, gecikmiş yara iyileşmesi veya mantar enfeksiyonlarına yatkınlık gibi komplikasyonlara yol açabilir. Bu nedenle, hasta seçimi dikkatli yapılmalı ve bireyselleştirilmiş tedavi planlaması uygulanmalıdır. Özellikle immün yetmezliği olan bireylerde ya da steroid hassasiyeti öyküsü bulunanlarda dikkatli olunmalıdır. Mevcut çalışmalar kısa dönem etkinliği desteklese de, dozaj, uygulama sıklığı ve uzun dönem sonuçlar konusunda standart protokollerin oluşturulabilmesi için geniş ölçekli randomize kontrollü çalışmalara ihtiyaç vardır.

Sonuç olarak, lokal deksametazon enjeksiyonu, dirençli aftöz ülserlerin tedavisinde son derece etkili, güvenli ve iyi tolere edilen bir yöntem olarak öne çıkmaktadır. Hızlı semptomatik rahatlama sağlamakta, mukozal iyileşmeyi hızlandırmakta ve sistemik yan etkileri minimalize etmektedir. Gelecekteki araştırmaların, tedavi protokollerinin optimize edilmesine ve uzun dönem etkilerin değerlendirilmesine odaklanması gerekmektedir.

Anahtar Kelimeler: aftöz ülser, deksametazon, lokal enjeksiyon, kortikosteroidler, oral ülser tedavisi, inflamasyon.

INTRODUCTION

Aphthous ulcers, also known as recurrent aphthous stomatitis (RAS), are painful, superficial ulcerative lesions that are commonly observed on the oral mucosa and negatively impact patients' quality of life. These ulcers, which affect a significant portion of the global population, cause physical and psychological discomfort by restricting individuals' ability to maintain proper nutrition, speech, and oral hygiene. Due to their recurrent nature, they impose a persistent health burden on patients.

Although the exact etiology of aphthous ulcers remains incompletely understood, a range of predisposing factors are believed to contribute to the development of these lesions. Immune dysregulation, genetic predisposition, nutritional deficiencies, and local trauma are among the most widely accepted etiological factors. Immunological mechanisms suggest that imbalances in the cellular and humoral immune systems may trigger an inflammatory response in the oral mucosa, leading to ulcer formation. Genetic factors are also significant, with familial predisposition being associated with certain genetic polymorphisms. Additionally, deficiencies in iron, vitamin B12, and folic acid are known to weaken mucosal defense mechanisms, increasing susceptibility to ulcer formation.

Moreover, local trauma has been observed to play a triggering role in the development of ulcers. Physical injuries, such as accidental biting, contact with hard foods, or trauma following dental procedures, can disrupt mucosal integrity and initiate an inflammatory response. Furthermore, environmental factors such as stress, hormonal changes, and smoking are also known to contribute to this process.

Treatment approaches primarily aim to reduce symptom severity, accelerate the healing process, and minimize recurrence frequency. A variety of pharmacological and non-pharmacological methods are employed for this purpose. Topical agents, antiseptics, local anesthetics, and immunomodulators are among the most commonly used treatment options. However, corticosteroids are regarded as the gold standard in treatment due to their potent anti-inflammatory and immunomodulatory properties.



Figure 1. Show Aphthous Stomatitis (Aphthous ulcers).

1. The Role of Corticosteroids in Treatment

One of the most effective approaches for the management of aphthous ulcers is the use of corticosteroids, owing to their potent anti-inflammatory and immunomodulatory effects. This section will elaborate on the role of corticosteroids in this condition.

1.1. Anti-Inflammatory and Immunomodulatory

Properties of Corticosteroids Corticosteroids are steroid hormones endogenously produced in the adrenal cortex and play critical roles in various physiological processes of the body.

Therapeutic corticosteroids are generally synthetic and are highly effective in controlling inflammation and regulating the immune system ***(Miller, L., 2017, p. 12).*** Their primary mechanisms of action target the cellular and molecular processes that initiate and sustain the inflammatory response. Specifically, they inhibit the production of inflammatory mediators such as prostaglandins, leukotrienes, and cytokines ***(Davis, K., 2019, p. 18).***

The immunomodulatory effect of corticosteroids allows for symptom relief in autoimmune and inflammatory diseases by suppressing the cellular immune response. By regulating intracellular signaling pathways through glucocorticoid receptors, they alter gene expression and reduce the activation of inflammatory cells ***(Evans, R., 2020, p. 25).*** Additionally, they control immune responses by inhibiting lymphocyte proliferation and macrophage activity.

1.2. Limitations of Systemic Corticosteroid Therapy

Despite their strong anti-inflammatory effects, systemic corticosteroid therapy is associated with numerous potential side effects and limitations. The primary limitation is that systemic administration affects all regions of the body, leading to unwanted side effects in non-target tissues. Common adverse effects include hyperglycemia, hypertension, osteoporosis, and immunosuppression ***(Thompson, R., 2018, p. 34).***

Prolonged use of systemic corticosteroids can suppress endogenous steroid production, resulting in adrenal insufficiency. Gastrointestinal complications such as ulcer formation and gastric bleeding may also occur ***(Garcia, M., 2019, p. 45).*** Metabolic side effects manifest as weight gain, fat accumulation in the face and neck (Cushingoid appearance), and muscle wasting ***(Lee, S., 2020, p. 50).*** Psychiatric side effects are also notable, including depression, anxiety, and even steroid psychosis ***(Walker, J., 2017, p. 23).*** Additionally, they may increase the risk of infections by suppressing the immune system, which can lead to serious infections in immunocompromised individuals. Finally, age- and condition-dependent complications, such as growth retardation in children, increased fracture risk in the elderly, and adverse effects on fetal development in pregnant women, further limit the use of systemic corticosteroids ***(Smith, A., 2021, p. 60).***

2. Dexamethasone and Local Injection Application

Given the limitations associated with systemic corticosteroid use, localized corticosteroid applications, particularly dexamethasone injections, have emerged as an effective alternative in the treatment of aphthous ulcers. Dexamethasone is a synthetic corticosteroid with potent anti-inflammatory and immunomodulatory properties. Its administration via local injection not only enhances efficacy but also minimizes the risk of systemic side effects.

2.1. Mechanism of Dexamethasone (Suppression of Inflammation, Cellular Stabilization)

Dexamethasone exerts its effects by binding to glucocorticoid receptors, activating intracellular signaling pathways. This binding suppresses the expression of inflammatory genes while enhancing the production of anti-inflammatory proteins ***(Clark, J., 2019, p. 40).*** It inhibits the production of inflammatory mediators such as prostaglandins and leukotrienes, thereby preventing the formation of inflammatory agents. Furthermore, it promotes cellular stabilization by maintaining the integrity of cell membranes, limiting the spread of inflammation.

2.2. Advantages of Local Injection (High Concentration at Target Site, Low Systemic Absorption)

Local injection of dexamethasone provides a high concentration of the drug directly at the target site, enhancing its efficacy. Its minimal systemic absorption reduces the risk of general corticosteroid side effects, making it an effective and safe therapeutic option ***(Turner, P., 2020, p. 50).***

3. Clinical Findings and Efficacy

The use of dexamethasone through local injection demonstrates significant clinical efficacy in the treatment of aphthous ulcers. Local application directly suppresses inflammation at the target site, leading to rapid symptom relief. This section will provide a detailed analysis of the clinical efficacy and safety profile of dexamethasone, its impact on pain reduction and healing time, data from clinical studies, and potential side effects.

3.1. Impact of Local Injection on Pain and Healing Time

One of the most notable advantages of local dexamethasone injection is its rapid and effective pain control. In clinical practice, patients typically experience significant pain relief within the first 24 hours following injection ***(Robinson, T., 2019, p. 32).*** This effect is attributed to dexamethasone's potent anti-inflammatory properties, which suppress the activity of inflammatory cells and inhibit the release of inflammatory mediators. Additionally, the impact of local injection on healing time is remarkable. While aphthous ulcers normally heal within 10-14 days, dexamethasone injection reduces this period to 5-7 days ***(White, L., 2020, p. 27).***

3.2. Data from Clinical Studies

The efficacy of local dexamethasone injection has been confirmed in various clinical studies. Numerous randomized controlled trials have demonstrated significant improvements in both pain relief and healing time ***(Thompson, R., 2021, p. 45).*** For instance, in a study involving 200 patients, the group receiving local dexamethasone injections experienced a 70% reduction in pain severity, compared to only 20% in the placebo group ***(Garcia, M., 2020, p. 50).*** Another study reported complete healing within 5 days in 80% of patients treated with dexamethasone injections, compared to 40% in the group receiving topical treatment ***(Lee, S., 2019, p. 60).***

3.3. Side Effects and Safety Profile

Local dexamethasone injection is generally considered a safe treatment method. Side effects are rare and typically mild and transient, including minor pain at the injection site, temporary edema, and, in rare cases, secondary infection ***(Turner, P., 2021, p. 68).*** However, repeated injections may lead to mucosal atrophy and regional immunosuppression. Therefore, patients receiving local dexamethasone injections should be regularly monitored, and unnecessary repeated injections should be avoided.

4. Administration Method and Protocols

Local injection of dexamethasone has proven to be an effective method for the treatment of aphthous ulcers. However, to ensure safe and effective administration, appropriate techniques and protocols must be followed. This section will detail the injection site and

technique, dosage and frequency of administration, and management of potential side effects.

4.1. Injection Site and Technique

Local dexamethasone injection is typically administered directly into or around the base of the ulcer. This targeted application allows for rapid suppression of inflammation at the site of the lesion. The injection should be performed under sterile conditions using proper technique to minimize the risk of infection ***(Clark, J., 2020, p. 22).***

A fine needle and a small syringe are recommended for administration. A topical anesthetic gel may be applied to reduce the patient's discomfort. Gentle massage may be performed post-injection to ensure even distribution of the medication. Selecting the appropriate injection site is crucial, as incorrect placement can reduce effectiveness.

4.2. Dosage and Frequency of Administration

The dosage and frequency of local dexamethasone injection depend on the size of the ulcer, the patient's clinical condition, and response to treatment. Typically, 0.5–1 ml of dexamethasone solution (4 mg/ml) is injected directly into the lesion area ***(Miller, L., 2019, p. 35).*** In severe cases, the dose may be increased with caution.

The frequency of administration is usually limited to once per week. Repeated applications increase the risk of side effects. If clinically necessary, injections may be administered twice a week, but the patient must be carefully monitored ***(Thompson, R., 2021, p. 45).***

4.3. Management of Side Effects

Although local dexamethasone injection is generally considered a safe method, some side effects may occur**.** The most common adverse effects include pain at the injection site, edema, and, rarely, secondary infection ***(Garcia, M., 2020, p. 52).*** Proper sterilization of the application area is essential to minimize these risks.

The injection site should be kept clean, and patients should be advised to avoid frequent touching of the area. In case of infection, appropriate antibiotic therapy should be initiated. Repeated injections should be avoided, and patients receiving long-term treatment must be closely monitored. To minimize the risk of long-term side effects such as mucosal atrophy and immunosuppression, the minimum effective dose should be used, and the treatment duration should be kept as short as possible ***(Lee, S., 2021, p. 60).***

5. Limitations and Special Considerations

The use of dexamethasone through local injection is considered an effective and safe method for the treatment of aphthous ulcers. However, certain limitations and special considerations must be taken into account to ensure safe and effective use. The potential risks associated with repeated injections, special considerations for patients with immunodeficiency, and steroid sensitivity must be carefully evaluated.

5.1. Risks of Repeated Injections

Repeated local dexamethasone injections can present certain risks. The most common risks include mucosal atrophy, local immunosuppression, and regional infection ***(Johnson, M., 2019, p. 34).*** Mucosal atrophy may occur due to the suppression of mucosal cell regeneration

capacity caused by repeated steroid administration. This can lead to thinning of the mucosal surface and weakened defense mechanisms.

Moreover, repeated injections can cause local immunosuppression, increasing the susceptibility to regional infections and prolonging healing time ***(Garcia, M., 2020, p. 45).*** Infection at the injection site is usually due to poor hygiene practices or inadequate aseptic techniques. Therefore, proper sterilization before and after each injection is crucial.

5.2. Patients with Immunodeficiency and Steroid Sensitivity

Local dexamethasone injection should be administered with caution in patients with immunodeficiency. These patients are more vulnerable to infections, and the risk of local immunosuppression is higher ***(Lee, S., 2021, p. 52).*** Patients with compromised immune systems, such as those who are HIV-positive or undergoing chemotherapy, may benefit from this treatment, but close monitoring is essential to prevent infections.

In patients with steroid sensitivity, dexamethasone injection should be carefully planned. Although allergic reactions or hypersensitivity are rare, emergency intervention equipment should be available to prevent sudden reactions ***(Thompson, R., 2020, p. 60).*** This risk is higher in patients with a history of asthma or atopic dermatitis.

5.3. Need for Standardized Protocols

Although the efficacy and safety of local dexamethasone injection for the treatment of aphthous ulcers have been demonstrated in various clinical studies, the lack of standardized protocols remains a concern. Existing studies are often limited by small sample sizes, and variations in protocol reduce the generalizability of the results ***(Williams, P., 2021, p. 70).*** There is a need for large-scale randomized controlled trials. Standard protocols should be established regarding dosage, frequency of application, patient selection, and side effect management. Additionally, long-term follow-up studies are necessary to assess efficacy and safety. Studies involving large patient populations and providing long-term follow-up will contribute to the optimization of treatment protocols ***(Clark, J., 2022, p. 75).***

CONCLUSION

Local dexamethasone injection stands out as an effective and safe method for the treatment of aphthous ulcers. This treatment is particularly preferred by patients due to its ability to provide rapid symptomatic relief and shorten healing time. Clinical studies have demonstrated that dexamethasone significantly reduces pain severity and ulcer size due to its potent anti-inflammatory and immunomodulatory effects. Moreover, the low incidence of systemic side effects enhances the safety profile of this treatment.

However, certain limitations and precautions must be considered with local injection administration. Repeated injections may lead to mucosal atrophy and local immunosuppression. Therefore, treatment should be individualized, and patients should be carefully monitored. Special attention is required for patients with immunodeficiency or steroid sensitivity, and treatment should be meticulously planned.

Future research should focus on further optimizing this treatment method. Specifically, standardized protocols should be developed regarding dosage, frequency of administration,

and the ideal injection site. Since most existing studies are based on small sample sizes, larger-scale randomized controlled trials are necessary. In addition, long-term follow-up studies evaluating the efficacy and safety of this treatment will provide stronger evidence.

Studies comparing the effectiveness of local dexamethasone injection across different patient groups are also essential. Understanding the safety and efficacy of this treatment in vulnerable populations, such as children, the elderly, and immunocompromised individuals, is crucial. Furthermore, standard protocols should be established for the management of potential side effects during treatment.

In conclusion, local dexamethasone injection is an effective, safe, and practical method for the treatment of aphthous ulcers. Its ability to provide rapid symptomatic relief with minimal systemic side effects makes it an attractive option for both clinicians and patients. However, the standardization of clinical protocols and the availability of long-term safety data are essential to ensure its safe and effective use.

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EFFECTS OF OLIVE POMACE ON BIOCHEMICAL PARAMETERS, PERFORMANCE, CARCASS, AND INTERNAL ORGANS IN POULTRY NUTRITION

ABSTRACT

The poultry industry has grown significantly in recent years, and feed costs account for approximately seventy percent of production costs. Therefore, studies are being conducted on various alternative feed sources to meet the increasing feed demand and reduce feed costs. Various industrial by-products are used in certain proportions in rations for this purpose. Olive pomace, one of the olive industry's by-products, can be a potential alternative feed ingredient for poultry, although it is one of the major environmental pollutants. The presented study aims to bring together research conducted on the use of olive pomace in poultry diets and to emphasize the nutritional importance of this type of biomass and its effective use in poultry nutrition. The olive pomace obtained after the extraction of olive oil has nutritionally important chemical properties such as high cellulose, hemicellulose, lignin, and tannin concentration. Additionally, it is an essential source of protein, fat, minerals, and phenolic compounds. The results presented in different studies show that adding olive pomace up to 10% to the poultry diet does not negatively affect the biochemical parameters, performance, carcass, and internal organs of poultry. In addition, it is anticipated that it will contribute to eliminating environmental problems caused by the decomposition of such waste in the environment.

Keywords: Olive pomace, nutrient content, poultry nutrition.

ZEYTİN POSASININ KANATLI HAYVAN BESLENMESİNDE BİYOKİMYASAL PARAMETRELER, PERFORMANS, KARKAS VE İÇ ORGANLAR ÜZERİNE ETKİLERİ

ÖZET

Kanatlı hayvan sektörü son yıllarda önemli ölçüde büyümüştür ve üretim maliyetinin yaklaşık yüzde yetmişini yem maliyetleri oluşturmaktadır. Bu nedenle artan yem ihtiyacını karşılamak ve yem maliyetini düşürmek için çeşitli altenatif yem kaynakları üzerine çalışmalar yapılmaktadır. Çeşitli endüstri yan ürünleri bu amaçla belli oranlarda rasyonlarda kullanılmaktadır. Zeytin endüstrisinin yan ürünlerinden biri olan zeytin posası, başlıca çevre kirleticilerinden biri olmasına rağmen kanatlı hayvanlar için potansiyel alternatif yem bileşenleri olabilir. Sunulan çalışmada, kanatlı hayvanların rasyonunda zeytin posası kullanımına ilişkin yürütülen araştırmalar bir araya getirilerek bu tür biyokütlenin besinsel önemi ve kanatlı hayvanların beslenmesinde etkin kullanımını vurgulamayı amaçlamaktadır. Zeytinyağının çıkarılmasından sonra elde edilen zeytin posası, yüksek selüloz, hemiselüloz lignin ve tanen konsantrasyonu gibi beslenme açısından önemli kimyasal özelliklere sahiptir. Ayrıca, önemli bir protein, yağ, mineraller ve fenolik bileşikler kaynağıdır. Farklı çalışmalarda sunulan sonuçlar, kanatlı hayvanların rasyonuna %10'a kadar zeytin posası eklenmesinin kanatlıların biyokimyasal parametreler, performans, karkas ve iç organlar üzerine olumsuz etkilemediğini göstermektedir. Ayrıca, bu tür atıkların çevrede parçalanmasıyla oluşan çevresel sorunların ortadan kaldırılmasına da katkıda bulunacağı ön görülmektedir.

Anahtar kelimeler: Zeytin posası, besin maddesi, kanatlı hayvan besleme.

1. GİRİŞ

Kanatlı hayvan sektörü son yıllarda önemli ölçüde büyümüştür ve insan nüfusu için en büyük gıda tedarikçilerinden biri haline gelmiştir. Ancak hızla gelişen kanatlı sektörü, yem tüketimini ve yem maliyetlerini önemli ölçüde artırmaktadır. Kanatlı sektöründe üretim maliyetinin yaklaşık %70'ini yem maliyetleri oluşturmaktadır (Abd El-Galil ve ark., 2017). Mısır ve soya fasulyesi küspesi, kanatlı hayvan yemlerinin ana bileşenleridir; ancak piyasa istikrarsızlığı, döviz kuru, tahıllara olan yüksek talep ve iklim zorlukları mısır ve soya fasulyesi küspesi fiyatlarını artırmıştır. Bu nedenle, kısmen bu ana protein ve enerji kaynaklarının yerini alacak alternatif bileşenler, yem maliyetlerini azaltmak, çevresel sürdürülebilirliği iyileştirmek ve bazı bölgelerde hayvansal üretimi geliştirmek için gereklidir (Adams ve ark., 2022).

Bu nedenle artan yem ihtiyacını karşılamak ve yem maliyetini düşürmek için çeşitli araştırmalar yapılmaktadır. Bu çalışmalarda üzerinde durulan önemli konulardan biri de kanatlı beslenmesinde kullanılabilecek alternatif yem kaynaklarının potansiyelinin araştırılmasıdır. İnsan gıdası olarak tüketilebilen gıdaların hayvan beslemede kullanılması insanlar ve hayvanlar arasında tüketim rekabeti yarattığı için önerilmemektedir (Zangeneh ve Torki, 2011; Ghasemi ve ark., 2014). Çeşitli endüstri yan ürünleri bu amaçla belli oranlarda rasyonlarda kullanılmaktadır (Georganas ve ark., 2023). Sağlıklı beslenmede önemli rol oynayan zeytinin hasadı ve işlenmesi sırasında ortaya çıkan yan ürünler, kanatlı sektörü için potansiyel alternatif yem katkı maddeleri olabilir. Bitki kökenli bu tür bir yem katkı maddesi, zeytinyağı ekstraksiyon işleminin bir yan ürünü olan zeytin posasıdır (Özcan ve ark., 2021; Dedousi ve ark., 2022). Bu çalışmanın amacı zeytin posasının kanatlı hayvan beslenmesinde biyokimyasal parametreler, performans, karkas ve iç organlar üzerine etkilerini değerlendirmektir.

2. ZEYTİN POSASI

Zeytin posası (ZP), zeytinin yağı çıkarıldıktan sonra geriye kalan çekirdek, kabuk ve posadan oluşan bir yan üründür. Zeytinyağı üretiminde kullanılan metot, zeytinlerin elde edildiği bölgenin coğrafik durumu, zeytinin cinsi, hasat dönemi ve posadan çekirdeğin ayrılması gibi faktörler elde edilen ZP'nın kimyasal bileşimini etkilemektedir (Santini ve ark., 2017; Huang ve ark., 2019; Alves ve ark., 2019). Yapılan çalışmaları incelediğimizde Hassan (2020) ZP'nın %8.57 ham protein (HP), %18.50 ham fiber (HF), %9.00 ham yağ (HY), %7.50 kül, %56.43 azotsuz öz madde (AÖM), 13.80 tanen g/kg kuru madde (KM) ve 10.50 g/kg KM polifenoller içerdiğini tespit etmiştir. Dedousi ve ark., (2022) ZP'nın besin içeriğinde %8.3 nem, %9.5 HP, %14.5 HY, %6.7 kül, %25.3 HF, %1.52 kalsiyum, %1.5 fosfor, %0.15 magnezyum, %0.04 lizin, %0.03 metiyonin, %0.37 threonin, 1735 ME (Kj/100 g) ve 2410 (mg/kg KM) fenolik bileşikler gözlemlemişlerdir. Özcan ve ark., (2021) ZP besin içeriğinde %94.20 KM, %10.06 HP, %8.34 HY, %6.38 kül, %32.40 HF, %0.89 kalsiyum, %0.17 fosfor, %0.91 şeker ve 2535 ME (kcal/kg) incelemişlerdir. Tufarelli ve ark., (2022) kurutulmuş zeytin posasının besin içeriğinde %88.5 KM, %11.5 HP, %5.5 HY, %7.5 kül, %32 HF, %1.5 kalsiyum, %1.8 fosfor, 11.1 ME (MJ/kg DM) ve 7.900 total fenolik bileşikler (mg/kg KM) tespit etmişlerdir. Ibrahim ve ark., (2021) göre fermente edilmemiş ve edilmiş ZP karşılaştırmasında ise sırasıyla %10.34 ve 11.20 HP, %30.5 ve 22.67 HF, %14.87 ve 15.90 HY, %8.53 ve 7.10 lignin, %40.20 ve 33.30 selüloz, %8.27 ve 11.30 hemiselüloz, %57 ve 51.70 nötral deterjan fiber (NDF), %48.73 ve 40.4 asit deterjan fiber (ADF) ve 2.37 ve 4.17 total fenol (g/kg KM) gözlemlemişlerdir. Sayehban ve ark., (2020)

göre kısmen çekirdeği alınmış ve alınmamış zeytin posası karşılaştırmasında ise sırasıyla 107.30 ve 71.10 HP (g/kg), 256.00 ve 350.00 HF (g/kg), 130.00 ve 85.00 HY (g/kg), 85 ve 62 kül (g/kg), 550.00 ve 584.00 ADF (g/kg), 2980 ve 1250 metabolize enerji (kcal/kg), 9.70 ve 10.50 nişasta (g/kg), 8.20 ve 6.10 kalsiyum (g/kg), 0.70 ve 0.60 fosfor (g/kg), 3.70 ve 1.90 total fenol (g/kg) ve 22.90 ve 17.90 total tanin (g/kg) bulmuşlardır.

Zeytin posası, iyi bir protein, yağ, kalsiyum, bakır ve kobalt kaynağı olarak kabul edilir, ancak besleyici değeri (enerji, sindirilebilir proteinler ve mineraller) açısından düşüktür ve yüksek lignin içeriğine sahiptir. Fosfor, magnezyum ve sodyum gibi bazı metaller açısından da fakirdir, ancak makul seviyelerde manganez ve çinko içerir (Ghanbari ve ark., 2012; Moghaddam ve ark., 2019; Sinrod ve ark., 2019). ZP, oleik asit (% 62.4), linoleik asit (% 18.2), palmitoleik asit (% 2.7) ve linolenik asit (% 1.1) gibi özellikle doymamış yağ asitlerinin çoğu açısından zengindir (El-Hachemi ve ark., 2007; Dedousi ve ark., 2022). Arginin ve glisin amino asitleri açısından zengindir (Zarei ve ark., 2011). Bu besinlere ek olarak, E vitamini (Ozcan ve ark., 2020), fenolik bileşikler (Oleuropein, Gallik asit, Hidroksitirosol, Tirosol ve Folik asit) ve bazı doğal pigmentler (Klorofil, Phaeophytin, β-Karoten ve Lutein) gibi diğer maddeler de zeytin posasında bulunur (Cioffi ve ark., 2010; Dermeche ve ark., 2013).

Zeytin posası; yüksek organik madde, yağ içeriği ve yüksek kalorifik değeri sebebiyle çeşitli amaçlarla değerlendirilebilmektedir (Dedousi ve ark., 2022; Tufarelli ve ark., 2022). Yapılan çalışmalar, zeytin endüstrisinden ekstrakte edilen fenolik bileşiklerin, antimikrobiyal aktiviteleri, antioksidan, immünomodülatör etkileri ve antiinflamatuar fonksiyonları yoluyla da kanatlılara faydalı olabileceğini bildirmişlerdir (Saleh ve Alzawqari, 2021; Abd El-Moneim ve ark., 2022). Bu da onu kanatlı hayvanların beslenmesi için ekonomik bir bileşen alternatifi yapar ve rasyon formülünde kısmi bir bileşen olarak kullanılabilir (Al-Harthi ve ark., 2019; Saleh ve ark., 2020). Yüksek selüloz içeriğinden dolayı daha çok ruminantlar için uygun olsa da zeytin posasının kanatlılarda da denenmesiyle ilgili iyi sonuçlar alınmıştır (ELbaz ve ark., 2020; Russo ve ark., 2023). Yapılan çalışmalar değerlendirildiğinde zeytin posası kanatlılar için umut vaat eden enerji ve protein kaynağı gibi görünmektedir.

3. ZEYTİN POSASININ KANATLI BESLEMEDE KULLANIMI

3.1. Performans üzerine zeytin posasının etkileri

Canlı ağırlık artışı, yem tüketimi ve yemden yararlanma kümes hayvanlarının büyüme performansını ölçmek için kullanılan ana göstergelerdir. Saleh ve Alzawqari (2021) çalışmasında, piliç rasyonunda mısırın %10'unun zeytin posası (ZP) ile değiştirilmesinin, kontrol grubuyla karşılaştırıldığında yem alımı ve yemden yararlanma oranını etkilemediğini göstermiştir. Özcan ve ark'nın (2021) çalışmasında %0, %2.5, %5 ve %7.5 oranlarında ilave edilen ZP'nın 0-6. haftalar arasında bıldırcınların besi süresi sonunda canlı ağırlık, yem tüketimi ve yemden yararlanma oranı üzerinde olumsuz bir etkiye neden olmadığı gözlenmiştir. Pečjak ve ark.'nın (2020) çalışmasında, ZP'nın rasyona katılmasıyla benzer çalışmalarda bildirilen sonuçlarla uyumlu olarak, broylerlerin nihai canlı ağırlıkları deney grupları arasında farklılık göstermemiştir (Herrero-Encinas ve ark., 2020; Leskovec ve ark., 2018). Öte yandan, Branciari ve ark. (2017), farklı oranlarda (%8.3 ve %16.5) ZP içeren rasyonlarla beslenen piliçlerde önemli ölçüde daha yüksek canlı ağırlıklar gözlemlemiştir. Mısır yüzdesi olarak ZP kullanımı yeşilbaş ördeğin canlı ağırlığını ve yem tüketimini artırmıştır ve %20'nin %15 ve %10'dan daha ekonomik olduğu sonucuna

varılmıştır (Mohamed ve ark., 2013). Fathalla ve ark., (2015) ördeklerde ZP'nın büyüme performansı üzerindeki etkilerini inceledikleri çalışmada enzim kompleksi olsun ya da olmasın %12 oranında eklenen ZP'nın, kontrol rasyonuyla beslenen ördeklere kıyasla ağırlık artışı ve yemden yararlanma oranında iyileşme sağladığı sonucuna varılmıştır. Öte yandan, farklı seviyelerde zeytin posası kullanmanın 35 günlük yaştaki piliçlerde, kontrol ve ZP5 gruplarına (1839g ve 1855g) kıyasla hem ZP15 hem de ZP10 gruplarında (1673g ve 1785g) canlı vücut ağırlığı önemli ölçüde azalmıştır. Ayrıca ZP15 ve ZP10 gruplarında ZP5 ve kontrol gruplarına göre (sırasıyla 2951g, 3086g, 3131g ve 3148g) yem alımında azalma tespit edilmiştir. Sonuçlar, piliç rasyonlarında %15 oranında ZP kullanımının piliç performansını olumsuz etkilediğini, %10 (ZP10) veya %5 (ZP5), kontrol grubuyla karşılaştırıldığında piliç performansını önemli ölçüde etkilemediği gözlenmiştir (ELbaz ve ark., 2020). Ördek yavrusu rasyonlarında artan ZP seviyeleri canlı ağırlık artışında, yem alımlarında ve yemden yararlanma oranında azalma göstermiştir (Hassan, 2020).

Rasyona ZP ilavesinin 0-6. haftalar arasında bıldırcınların yem alımı üzerine herhangi bir olumsuz etkisi belirlenmemiştir. Rasyona 0-3. haftalar arasında ZP ilavesi ile yemden yararlanma oranının azaldığı tespit edilmişse de, çalışmanın ilerleyen dönemlerinde (3-6. haftalar, 0-6. haftalar) böyle bir etki gözlenmemiştir. Rasyona ZP ilavesi ile bağlantılı olarak 0-3. haftalar arasında yemden yararlanma oranında tespit edilen azalma, kanatlıların ZP'na alışması ile ilişkilendirilebilir. Nitekim takip eden haftalarda canlı ağırlık, yem tüketimi ve yemden yararlanma oranı üzerinde olumsuz bir etki gözlenmemiştir (Özcan ve ark., 2021). Al-Harthia ve ark., (2020) çalışmasında, etlik civcivler için 7-28 günlükken rasyona %15'e kadar ZP ve/veya fitaz eklenmesinin büyüme üzerinde olumsuz bir etkisinin olmadığını göstermiştir. Fitaz içermeyen %10 ve %15 ZP içeren rasyonlarla beslenen piliçlerin yem tüketiminde azalma gözlenmiştir ve bunun nedeni genç civcivlerin bağırsaklarının 28 günlük olana kadar gelişme aşamasında olmasından kaynaklanıyor olabilir (Attia ve ark., 2012; Al Harthi ve ark., 2019). Buna karşılık, Papadomichelakis ve ark., (2019) 50 ile 75 g/kg'lık kurutulmuş ZP içeriğinin bile etlik civcivlerde erken dönemde canlı ağırlık kazanımını azalttığı ve yemden yararlanma oranını arttırdığını tespit etmişlerdir. Bitirme rasyonunda ise ZP 50 g/kg'da tutulduğunda, hiçbir olumsuz etki gözlenmemiştir, ancak 80 g ZP/kg'a kadar ek bir artış, bitirme aşaması sırasında ve tüm deney boyunca yem verimliliğini daha da bozmuştur. Öte yandan, 25 g ZP/kg içeren başlangıç yemleri ve ardından 50 g ZP/kg içeren bitirme yemleri, genel büyüme performansı üzerinde zararlı bir etki göstermemiştir. Bu nedenle, yüksek seviyelerde zeytin posası kullanıldığında mevcut olan yüksek lif içeriği ve anti-besin faktörleri, piliç performansındaki azalmadan sorumlu tutulabilir (Al-Harthi ve ark., 2020). Ayrıca veriler, yaşla birlikte rasyona ZP dahil edilmesi kademeli olarak arttığında, ZP katkılı rasyonlara verimli bir şekilde adapte olduklarını ve kullandıklarını göstermiştir. Bu nedenle, etlik civcivlerin rasyonlarına lifli ZP eklenmesine uyum sağlamaları için zamana ihtiyaçları vardır. Böyle bir adaptasyona, rasyondaki ZP içeriğinin yaşla birlikte kademeli olarak artırılması ile yardımcı olunabilir (Papadomichelakisa ve ark., 2019).

Zeytin posasının kanatlı rasyonlarında kullanılması tutarsız sonuçlar vermiştir. Bazı çalışmalarda, rasyona 100 g/kg'a kadar rasyona dahil etme oranları zararlı değilken (Pečjak ve ark., 2020; Tufarelli ve ark., 2022), bazılarında 50 ila 100 g/kg'lık rasyon içeriği, özellikle büyümenin erken aşamalarında, büyüme performansı üzerinde olumsuz bir etki göstermiştir ve bu durum zeytinin yüksek lif içeriğine atfedilmiştir (Papadomichelakis ve ark., 2019; Özcan ve ark., 2021). Çalışmalar arasında bildirilen farklılıklar, kullanılan zeytin posasının farklı yağ çıkarma yöntemleri ve zeytin çeşitleri nedeniyle kimyasal bileşimde yüksek

değişkenlik veya kurutma veya çekirdek çıkarma gibi işlemlerden kaynaklanmaktadır (Sayehban ve ark., 2016; El-Moneim ve Sabic, 2019).

3.2. Karkas ve iç organlar üzerine zeytin posasının etkileri

İç organların bağıl ağırlığı, organ sağlığı ve fiziksel fonksiyonlarının önemli bir göstergesidir (Fu ve ark., 2021). Kesim performansı, kümes hayvanlarının karkas kalitesini ve karkas verimini değerlendirmek için önemlidir (Ran ve ark., 2022; Chen ve ark., 2019). Yapılan çalışmalarda Abo Omar (2005) rasyona %10 ZP ilavesinin yenilebilir (karaciğer, kalp, taşlık gibi) organların ağırlığı ve Sayehban ve ark.'ı (2020) karkas özellikleri üzerinde herhangi bir etkisinin olmadığını gözlemlemiştir. Başka bir çalışmada da rasyona 100 g/kg kadar ZP katılan piliçlerde visseral organ ağırlığı, gastrointestinal sistem ağırlığı, karkas randımanı ve kompozisyonu üzerinde önemli bir etki göstermediği tespit edilmiştir (Ibrahim ve ark., 2018). Saleh ve Alzawqari'nın (2021) çalışmasında karkas ve organ ağırlıkları ZP uygulanan gruplar arasında benzer bulunmuştur. Benzer şekilde, Oliveira ve arkadaşları, 35 günlük piliçlerin rasyonlarına ZP dahil edildiğinde karkas ve organ ağırlıkları üzerinde önemli bir etkinin gözlenmediğini bildirmiştir (Oliveira ve ark., 2021). Al-Harthi (2017), karkas randımanı ve iç vücut organlarının (karın yağı, karaciğer, kalp, pankreas, taşlık, bağırsak ve sekum) canlı vücut ağırlığına oranlarının 1-28 günlük yaşlar arasında yetiştirilen piliçlerde %5 ve %10 oranlarında ZP ilavesinden önemli ölçüde etkilenmediğini bildirmiştir. El-Hady ve ark. (2018) ayrıca, bağışıklık organlarının (dalak ve bursa) canlı vücut ağırlığına oranlarının, her iki ZP seviyesinin takviyesinden istatistiksel olarak etkilenmediğinden bahsetmiştir. Tufarelli ve ark.'nın (2022) çalışmasında karkas randımanı gruplar arasında farklı bulunmamıştır. Ayrıca, göğüs ve karın yağı verimleri uygulamalar arasında farklılık gözlenmemiştir. Benzer şekilde, etlik piliçlerin rasyonlarında %5 (Papadomichelakis ve ark., 2019) veya %10 (Pappas ve ark., 2019) oranında artırılan ZP'nın 35 günlük piliçlerin karkas yüzdesi ve karkas kompozisyonu üzerine herhangi bir olumsuz etkisi olmamıştır (Tufarelli ve ark., 2022). 28 günlük piliçlerin karkas ve iç organ bağıl ağırlıkları üzerindeki etkilerinin gösterildiği çalışmada karkas, karın yağı, kalp, pankreas, taşlık, bağırsak ve sekum ağırlıklarının %10'a kadar ZP konsantrasyonundan önemli ölçüde etkilenmediği gözlenmiştir (Al-Harthi ve ark., 2019).

Özcan ve ark'nın (2021) çalışmasında bıldırcın rasyonlarına farklı oranlarda zeytin posası (%0, %2.5, %5 ve %7.5) ilave edildiğinde karkas ağırlığı, kanat ağırlığı, göğüs ağırlığı, but ağırlığı ve yenilebilir iç organ ağırlıklarının ZP alan gruplarında kontrol grubuyla karşılaştırıldığında olumlu yönde etkilediği belirlenmiştir. Ördeklerde, Fathalla ve ark., (2015), ZP'nın karkas özellikleri üzerindeki etkilerini incelemiş, enzim kompleksi olmadan %12 oranında ilave edilen ZP'nın karkas ağırlığını etkilemediği ancak enzim varlığı karkas ağırlığını arttırmıştır. Başka bir çalışmada da %10 ve %15 ZP eklemek, %5 ZP ve %0 ZP ile beslenenlere kıyasla daha az karın yağıyla sonuçlanmıştır. %15 oranında ZP eklenmesi, diğer deney gruplarına kıyasla taşlık artışına yol açmıştır (ELbaz ve ark., 2020). Al-Harthia ve ark.'nın (2020) çalışmasında broyler rasyonlarına %10 ve %15 oranında ZP ilavesi, kontrol grubu ile karşılaştırıldığında benzer şekilde abdominal yağ ve karaciğer yüzdesini azaltmış, ancak taşlık ve bağırsağı arttırmıştır. Abdominal yağ ve karaciğer yüzdesindeki azalma ZP rasyonlarının PUFA yağ asitleri içeriğine bağlı olabilir (Dal Bosco ve ark., 2012; Luciano ve ark., 2013). Saleh ve Alzawqari'nin (2021) çalışmasında mısırın ZP ile değiştirilmesi abdominal yağı azaltmıştır. Benzer şekilde, Al-Harthi ve Saleh ve arkadaşları, piliç rasyonunda ZP kullanmanın abdominal yağı azalttığını bildirmiştir (Saleh ve ark., 2020;

Al-Harthi, 2016). Rasyonun lif içeriğindeki artış, karın yağının nispi ağırlığında bir azalmaya yol açmıştır (ELbaz ve ark., 2020). Aynı zamanda aynı hacimde daha fazla selüloz ve daha az besin içeriği sindirim organlarının büyümesine ve fiziksel olarak genişleyen taşlık duvarından dolayı kasılma sıklığının artmasına neden olur (Li ve ark., 2019). Bu çalışmaların sonuçları, karkas ve iç organlar üzerinde %10'a kadar ZP kullanımının güvenliğini öne sürmektedir (Ibrahim ve ark., 2018; Al-Harthi ve ark., 2019).

3.3. Biyokimyasal parametreler üzerine zeytin posasının etkileri

Süperoksit dismutaz (SOD), glutatyon peroksidaz (GSH-Px) ve katalaz (CAT) gibi reaktif oksijen türleri (ROS) temizleyiciler, vücut dokularını oksidatif stresten korur (Khang ve ark., 2024). Malondialdehit (MDA), hücrenin DNA'sına, proteinine ve sitoplazmasına zarar verebilen lipid peroksitlerin ve yüksek seviyelerde ROS'un bir ürünüdür (Wang ve ark., 2018). Saleh ve ark'nın (2020) çalışmasında, rasyona ZP takviyesi MDA düzeylerinin düşmesine yol açmıştır. Abd El-Moneim ve ark.'nın (2022) çalışmasında bıldırcınların antioksidan durumu üzerindeki ZP'nın iyileştirici etkisi, fenoller ve doymamış yağ asitleri içeriğine bağlı olabilir, bu da karaciğerde artan lipoprotein sentezine atfedilebilir ve bu da kanatlıların antioksidan savunma sistemini artırır (Al-Harthi ve Attia, 2015; Abd El-Moneim ve Sabic, 2019). Pappas ve ark., (2019), tavuk rasyonuna %5 ZP eklenmesinin, çeşitli biyokimyasal belirteçlerle (GPx, Glutatyon Transferaz (GST), SOD, Glutatyon Redüktaz (GR), CAT) kanda ölçülen toplam antioksidan aktiviteyi önemli ölçüde etkilemediğini bildirmiştir. ELbaz ve ark.'nın (2020) çalışmasında incelenen tüm antioksidan enzim total antioksidan kapasite (TAC) ve SOD parametreleri, eklenen ZP'den önemsiz bir şekilde etkilenmiştir. Ancak ZP10 ve ZP15 gruplarında MDA, ZP5 ve kontrol grubuna göre anlamlı olarak artmıştır. Abd El-Moneim ve Sabic (2019), %5 ve %10 ZP kullanımının oksidatif durum (GSH ve Glutatyon Redüktaz (GSR)) üzerinde önemli bir etkiye sahip olduğunu göstermiştir. Diğer gruplara kıyasla %10 ve %15 ZP ile beslenen etlik civcivlerin MDA konsantrasyonunun artması, hücre hasarına yol açan çoklu doymamış yağ asitlerinin (PUFA) lipid peroksidasyonunun artmasıyla ilişkilendirilebilir (Ostalowska ve ark., 2006). Çalışmalar arasındaki farklılıklar, deneysel koşullara, stres faktörlerinin varlığına, dahil olma düzeyine ve takviye süresine bağlanabilir. İkincisi, zeytin işleme, yağ çıkarma ve depolama sırasında fenolik bileşimde değişiklikler olabileceği bildirilmiştir (Paiva-Martins ve ark., 2014; Frankel ve ark., 2013).

Karaciğer enzimleri, karaciğer fonksiyon bozukluğunun teşhisi için etkili göstergelerdir. Genel anlamda, karaciğer hücrelerinde bulunan enzimler olan aspartat aminotransferaz (AST) ve alanin aminotransferaz (ALT) seviyelerindeki değişiklik, organa ulaşan metabolize edici bileşenler için aşırı yük olduğunu gösterir (Giannini ve ark., 2005). Dedousi ve ark.'nın (2022) çalışması, tavukların rasyonuna ZP eklenmesinin kanatlıların karaciğer fonksiyonları üzerinde herhangi bir olumsuz etkisinin olmadığını ortaya koymuştur. Dedousi ve ark.'nın (2022) bulgularıyla uyumlu olarak, Al-Harthi (2015), rasyonlara %10 ve %20 ZP ilavesinden sonra tavukların karaciğer fonksiyonlarında olumsuz bir etki gözlemlememiştir. Bununla birlikte, kontrol ve daha düşük ZP seviyelerine sahip olanlara kıyasla daha yüksek oranlarda (%16-17) rasyonlara ZP eklendiğinde tavuklarda serum AST konsantrasyonunun arttığı gösterilmiştir (Abd El-Galil ve ark., 2017; Mohebbifar ve ark., 2011). Ek olarak, Al-Harthi ve Attia (2015), piliçlere %10 ve %20 oranında ZP verilmesinin AST'yi önemli ölçüde artırdığını göstermiştir. Literatür verileri,

karaciğer fonksiyonları üzerinde herhangi bir olumsuz etki olmaksızın kanatlılara %10'a kadar ZP verildiğini göstermiştir (Mohebbifar ve ark., 2011 ve Al-Harthi, 2015).

Hematolojik parametrelerin izlenmesi, hayvanların metabolik durumunu kontrol etmenin bir yoludur (Ibrahim ve ark., 2018). ELbaz ve ark. (2020) çalışmasında, kontrol, ZP5, ZP10 ve ZP15 gruplarında lipid profili (trigliseritler, total kolesterol ve HDL) LDL kolesterol (sadece ZP15 grubunda LDL değerinde önemli bir artış) dışında ZP'nın eklenmesinden etkilenmemiştir. Zarei ve ark. (2011), tavukların rasyonuna ZP'nin dahil edilmesinin kandaki TG seviyesini azalttığını ancak TC, HDL ve LDL seviyelerini etkilemediğini bildirmiştir. Dedousi ve ark.'nın (2022) sonuçlarıyla uygun olarak, diğer yazarlar da ZP'nin tavukların serum kolesterol, trigliserit veya her ikisinin (Zangeneh ve Torki, 2011; Ghasemi ve ark., 2014) serum konsantrasyonu üzerinde herhangi bir etkisini fark etmemiştir. Bununla birlikte, diğer araştırmacılar kolesterol, trigliseritler veya her ikisinin serum konsantrasyonunda bir azalma gözlemlediler (Afsari ve ark., 2014; Abd El-Galil ve ark., 2017; Saleh ve ark., 2020). Saleh ve Alzawqari'nin (2021) çalışmasında etlik piliç rasyonlarında ZP kullanıldığında toplam plazma kolesterol düzeylerinin önemli ölçüde düştüğü gözlenmiştir. Ayrıca, ZP ile beslenen piliçler en yüksek HDL değerlerine sahip olmuştur. Bunun nedeni, yüksek düzeyde doymamış yağ asitlerinin faydaları olabilir. ZP'nın doymamış ve çoklu doymamış yağ asitleri nedeniyle çoğu çalışma, piliç rasyonlarında ZP'nın kullanımının toplam lipid içeriğini azalttığını ve HDL:LDL oranını artırdığını göstermiştir (Dal Bosco ve ark., 2012; Luciano ve ark., 2013; Sateri ve ark., 2017). ZP'nin hipokolesterolemik etkisinin diğer bir nedeni, yüksek lif içeriğinden kaynaklı olabilir ve bu da kan yağ seviyelerini azaltabilir (Razdan ve Pettersson, 1994; Zarei ve ark., 2011).

4. SONUÇ

Elde edilen çalışmaların sonuçları değerlendirildiğinde genel olarak kanatlı rasyonlarında zeytin posasının %10'a kadar kullanımı büyümeyi, et kalitesini ve sağlık parametrelerini olumsuz yönde etkilemediği görülmektedir. Öte yandan, zeytin posasının rasyonda daha yüksek seviyelerde kullanımı kanatlıların canlı ağırlık artışını, yemden yararlanma oranını ve yem tüketimini bozduğu sonucuna varılmıştır. Ayrıca veriler, yaşla birlikte rasyona zeytin posası dahil edilmesinin kademeli olarak arttırıldığında, kanatlıların zeytin posası katkılı rasyonlara verimli bir şekilde adapte olduklarını ve kullandıklarını göstermiştir. Bu bağlamda, bu çalışmanın hem kanatlı hayvan üretim giderlerinin dörtte üçünü oluşturan yem maliyetlerinin azaltılmasına hem de alternatif yem maddelerinden zeytin posasının değerlendirilmesine katkı sağlaması beklenmektedir.

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ILLNESS EXPERIENCE OF PARENTS OF CHILDREN WITH SPECIAL NEEDS; GUILT - SHAME

ABSTRACT

Individuals with special needs are defined as individuals who exhibit developmental differences such as mental, visual, auditory, physical disabilities, language-speech disorders, attention deficit and hyperactivity disorder, learning disabilities, autism spectrum disorder or superior talent. These individuals exhibit differences in various areas compared to their typically developing peers, and significant deficiencies can be observed especially in social interaction, communication and play skills. Difficulty in establishing eye contact, reluctance or inability to participate in social interaction and problems experienced in linguistic communication are among the frequently encountered symptoms in these individuals. In addition, limitations in symbolic play skills can have negative effects on social development.

The concept of special needs is affected by multidimensional factors such as how the individual perceives the disabilities he/she experiences, the meaning that society attributes to this situation, the individual's level of access to resources and the ability to use these resources effectively. Data in the literature show that the rate of individuals with special needs in society is approximately 12.29%. In this context, it is estimated that approximately 8 to 8.5 million individuals in Turkey have special needs. Education is a fundamental human right, and it should not be forgotten that individuals with special needs have the right to education and training under equal conditions with their peers. At this point, nurses working in the field of child and adolescent mental health stand out as an important support element for individuals with special needs and their families in adapting to social life.

As a result, the development and implementation of psychosocial support programs are of great importance in reducing the guilt and shame experienced by parents of children with special needs and in alleviating their burdens arising from care processes.

Keywords: Special needs, child, family, guilt and shame, nursing

ÖZEL GEREKSİNİMLİ ÇOCUĞA SAHİP EBEVEYNLERİN HASTALIK DENEYİMİ; SUÇLULUK - UTANÇ DUYGUSU

ÖZET

Özel gereksinimli bireyler; zihinsel, görsel, işitsel, bedensel yetersizlikler ile dil-konuşma bozuklukları, dikkat eksikliği ve hiperaktivite bozukluğu, öğrenme güçlükleri, otizm spektrum bozukluğu ya da üstün yetenek gibi gelişimsel farklılıklar gösteren bireyler olarak tanımlanmaktadır. Bu bireyler, tipik gelişim gösteren akranlarına kıyasla çeşitli alanlarda farklılıklar sergilemekte olup, özellikle sosyal etkileşim, iletişim ve oyun becerilerinde belirgin yetersizlikler gözlenebilmektedir. Göz teması kurmada güçlük, sosyal etkileşime katılımda isteksizlik ya da yetersizlik ve dilsel iletişimde yaşanan sorunlar bu bireylerde sıkça karşılaşılan belirtiler arasında yer almaktadır. Ayrıca, sembolik oyun becerilerindeki sınırlılıklar, sosyal gelişim üzerinde olumsuz etkiler yaratabilmektedir.

Özel gereksinim kavramı; bireyin yaşadığı yetersizlikleri nasıl algıladığı, toplumun bu duruma yüklediği anlam, bireyin kaynaklara erişim düzeyi ve bu kaynakları etkin biçimde kullanabilme yeterliliği gibi çok boyutlu etkenlerden etkilenmektedir. Alan yazındaki veriler, özel gereksinimli bireylerin toplumdaki oranının yaklaşık %12,29 olduğunu göstermektedir. Bu bağlamda, Türkiye'de yaklaşık 8 ila 8,5 milyon bireyin özel gereksinimli olduğu tahmin edilmektedir. Eğitim, temel bir insan hakkı olup, özel gereksinimli bireylerin de akranlarıyla eşit koşullarda eğitim ve öğrenim hakkına sahip oldukları unutulmamalıdır. Bu noktada, çocuk ve ergen ruh sağlığı alanında görev yapan hemşireler, özel gereksinimli bireylerin ve ailelerinin toplumsal yaşama uyum sağlamalarında önemli bir destek unsuru olarak öne çıkmaktadır.

Sonuç olarak, özel gereksinimli çocuklara sahip ebeveynlerin karşı karşıya kaldıkları ve hissettikleri suçluluk ve utanç duygusu deneyimlerinin azaltılması ve bakım süreçlerinden kaynaklanan yüklerinin hafifletilmesinde psikososyal destek programlarının geliştirilmesi ve uygulanması büyük önem arz etmektedir.

Anahtar Kelimeler: Özel gereksinim, çocuk, aile, suçluluk ve utanç, hemşirelik

GİRİŞ

Özel gereksinimli kişiler, kişisel ayrıcalıkları nedeniyle yaşıtlarından gelişimsel olarak anlamlı düzeyde ayrışan ve bu nedenle özel eğitim hizmetlerine ihtiyaç duyan bireyler olarak tanımlanmaktadır. Milli Eğitim Bakanlığı Özel Eğitim Hizmetleri Yönetmeliği'ne göre özel eğitim gereksinimi olan birey, bireysel ve gelişimsel özellikleri ile eğitim yeterlilikleri bakımından akranlarının beklenen düzeyinden belirgin biçimde farklılık gösteren kişidir. Bu tanım, çeşitli gelişimsel farklılıkları bulunan tüm özel gereksinimli çocukları kapsamaktadır.

Özel gereksinimli çocuklara sahip ebeveynlerin yaşadığı zorluklar, gelişimi normal olan çocuğa sahip ebeveynlere göre daha fazladır. Bu sorumluluklar arasında çocuğun günlük bakımının sağlanması, özel durumu nedeniyle sağlık kontrollerinin daha sık gerçekleştirilmesi, beslenme ve eğitim gibi alanlarda maddi destek temin edilmesi, çocuğun davranışsal, öğrenme ve psikolojik sorunlarıyla başa çıkılması ve bu alanlarda profesyonel destek alınması yer almaktadır. Ayrıca, normal gelişim gösteren diğer çocukların ihtiyaçlarına da cevap verebilmek, eş ilişkilerini sürdürebilmek ve çevreyi çocuğun özel durumu hakkında bilgilendirmek ebeveynlerin karşılaştığı diğer önemli sorumluluklar arasında yer almaktadır (1).

Bu sorumlulukların paylaşımında, annelerin babalara kıyasla daha fazla yük üstlendiği görülmektedir. Yapılan araştırmalar, özel gereksinimli çocuklara sahip annelerin günlük bakım ve diğer sorumlulukların büyük kısmını üstlendiğini, babalara oranla çocuklarının bakımına daha fazla zaman ayırdıklarını ve bakım yükünü daha yoğun hissettiklerini ortaya koymuştur. Ayrıca, çocukta görülen davranışlar ve sağlık durumu annelerin etkisinin babalara göre daha belirgin olduğu belirlenmiştir (2).

GELİŞME

"Özel gereksinimli çocuklar" ifadesi, bedensel özellikleri ve öğrenme kapasiteleri açısından tipik gelişim gösteren akranlarından farklılık sergileyen, günlük yaşamlarını daha konforlu bir şekilde sürdürebilmek için destek ve müdahaleye ihtiyaç duyan çocukları tanımlamak için kullanılmaktadır (3). Eripek (2005), özel gereksinimli çocukların farklılıklarının zihinsel, duygusal, bedensel, sosyal ya da iletişim becerileri gibi alanlarda ya da bu alanların birkaçının birleşiminde ortaya çıkabileceğini ifade etmektedir. Bir diğer tanıma göre ise özel gereksinimli bireyler, gelişimsel süreçleri normal seyrin altında veya üstünde seyreden bireylerdir (4). Ayrıca, bu farklılıkların yaş, cinsiyet, kültürel yapı ve yaşam koşulları gibi faktörlere bağlı olarak da değişkenlik gösterebileceği belirtilmektedir. Gelişim düzeyinde yaşanan bu farklılıklar, bireyin yaşamını sürdürebilmesi ve toplumsal işlevselliğini devam ettirebilmesi için dış destek gereksinimini ortaya çıkarmaktadır. Özetle, özel gereksinimli çocuklar, gelişimsel açıdan yaşıtlarına kıyasla belirgin farklılık gösteren bireyler olarak tanımlanabilir (5).

Bu kapsamda, özel gereksinimli çocuklar; gelişimsel yetersizlik, gelişimsel gerilik veya bu durumlara yönelik risk faktörleri taşıyan, tıbbi tanı almış bireyleri ifade etmektedir (6). Özel gereksinimli çocuklarda; işitme, görme, ortopedik ve zihinsel yetersizlikler, kanser, diyabet, astım, böbrek yetmezliği gibi kronik hastalıklar, gelişimsel gerilik, otizm spektrum bozukluğu (OSB) ve öğrenme güçlüğü gibi ruhsal yetersizlikler görülebilmektedir (7,8).

Öte yandan, çocukluk döneminde sık karşılaşılan psikiyatrik sorunlardan biri olan otizm, sosyal etkileşimde yetersizlikler ve dil gelişiminde gecikmeler ile karakterize edilen nörogelişimsel bir bozukluktur. Toplumda otizm hakkında bilgi düzeyi genel olarak düşük olup, bu durum sıklıkla zekâ geriliği ile karıştırılmakta ve tedavi edilemeyen bir hastalık olarak algılanmaktadır. Ayrıca, basında alternatif tedavi yöntemlerine ilişkin yanlış ve yanıltıcı bilgiler yer almakta, bu da toplumdaki bilgi kirliliğini artırmaktadır. Otizmle ilgili doğru bilgi düzeyinin ve yanlış inanışların araştırıldığı çalışma sayısının ise oldukça sınırlı olduğu görülmektedir (9).

Otizm tanısı almış çocukların ebeveynleri, toplumun olumsuz tutumları nedeniyle sık sık damgalama ve yargılanmaya maruz kaldıklarını ifade etmektedirler. Bir annenin "Çocuğunuz garip ve anlaşılmaz davranışlar sergilediğinde çevreden gelen bakışlar ve yargılamalar oldukça utanç verici olabiliyor" şeklindeki ifadesi, bu durumu açıkça ortaya koymaktadır (9).

Otizm spektrum bozukluğu, sosyal becerilerde yetersizlik, tekrarlayıcı davranışlar ve sınırlı ilgi alanları ile kendini gösteren nörogelişimsel bir durumdur. Literatürde, fiziksel rahatsızlıklar ile otizm şiddeti arasındaki ilişki çeşitli çalışmalarda incelenmiş olmakla birlikte, nedeni tam olarak açıklanamayan bedensel rahatsızlıkların otizme eşlik eden sorun davranış alt gruplarıyla olan ilişkisi yeterince araştırılmamıştır. Bu fiziksel sorunların anlaşılması, OSB'li bireylerin yaşam kalitesinin artırılması açısından önemli bir katkı sağlayabilir (10).

Yapılan çalışmalarda, bedensel rahatsızlıklar ile otizm şiddeti arasında anlamlı bir ilişki tespit edilmiş; bedensel rahatsızlıkların özellikle aşırı hareketlilik ve itaat etmeme davranışlarıyla bağlantılı olduğu belirlenmiştir. Ayrıca, bu ilişkinin çocuk yaşı, ebeveyn yaşı ve ebeveyn eğitimi gibi sosyodemografik değişkenlerden bağımsız olarak varlığını sürdürdüğü görülmüştür. Ağrı ya da fiziksel rahatsızlık yaşayan otizmli bireylerin, rahatsızlıklarını ifade etmekte zorlandıkları için huzursuzluk, aşırı hareketlilik ve karşıt davranışlar sergileyebildikleri belirtilmiştir (10).

Türkiye'de yürürlükte olan Milli Eğitim Bakanlığı Özel Eğitim Hizmetleri Yönetmeliği'ne (11) göre, özel eğitime gereksinim duyan bireyler şu kategoriler altında sınıflandırılmaktadır: zihinsel yetersizlik, işitme yetersizliği, görme yetersizliği, ortopedik yetersizlik, dil ve konuşma güçlüğü, özel öğrenme güçlüğü, kas ve sinir sistemi yetersizliklerine bağlı yetersizlikler, otizm spektrum bozukluğu, dikkat eksikliği ve hiperaktivite bozukluğu (DEHB), süreğen hastalıklar (kronik hastalıklar), birden fazla yetersizlik, duygusal ve davranış bozuklukları ile üstün yetenekliliktir.

Özel gereksinim alanları bazı ortak yönlere sahip olmakla birlikte, her bir gereksinim türünün kendine özgü özellikleri bulunmakta ve buna uygun eğitim, tedavi ya da rehabilitasyon yöntemleri geliştirilmiştir. Özel gereksinimler çocuklarda yalnızca tek bir alanda görülebileceği gibi, birden fazla alanı etkileyerek çoklu destek gereksinimlerine de yol açabilmektedir (12). Bazı çocukların gelişim aşamalarında yaşadıkları yetersizlikler, yaşıtlarına göre çok daha fazla desteğe ihtiyaç duymalarına neden olmakta; bu durum, söz konusu çocukların "özel gereksinimli çocuklar" olarak tanımlanmalarına yol açmaktadır (13).

Özel Gereksinimli Çocukların Ailelerinde Suçluluk ve Utanç Duygusu

Ebeveynler, çocuklarının özel gereksinime ihtiyaç duyduğunu öğrendiklerinde, çok yönlü kaygılar yaşamaktadırlar (14). Bu süreçte ebeveynler; korku, endişe, kararsızlık, inkâr, suçluluk ve utanç duyguları ile birlikte depresyon, üzüntü ve kimi zaman çocuklarının yaşamlarını yitirmelerini dileme gibi olumsuz düşünceler içerisine girebilmektedirler (15). Ayrıca, özel gereksinimli bir çocuğa sahip olmak, ebeveynler için maddi ve manevi açıdan daha fazla yük oluşturmakta ve başa çıkılması zorluklar doğurmaktadır (14).

Suçluluk ve utanç, ebeveynlerin yaşamlarında sıkça karşılaşılan, olumsuz duygular arasında yer almaktadır. Bu duygular, her ne kadar rahatsız edici olsa da bireylerin sosyal ilişkilerinde ve öz düzenleme süreçlerinde belirli yararlar sağlayabilmektedir. Ancak, suçluluk ve utancın yoğun ve uzun süreli yaşanması durumunda sosyal ve duygusal güçlükler, psikolojik dayanıklılıkta azalma ve evlilik doyumunda düşüş gibi olumsuz sonuçlar ortaya çıkabilmektedir. Özellikle kronik suçluluk ve utanç duyguları, öfke, huzursuzluk ve evlilikte doyum kaybı gibi durumlarla ilişkilendirilmektedir. Ayrıca, utanç duygusunun narsistik, antisosyal ve sınır kişilik bozukluklarının gelişiminde belirleyici bir rol oynayabileceği belirtilmektedir. Suçluluk duygusunun, utanç duygusuna kıyasla daha işlevsel olduğu ve bireyin zarar verdiği kişiye yönelik tamir edici davranışlara yönelmesini sağladığı ifade edilmektedir (16).

Özel gereksinimli bir çocuğun varlığı, ebeveynler üzerinde ciddi psikolojik baskılar oluşturabilmektedir. Ebeveynler, karmaşık duygularla birlikte, özel gereksinimli çocuklarının getirdiği aşırı sorumluluklar nedeniyle sürekli başarısızlık, mutsuzluk ve hayal kırıklığı hissetmektedirler. Toplumun beklentileri ve çevreden gelen yargılayıcı tutumlar, ailelerin dışlandıkları ya da kötü ebeveynler oldukları hissine kapılmalarına neden olabilmektedir (17). Şener (2017) tarafından yapılan bir çalışmada, özel gereksinimi olan çocuğa sahip ailelerin yaşam doyumu ile hissettikleri suçluluk ve utanç düzeyleri incelenmiş, suçluluk ve yaşam doyumu düzeylerinde anlamlı bir farklılık saptanmamakla birlikte, zihinsel yetersizliği olan çocukların ebeveynlerinde utanç duygusunun, yaygın gelişimsel bozukluk tanılı çocukların ebeveynlerine göre daha yüksek olduğu bulunmuştur (18).

Özel gereksinimli çocuklarda, özellikle Otizm Spektrum Bozukluğu (OSB) tanılı bireylerde, aşırı hareketlilik, sinirlilik, dürtüsellik, agresif davranışlar, göz temasından kaçınma, çevreye ilgisizlik, obsesif davranışlar, dil ve konuşma becerilerinde gerilik, sebepsiz yere gülme, öfke nöbetleri, inatçılık, saç çekme, bağırma, ağlama gibi davranış sorunları görülebilmektedir. Ayrıca uyku, yeme ve cinsel gelişimle ilgili problemler de sıklıkla bildirilmektedir. Bu çocukların, kronik sağlık sorunları nedeniyle akademik başarılarının olumsuz etkilenebildiği ve sosyal dışlanma yaşadıkları belirtilmiştir (19). Özel gereksinimli çocuğa sahip aileler, yalnızca bakım sürecinde yaşadıkları zorluklarla değil, aynı zamanda toplumsal damgalama ile de mücadele etmek zorunda kalmaktadırlar (20). Toplumda, özel gereksinimli bireylerin davranışlarının "tuhaf" olarak algılanması sonucu, ailelerin incitici sözlere ve bakışlara maruz kaldıkları; bu durumun da ailelerin sosyal yaşamdan izole olmalarına yol açtığı tespit edilmiştir. Aileler, toplumun yargılayıcı bakışlarından kaçınmak amacıyla yalnızca kendilerini anlayacaklarına inandıkları yakın akrabalarla veya benzer deneyime sahip diğer özel gereksinimli çocuk aileleriyle iletişim kurmayı tercih ettiklerini ifade etmektedirler (9).

Utanç ve suçluluk, insan doğasına özgü zengin duygular arasında yer almakta olup hem bireysel hem de kişilerarası düzeyde önemli işlevler üstlenmektedir. Bu duyguların bireyin davranışlarını yönlendirdiği ve başkalarının gözündeki imajını etkilediği ileri sürülmektedir.

Ayrıca, suçluluk ve utanç duygularının erken dönem kişilerarası deneyimlerle, aile ve diğer önemli sosyal ilişkiler aracılığıyla geliştiği, benlik bilincine dayalı ve ahlaki içerikli duygular olduğu belirtilmektedir (21).

Özel gereksinimli bireylerin eğitim ve diğer temel hakları, başta Anayasamız olmak üzere, 573 sayılı Kanun Hükmünde Kararname ve 5378 sayılı "Engelliler Hakkında Kanun" ile güvence altına alınmıştır. Bu düzenlemeler, özel gereksinimli bireylerin farklılıkları dikkate alınarak, yaşadıkları çevrede bütünleştirilmiş ortamlarda eşitlik temelinde, hayat boyu eğitim hakkından ayrımcılık yapılmaksızın yararlanmalarını amaçlamaktadır. Ayrıca, genel eğitim sistemi içinde engelli bireylerin her seviyede eğitim alabilmesi için bütünleştirici planlamalar yapılması gerektiği vurgulanmıştır.

Ruhsal bozukluklara yönelik toplumsal damgalamaya ilişkin çok sayıda araştırma yapılmasına karşın, hasta ailelerinin kendilerine yönelik suçluluk ve utanç duyguları konusundaki çalışmaların sayısının sınırlı olduğu görülmektedir (22).

Literatür incelendiğinde, özel gereksinimli çocuklara sahip ebeveynlerin çocuklarının günlük bakımıyla ilgili ağır sorumluluklar üstlendikleri ve toplumsal yaşamda çeşitli güçlüklerle karşılaştıkları belirtilmektedir. Tanının konulması sürecinde ebeveynlerin şok, inkâr, reddetme, öfke, korku, hayal kırıklığı, suçluluk, kaygı ve depresyon gibi yoğun duygusal tepkiler geliştirdiği görülmektedir. Ayrıca, özel gereksinimli çocuğa sahip ebeveynlerin psikolojik iyilik halleri, normal gelişim gösteren çocuklara sahip ebeveynlere kıyasla daha düşük düzeyde seyretmektedir. Ebeveynlerin karşılaştığı güç yaşam koşulları bireylerde stres düzeyini artırmakta; bu stresin uzun süre devam etmesi durumunda depresyon ve kaygı gibi ruh sağlığı sorunlarının ortaya çıkmasına zemin hazırlamaktadır. Toplumsal yapının ve bireylerin farklılıklara yönelik olumsuz tutumları da ebeveynlerin sosyal çevrelerinden kopmalarına neden olabilmektedir (23).

Özel gereksinimli çocuğa sahip anneler ile herhangi bir özel gereksinimi olmayan çocuğa sahip annelerin atılganlık ve suçluluk-utanç düzeyleri karşılaştırıldığında, özel gereksinimli çocuğa sahip annelerin suçluluk ve utanç duygularının anlamlı düzeyde daha yüksek olduğu saptanmıştır (24,25).

SONUÇ

Sonuç olarak geniş çaplı çalışmaların arttırılması gerekir. İlerleyen araştırmalarda özel gereksinimi olan çocuğa sahip ailelerin hastalık deneyimleri ve başetme ile ilgili geniş çapta çalışmalar yürütülebilir.

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DIGITAL IDENTITY AND ACCESS PROBLEMS OF DISABLED INDIVIDUALS AFTER DISASTERS: A STUDY ON CRYPTO TECHNOLOGIES AND BLOCKCHAIN-BASED SOLUTIONS

ABSTRACT

Introduction: Disasters pose a serious threat by deeply affecting the infrastructures of societies and the daily lives of individuals, making survival and reintegration processes particularly difficult for individuals with disabilities. During disasters, these individuals face various problems such as the accuracy, security and accessibility of their digital identities, which creates serious barriers that prevent them from accessing post-disaster aid and support systems. Traditional centralized systems may be inadequate in terms of ensuring the security and accessibility of digital identity data in disaster conditions, which makes it difficult for individuals with disabilities to access vital aid on time. In this context, blockchain and crypto technologies can enable the decentralized, secure and transparent storage and verification of digital identities, allowing individuals with disabilities to access aid mechanisms more quickly, safely and effectively after a disaster.

Objective: This study aims to examine how blockchain-based technologies can provide solutions to these problems in the context of security, accessibility and system efficiency by addressing the digital identity and access problems encountered by individuals with disabilities in post-disaster processes.

Method: The study was conducted using the literature review method.

Results: In line with the literature reviewed, it has been observed that crypto technologies and blockchain-based systems allow digital identities to be stored securely and verifiably. It has been determined that these technologies provide speed, security and transparency in the access of disabled individuals to aid and support services in post-disaster processes. In addition, it has been determined that decentralized structures reduce the risk of systemic collapse in times of disaster and make digital identity verification processes sustainable.

Conclusion: The study has revealed that blockchain-based digital identity solutions offer a strong potential in reducing the digital access problems of disabled individuals after disasters. It has been concluded that decentralized and secure systems supported by crypto technologies can contribute to the development of holistic and inclusive approaches in disaster management policies by facilitating the timely access of disabled individuals to the necessary aid in disaster situations.

Keywords: Disasters, disabled individuals, digital identity, access, blockchain, crypto technologies

AFETLER SONRASI ENGELLİ BİREYLERİN DİJİTAL KİMLİK VE ERİŞİM SORUNLARI: KRİPTO TEKNOLOJİLERİ VE BLOCKCHAİN TABANLI ÇÖZÜMLER ÜZERİNE BİR İNCELEME

ÖZET

Giriş: Afetler, toplumların altyapılarını ve bireylerin günlük yaşamlarını derinden etkileyerek, özellikle engelli bireyler için hayatta kalma ve yeniden entegrasyon süreçlerini önemli ölçüde zorlaştıran ciddi bir tehdit oluşturmaktadır. Bu bireyler, afetler sırasında dijital kimliklerinin doğruluğu, güvenliği ve erişilebilirliği gibi çeşitli sorunlarla karşılaşmakta ve bu da afet sonrası yardım ve destek sistemlerine erişimlerini engelleyen ciddi bariyerler yaratmaktadır. Geleneksel merkezi sistemler, afet koşullarında dijital kimlik verilerinin güvenliğini ve erişilebilirliğini sağlama noktasında yetersiz kalabilmekte, bu durum ise engelli bireylerin hayati yardımlara zamanında ulaşabilmelerini zorlaştırmaktadır. Bu bağlamda, blockchain ve kripto teknolojileri, dijital kimliklerin merkeziyetsiz, güvenli ve şeffaf bir şekilde depolanmasını ve doğrulanmasını mümkün kılarak, afet sonrası engelli bireylerin yardım mekanizmalarına daha hızlı, güvenli ve etkili bir şekilde erişebilmelerini sağlayabilir.

Amaç: Bu çalışma, afet sonrası süreçlerde engelli bireylerin karşılaştığı dijital kimlik ve erişim sorunlarını ele alarak, blockchain tabanlı teknolojilerin bu sorunlara nasıl çözüm sunabileceğini güvenlik, erişilebilirlik ve sistemsel verimlilik bağlamında incelemeyi amaçlamaktadır.

Yöntem: Çalışma, literatür taraması yöntemi kullanılarak gerçekleştirilmiştir.

Bulgular: İncelenen literatürler doğrultusunda, kripto teknolojileri ve blockchain tabanlı sistemlerin dijital kimliklerin güvenli ve doğrulanabilir şekilde saklanmasına olanak tanıdığı görülmüştür. Bu teknolojilerin, afet sonrası süreçlerde engelli bireylerin yardım ve destek hizmetlerine erişiminde hız, güvenlik ve şeffaflık sağladığı tespit edilmiştir. Ayrıca, merkeziyetsiz yapıların, afet anlarında sistemsel çökme riskini azaltarak dijital kimlik doğrulama süreçlerini sürdürülebilir kıldığı belirlenmiştir.

Sonuç: Çalışma, blockchain tabanlı dijital kimlik çözümlerinin, afet sonrası engelli bireylerin dijital erişim sorunlarını azaltmada güçlü bir potansiyel sunduğunu ortaya koymuştur. Kripto teknolojileri ile desteklenen merkeziyetsiz ve güvenli sistemlerin, engelli bireylerin afet durumlarında gerekli yardımlara zamanında ulaşmasını kolaylaştırarak, afet yönetimi politikalarında bütüncül ve kapsayıcı yaklaşımların geliştirilmesine katkı sağlayabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Afetler, engelli bireyler, dijital kimlik, erişim, blockchain, kripto teknolojileri

1. GİRİŞ

Afetler, dünya genelinde milyonlarca insanın yaşamını etkileyen, büyük kayıplara yol açan olaylardır (1). Ancak afetlerin en çok etkilediği gruplardan biri, yaşamlarını daha da zorlaştıran engelleri olan bireylerdir (2). Engelli bireyler, afet anlarında, hem fiziksel hem de dijital erişim açısından ciddi zorluklarla karşılaşmaktadırlar (3). Dijital kimliklerin güvenliği ve doğruluğu, afet durumlarında hayati bir rol oynar; bu kimliklerin doğruluğu, engelli bireylerin acil yardım, barınma ve sağlık hizmetlerine erişimlerini doğrudan etkiler (4). Ancak mevcut dijital kimlik sistemleri, özellikle afet koşullarında bu bireylerin ihtiyaçlarını karşılamakta yetersiz kalmaktadır (5,6).

Dijital kimlikler, bireylerin çevrimiçi ortamda kendilerini tanıtabilmesini, çeşitli hizmetlere erişim sağlayabilmesini ve sosyal güvenlik haklarından faydalanabilmesini mümkün kılar (7). Ancak afetler sırasında, merkezi sistemlerin alt yapısı genellikle zarar gördüğünden, dijital kimliklerin doğrulanması, erişimi ve güvenliği büyük ölçüde tehdit altına girer. Bununla birlikte, afet sonrası engelli bireylerin dijital kimliklerine erişim sorunu, onların hayatta kalmalarını ve afet sonrası yeniden entegrasyon süreçlerini daha da karmaşık hale getirebilir (8). Bu bağlamda, dijital kimliklerin yönetilmesinde blockchain teknolojileri ve kripto sistemlerinin sunduğu güvenlik ve erişilebilirlik avantajları, engelli bireylerin afet durumlarında daha etkili bir şekilde yardım alabilmesi için potansiyel bir çözüm sunabilmektedir.

Blockchain teknolojisi, merkeziyetsiz bir yapıya sahip olup, dijital kimliklerin güvenli bir şekilde depolanması ve doğrulanmasını sağlar. Bu, özellikle afet durumlarında engelli bireylerin kimliklerinin kaybolmaması veya bozulmaması açısından kritik bir önem taşır (5). Blockchain'in sunduğu şeffaflık, güvenlik ve erişilebilirlik, engelli bireylerin afet sonrası yardım süreçlerine hızlı ve güvenli bir şekilde erişmelerine olanak tanır. Blockchain'in avantajları, merkezi sistemlerin aksine, dijital kimliklerin merkezi olmayan bir ağda, şifreli ve güvenli bir biçimde saklanmasını sağlar. Böylece, afet sonrasında, dijital kimliklerin herhangi bir devlet ya da özel sektöre bağlı bir platformda kaybolması veya erişilememesi gibi sorunların önüne geçilmiş olur (7,9).

Kripto teknolojileri de bu süreçte önemli bir rol oynamaktadır. Dijital para birimlerinin ve kripto ödeme sistemlerinin gelişimi, afet durumlarında engelli bireylerin ihtiyaç duyduğu finansal yardım ve hizmetlere hızlı erişimini kolaylaştırabilir (10). Ayrıca, bu sistemler, dijital kimlik doğrulaması ile entegre çalışarak, bireylerin doğru kimlik bilgilerine dayalı şekilde yardım almasını sağlayabilir (5). Kripto teknolojilerinin sunduğu güvenlik, şeffaflık ve düşük işlem maliyetleri, afetlerde daha hızlı, verimli ve erişilebilir yardım süreçleri için yeni fırsatlar yaratmaktadır (11).

Bu çalışmanın amacı, afet sonrası engelli bireylerin dijital kimlik ve erişim sorunlarına, blockchain ve kripto teknolojileriyle çözüm getirme potansiyelini incelemektir. Blockchain tabanlı dijital kimlik yönetimi; sunduğu güvenlik, şeffaflık ve merkeziyetsizlik özellikleri sayesinde, afet anlarında engelli bireylerin yardım hizmetlerine daha hızlı ve güvenli şekilde ulaşmalarını sağlayabilir. Bu bağlamda, söz konusu teknolojilerin uygulanabilirliği değerlendirilerek, engelli bireylerin afet sonrası hayatta kalma oranlarının artırılması ve toplumsal entegrasyonlarının güçlendirilmesi hedeflenmektedir.

2. AFET

Afet, insanların yaşamını, mal varlığını ve çevresini tehdit eden, genellikle ani gelişen ve toplumda ciddi zararlara yol açan doğal veya insan kaynaklı olaylardır. Deprem, sel, yangın, heyelan gibi doğal afetlerin yanı sıra, teknolojik kazalar ve salgın hastalıklar da afet kapsamında değerlendirilir (12).

Türkiye, coğrafi konumu nedeniyle deprem, sel, heyelan, orman yangını ve kuraklık gibi çeşitli doğal afetlere sıklıkla maruz kalan bir ülkedir. Özellikle Kuzey Anadolu Fay Hattı üzerinde yer alması, ülkeyi yüksek riskli deprem bölgelerinden biri haline getirmektedir. AFAD verilerine göre, Türkiye'de her yıl yüzlerce deprem meydana gelmekte; 1999 Marmara Depremi gibi büyük afetler ise on binlerce insanın hayatını kaybetmesine ve milyonlarca kişinin etkilenmesine neden olmaktadır (13). Bunun yanı sıra, iklim değişikliğine bağlı olarak artan yağış rejimi değişiklikleri, sel ve taşkın risklerini de ciddi şekilde artırmıştır (13,14). Türkiye'de afet riski sadece fiziksel zararlarla sınırlı kalmamakta, aynı zamanda toplumsal eşitsizlikleri derinleştirerek dezavantajlı gruplar —özellikle engelli bireyler— üzerinde daha yıkıcı etkiler yaratmaktadır (15).

2.1.Afetlerin Engelli Bireyler Üzerindeki Etkileri

Engelli bireyler, afet durumlarında çeşitli zorluklarla karşılaşmakta ve bu durum, onların hayatta kalma oranlarını, sağlık durumlarını ve toplumsal entegrasyonlarını olumsuz yönde etkilemektedir (16).

2.1.1. Fiziksel Erişim ve Tahliye Zorlukları

Engelli bireyler, afet anında fiziksel engelleri nedeniyle tahliye süreçlerinde ciddi zorluklar yaşamaktadır. Özellikle hareket kabiliyeti kısıtlı bireyler, dar alanlarda veya engelli erişimine uygun olmayan binalarda mahsur kalabilmektedir. Bu durum, afet sonrası kurtarma ve yardım çalışmalarının etkinliğini azaltmakta, engelli bireylerin hayatta kalma şansını düşürmektedir (17).

2.1.2. Bilgiye Erişim Sorunları

Afet durumlarında, doğru ve zamanında bilgiye erişim hayati önem taşır. Ancak engelli bireyler, iletişim araçlarının yetersizliği veya erişilebilirliğinin olmaması nedeniyle bu bilgilere ulaşmada güçlük çekmektedir. Örneğin, işitme engelli bireyler için sesli uyarılar, görme engelli bireyler içinse yazılı bilgilendirmeler yetersiz kalmaktadır. Bu durum, afet sırasında doğru kararlar almayı ve güvenli alanlara ulaşmayı zorlaştırmaktadır (18).

2.1.3. Sağlık Hizmetlerine Erişim Engelleri

Afet sonrası sağlık hizmetlerine erişim, engelli bireyler için daha karmaşık hale gelebilmektedir. Sağlık tesislerinin engelli bireyler için uygun olmaması, ulaşım zorlukları ve özel bakım ihtiyaçları, bu bireylerin sağlık hizmetlerinden yeterince faydalanamamasına yol açmaktadır. Ayrıca, afet sonrası psikolojik destek ve rehabilitasyon hizmetlerine erişim de sınırlı olabilir (19,20).

2.1.4. Toplumsal Dışlanma ve Ayrımcılık

Afetler, engelli bireylerin toplumsal dışlanma deneyimlerini derinleştirebilmektedir. Afet sonrası yardımların ve kaynakların dağılımında engelli bireylerin ihtiyaçları genellikle göz

ardı edilmektedir (20). Ayrıca, afet durumlarında engelli bireylere yönelik ayrımcılık ve damgalama, onların toplumsal entegrasyonunu daha da zorlaştırmaktadır (21).

2.1.5. Aile ve Bakım Verenlerin Yükü

Engelli bireylerin afet durumlarında karşılaştıkları zorluklar, bakım veren aile üyeleri üzerinde de ek bir yük oluşturmaktadır. Aile bireyleri, engelli yakınlarının güvenliğini sağlamak, sağlık ihtiyaçlarını karşılamak ve psikolojik destek sunmak gibi sorumluluklarla karşı karşıya kalmaktadır. Bu durum, aile üyelerinin fiziksel ve psikolojik sağlıklarını olumsuz yönde etkileyebilir (20,21).

2.1.6. Sosyo-Ekonomik Etkiler

Afetler, engelli bireylerin sosyo-ekonomik durumunu da etkileyebilmektedir (Gür ve Nirgiz, 2024). Engelli bireyler, afet sonrası işlerini kaybetme, gelir kaynaklarının azalması ve yeniden iş bulma konusunda daha fazla zorluk yaşamaktadır. Ayrıca, afet sonrası yeniden yapılanma süreçlerinde engelli bireylerin ihtiyaçları genellikle göz ardı edilmekte, bu da onların ekonomik ve sosyal durumlarını daha da kötüleştirmektedir (22).

3. DİJİTAL KİMLİK ve ERİŞİM ENGELLERİ

Dijital kimlik, bireylerin dijital ortamda varlıklarını tanımlayan ve haklarına erişimlerini mümkün kılan temel bir araç olarak, günümüzün dijitalleşen toplumlarında hayati bir rol oynamaktadır. Sağlık, eğitim, finans ve sosyal hizmetler gibi alanlarda dijital kimliklerin güvenliği, doğruluğu ve erişilebilirliği; bireylerin bu hizmetlere eşit ve güvenli erişimini doğrudan etkileyen kritik unsurlardır (23). Ancak bu sistemler, özellikle görme, işitme, hareket ya da bilişsel engelleri bulunan bireyler açısından önemli erişim ve doğrulama sorunları barındırmaktadır (24).

Engelli bireyler, dijital kimliklerini kullanarak hizmetlere erişme sürecinde teknik altyapı eksiklikleri, tasarım yetersizlikleri ve kullanıcı dostu olmayan ara yüzler nedeniyle ciddi zorluklarla karşılaşmaktadır (24). Bu sorunlar, afetler ve acil durumlar gibi kriz anlarında daha da kritik hale gelmekte; çünkü afet sonrası yardım ve desteklerin zamanında ve doğru kişilere ulaştırılabilmesi büyük ölçüde dijital kimlik sistemlerinin işleyişine bağlıdır (25). Dijital kimliklerin güvenli ve erişilebilir olması, özellikle engelli bireylerin afet sonrası ihtiyaç duydukları hizmetlere hızlı şekilde ulaşabilmesi ve hayatta kalma oranlarının artırılması açısından büyük önem taşımaktadır (26). Bu nedenle, dijital kimlik sistemlerinin kapsayıcı, erişilebilir ve güvenilir biçimde tasarlanması; sadece bireysel hakların korunması değil, aynı zamanda toplumsal eşitliğin sağlanması ve afetlere karşı dirençli bir toplum inşa edilmesi açısından da kritik bir gerekliliktir.

Sonuç olarak, güvenlik açıkları, erişilebilirlik sorunları ve afet durumlarındaki zorluklar, dijital kimlik doğrulama sistemlerinin etkinliğini sınırlamaktadır. Bu eksikliklerin giderilmesi, dijital kimliklerin güvenli, erişilebilir ve dayanıklı hale getirilmesi için yeni teknolojilere olan ihtiyaç, daha da belirginleşmiştir. Blockchain gibi merkeziyetsiz ve güvenli teknolojilerin, dijital kimlik doğrulama süreçlerini güçlendirebileceği ve bu tür sınırlamaların üstesinden gelebileceği öngörülmektedir.

3.1. Blockchain Tabanlı Çözümler ve Kripto Teknolojileri

Son yıllarda, dijital dönüşümün hızla ilerlemesiyle birlikte, teknoloji dünyasında kripto para birimleri ve blockchain (blok zinciri) teknolojileri giderek daha fazla önem kazanmaktadır (27).

3.1.1. Blockchain

Blockchain, merkeziyetsiz ve güvenli veri depolama sistemleri sağlayarak, dijital dünyada bilgi alışverişi, kimlik doğrulama ve işlem güvenliği gibi kritik alanlarda devrim yaratmaktadır. Özellikle finansal hizmetlerden sağlık hizmetlerine, lojistikten devlet hizmetlerine kadar pek çok sektörde blockchain tabanlı çözümler, etkinliği, güvenliği ve şeffaflığı artırma potansiyeli taşımaktadır (28).

Blockchain, temel olarak, her türlü dijital işlemi güvenli ve şeffaf bir şekilde kaydeden dağıtık bir veri tabanı olarak işlev görür. Her bir işlem bir "blok" olarak kaydedilir ve bu bloklar bir zincir şeklinde birbirine bağlanır. Blockchain'in merkeziyetsiz yapısı, verilerin tek bir noktada toplanmaması sayesinde sistemin güvenliğini artırırken, her işlemin şeffaf bir şekilde takip edilebilmesini sağlar (27). Bu, özellikle dijital kimlik doğrulama, seçim güvenliği, akıllı sözleşmeler ve tedarik zinciri yönetimi gibi alanlarda devrim niteliğinde uygulamalara olanak tanır (29). Blockchain teknolojisinin sunduğu bu güvenlik ve şeffaflık özellikleri, afet sonrası yardım süreçlerinde, dijital kimlik doğrulama sistemlerinde ve sağlık hizmetlerine erişim gibi kritik alanlarda engelli bireyler için daha güvenli ve etkili çözümler sunabilir (5).

3.1.2. Kripto Teknolojileri

Kripto teknolojileri, blockchain altyapısı üzerine inşa edilen dijital para birimlerinden daha fazlasını ifade eder (29). Kripto para birimleri, özellikle uluslararası ödemelerde düşük işlem maliyetleri, hızlı işlem süreleri ve güvenlik sağlama potansiyeli ile öne çıkmaktadır. Bununla birlikte, kripto teknolojilerinin merkeziyetsiz yapısı, kullanıcıların finansal ve dijital kimlik bilgilerini kontrol etmelerine olanak tanıyarak, bireylerin verilerini daha güvenli bir biçimde yönetmelerine yardımcı olabilir (30).

Kripto ve blockchain teknolojilerinin bu denli önemli hale gelmesinin bir diğer nedeni, dijitalleşen toplumların daha fazla güvenlik, şeffaflık ve verimlilik talepleriyle paralel gelişmesidir. Özellikle devlet hizmetleri ve sağlık gibi hassas alanlarda, merkeziyetsiz yapılar, kişisel bilgilerin güvenliğini sağlamakla birlikte, verilerin manipülasyona karşı dayanıklı olmasını da temin eder. Bu teknolojiler, devletlerin ve kurumların bireylerin dijital kimliklerini ve verilerini güvenli bir biçimde yönetmelerine yardımcı olurken, aynı zamanda sistemdeki olası aksaklıkları ve hileleri ortadan kaldırır (31).

3.1.3. Blockchain ve Kripto Sistemlerinin Sürdürülebilirliği ve Uygulama Engelleri

Blockchain ve kripto sistemlerinin yaygınlaşması ve sürdürülebilirliği, pek çok teknik, ekonomik ve düzenleyici engelle karşı karşıyadır. Bu engellerin aşılması, bu sistemlerin geniş çapta benimsenmesi ve uzun vadeli başarıları için kritik öneme sahiptir (32).

Sürdürülebilirlik konusu, blockchain ve kripto sistemlerinin geleceği açısından büyük önem taşımaktadır. Özellikle, enerji tüketimi, çevresel etkiler ve ekonomik verimlilik gibi faktörler, bu teknolojilerin sürdürülebilirliği üzerinde önemli bir etkiye sahiptir. Bitcoin gibi popüler kripto paraların madencilik işlemleri, yüksek enerji tüketimi ile bilinir ve bu durum,

çevresel etkileri ve fosil yakıt kullanımıyla ilişkilendirilen ciddi eleştiriler almasına neden olmuştur. Bu yüksek enerji tüketimi, sadece ekonomik açıdan değil, aynı zamanda çevresel açıdan da önemli bir sürdürülebilirlik sorunu yaratmaktadır. Bununla birlikte, blockchain teknolojilerinin yenilenebilir enerji kaynaklarıyla entegrasyonu ve daha enerji verimli algoritmalar kullanılması gibi çözümler, bu sorunun aşılmasında umut verici bir yol sunmaktadır (32,33).

Bunun yanı sıra, blockchain ağlarının ölçeklenebilirlik sorunları da, teknolojilerin uygulama engelleri arasında yer almaktadır. Mevcut blockchain sistemlerinin işlem kapasitesi, geleneksel ödeme sistemleriyle karşılaştırıldığında sınırlıdır. Özellikle, Bitcoin ve Ethereum gibi ağlar, saniyede yalnızca birkaç işlem gerçekleştirebilirken, Visa gibi merkeziyetsiz olmayan sistemler saniyede binlerce işlem gerçekleştirebilmektedir. Bu da, blockchain teknolojilerinin geniş çapta benimsenmesi için büyük bir engel teşkil etmektedir. Ancak, Layer 2 çözümleri, sharding ve proof-of-stake (PoS) gibi yeni teknolojiler, bu ölçeklenebilirlik sorunlarını çözmeye yönelik potansiyel çözümler olarak dikkat çekmektedir (32).

Kripto sistemlerinin uygulama engellerinin bir diğeri ise regülasyon eksiklikleri ve hukuki belirsizliklerdir. Kripto paralar ve blockchain teknolojileri, mevcut yasal çerçevelerle uyumlu çalışmakta zorlanmaktadır. Dünyanın farklı bölgelerinde farklı yasal düzenlemeler uygulanmakta ve bu durum, küresel çapta bir standart oluşturmayı zorlaştırmaktadır. Kripto paraların yasal statüsü, vergilendirilmesi ve para aklama önlemleri gibi konular, pek çok ülkede hala netleşmemiştir. Bu hukuki belirsizlik, hem yatırımcıları hem de işletmeleri bu teknolojilerle ilgili daha temkinli ve kararsız hale getirebilir (34,35).

Bir diğer önemli engel, kullanıcı kabulü ve dijital okuryazarlık eksiklikleridir. Blockchain ve kripto sistemleri, birçok kişi için hala soyut ve karmaşık bir kavram olarak kalmaktadır. Bu teknolojilerin kullanıcılar tarafından anlaşılması, kabul edilmesi ve güvenle kullanılabilmesi için daha fazla eğitim ve farkındalık gereklidir. Özellikle gelişmekte olan ülkelerde, kripto sistemlerinin benimsenmesi, düşük dijital okuryazarlık oranları ve güvenlik endişeleri nedeniyle yavaş ilerlemektedir. Blockchain tabanlı sistemlerin daha geniş bir kullanıcı kitlesi tarafından benimsenebilmesi için, kullanıcı dostu arayüzler ve güvenlik özelliklerinin daha da geliştirilmesi önemlidir (36).

Son olarak, blockchain ve kripto teknolojilerinin veri gizliliği ve güvenlik açısından da zorlukları vardır. Blockchain üzerinde tüm işlemler şeffaf bir şekilde kaydedilse de, kullanıcıların kişisel bilgileri ve verileri üzerinde tam kontrol sağlamaları gerektiği bir durum söz konusudur. Özelleştirilebilen ve şifrelenmiş kimlik yönetimi çözümleri, bu teknolojilerin gizlilik sorunlarını giderebilir ve daha güvenli bir ortam sağlayabilir (29).

Tüm bu engeller ve sürdürülebilirlik sorunlarına rağmen, blockchain ve kripto sistemlerinin geleceği oldukça umut vericidir. Çeşitli araştırmalar ve inovasyonlar, bu sorunları çözmeye yönelik çözüm yolları geliştirmektedir. Enerji verimliliği, daha hızlı ve ölçeklenebilir ağlar, düzenleyici çerçevelerin netleştirilmesi ve kullanıcı dostu tasarımlar, blockchain ve kripto teknolojilerinin önündeki engelleri aşmak için kritik adımlardır. Geliştirilen yeni protokoller ve uygulamalar, bu teknolojilerin daha geniş bir kullanıcı kitlesi tarafından benimsenmesine ve sürdürülebilir bir şekilde kullanılmasına olanak tanıyacaktır.

4. KRİPTO VE BLOCKCHAİN'İN AFET DURUMLARINDA KULLANILABİLİRLİĞİ

Afet durumları, hem fiziksel altyapıyı hem de toplumsal düzeni derinden etkileyerek, acil yardım hizmetlerinden lojistik desteğe kadar birçok alanda büyük zorluklar yaratır (37). Bu tür durumlarda, özellikle afet mağdurlarının kimlik bilgileri, sağlık verileri ve yardım erişimi gibi kritik bilgilere güvenli ve hızlı bir şekilde ulaşabilmesi, kurtarma ve yeniden yapılandırma sürecinin başarıyla yönetilmesinde belirleyici rol oynamaktadır (38). Geleneksel sistemler, bu tür acil durumlar sırasında genellikle yetersiz kalır ve merkezi veri tabanlarının çökmesi, iletişim ağlarının bozulması ve güvenlik riskleri gibi sorunlar yaşanır. Ancak kripto teknolojileri ve blockchain, afet yönetiminde önemli bir çözüm sunma potansiyeline sahiptir. Bu teknolojiler, afet durumlarında güvenli, şeffaf ve merkeziyetsiz bir ortam sağlayarak, afet sonrası yardım süreçlerini daha verimli ve güvenli hale getirebilir (39).

Blockchain, verilerin merkeziyetsiz ve değiştirilemez bir şekilde depolanmasını sağlayarak, afet durumlarında kimlik doğrulama, yardımların izlenmesi ve acil durum yanıt süreçlerinin daha şeffaf hale getirilmesini mümkün kılar. Afet mağdurlarının kimlik bilgileri, sağlık verileri ve diğer kritik bilgiler, blockchain teknolojisi ile güvenli bir şekilde saklanabilir ve yalnızca yetkilendirilmiş taraflarla paylaşılabilir. Blockchain tabanlı sistemler, afet sırasında iletişim ağlarının çökmesi durumunda bile, afet mağdurlarının dijital kimlik bilgilerini hızlı bir şekilde doğrulayarak yardım alabilmelerini sağlar. Ayrıca, blockchain'in şeffaf yapısı sayesinde, yardım dağıtım süreçleri de izlenebilir hale gelir, böylece yardımların doğru kişilere ulaşıp ulaşmadığı, hangi bölgelere ne kadar yardım gönderildiği gibi bilgiler şeffaf bir şekilde kayıt altına alınabilir (39).

Afet durumlarında, kripto paralar da kritik bir rol oynar. Kripto paralar, merkeziyetsiz yapıları sayesinde afet bölgelerinde geleneksel bankacılık sistemlerine erişimi olmayan kişilere dahi hızlı ve güvenli finansal destek sağlamaktadır. Kripto paralar, fiziksel bankaların ve finansal altyapıların zarar görmesi durumunda bile, afet mağdurlarına dijital ortamda anında yardım göndermek için kullanılabilir. Bunun yanı sıra, kripto paraların düşük işlem maliyetleri, yüksek hızda işlem yapılabilmesi ve dijital ortamda hızlı bir şekilde transfer edilebilmesi, afet sonrası yardım sistemlerini daha verimli hale getirebilir. Özellikle engelli bireyler, yaşlılar ve diğer dezavantajlı gruplar, geleneksel bankacılık sistemlerine erişim güçlükleri nedeniyle kripto paralar sayesinde hızlı bir şekilde finansal yardım alabilirler (39,40).

Blockchain ve kripto teknolojileri, afet sonrası kriz yönetiminin birkaç farklı yönüne hizmet edebilir. Acil sağlık bilgisi yönetimi, afet sırasında sağlık hizmetlerine hızlı erişim sağlamak açısından çok önemlidir. Blockchain tabanlı sağlık kayıtları, afet mağdurlarının tıbbi geçmişini güvenli bir şekilde saklayarak, sağlık hizmeti sağlayıcılarının doğru ve güncel bilgilere hızlıca ulaşmasına olanak tanır. Kripto para kullanılarak, yardım kuruluşları ve hükümetler, afet mağdurlarına doğrudan finansal yardım gönderebilir, böylece aracılara olan ihtiyaç ortadan kalkar ve yardım süreci hızlanır. Ayrıca, blockchain teknolojisi, afet sonrası yeniden inşa süreçlerinde, mülk sahipliği ve kaynak yönetimi gibi bilgilerin güvenli bir şekilde saklanmasını sağlayarak, olası dolandırıcılık ve sahteciliği engelleyebilir (39).

Afet durumlarında bilgi güvenliği ve şeffaflık kritik öneme sahiptir. Blockchain, veri manipülasyonunu engelleyerek, acil durumlarda veri güvenliğini sağlar. Bu, özellikle afet sonrası kurtarma çalışmaları sırasında kritik bilgilere güvenli ve hızlı erişim sağlamak için gereklidir. Örneğin, afet bölgelerinde sağlık hizmetlerine erişim sağlayan kişilerin

kimliklerinin doğrulanması, sahtecilik ve kimlik hırsızlıkları gibi sorunları engeller. Blockchain'in sağladığı değiştirilemezlik özelliği, afet sonrası yardım süreçlerinde doğru bilgi paylaşımını güvence altına alırken, sahtecilik ve manipülasyon risklerini de ortadan kaldırır (7,9,41).

5. SONUÇ

Afet durumlarında, dijital kimlik sistemlerine erişim, özellikle engelli bireyler açısından hayati öneme sahiptir. Mevcut merkezi ve geleneksel kimlik doğrulama sistemleri, altyapı hasarları, internet kesintileri ve fiziksel engeller nedeniyle afet koşullarında işlevsiz hale gelebilmekte, bu da engelli bireylerin temel hizmetlere erişimini ciddi şekilde kısıtlamaktadır. Bu çalışma, bu sorunsal bağlamda blockchain ve kripto teknolojilerinin sunduğu merkeziyetsiz, güvenli ve erişilebilir çözümleri incelemiştir.

Blockchain tabanlı dijital kimlik sistemleri, merkezi bir otoriteye bağlı olmadan çalışabilme özellikleri sayesinde, afet gibi olağanüstü koşullarda bile kimlik doğrulama süreçlerini sürdürülebilir kılabilmektedir. Ayrıca bu sistemler, veri güvenliğini artırmakla kalmayıp, biyometrik verilerle desteklenebilen özelleştirilmiş kimlik çözümleri sayesinde engelli bireyler için daha kapsayıcı bir dijital ortam oluşturulmasına olanak tanımaktadır. Yenilenebilir enerji kaynaklarıyla entegre edilen enerji verimli blockchain altyapıları ise, bu teknolojilerin sürdürülebilirliğini destekleyen önemli bir faktör olarak öne çıkmaktadır.

Sonuç olarak, afet sonrası dijital erişim ve kimlik sorunlarının çözümünde blockchain ve kripto teknolojileri, yalnızca teknik bir alternatif değil, aynı zamanda toplumsal eşitlik ve açısından da dönüştürücü bir potansiyele sahiptir. Bu nedenle, bu teknolojilerin gelişimi ve uygulanabilirliği, yalnızca teknoloji politikaları çerçevesinde değil, aynı zamanda sosyal adalet perspektifinden de değerlendirilmelidir. Gelecekte, engelli bireylerin afet koşullarında dijital hizmetlere engelsiz erişimini sağlamak adına, bu yenilikçi çözümlerin daha fazla araştırılması ve kamu politikalarına entegre edilmesi gerekmektedir.

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THE NEW FACE OF CLIMATE CHANGE ON HEALTH: A PERIOD OF INCREASING ANTIBIOTIC RESISTANCE

ABSTRACT

Introduction: Climate change has serious and widespread impacts on global health, and antibiotic resistance is an important dimension of these impacts. Climatic changes such as temperature increase, extreme weather events, forest fires, and water pollution allow pathogens to multiply rapidly, while also contributing to the spread of antibiotic resistance. This process threatens public health by complicating the control of infectious diseases. In this context, healthcare professionals play a critical role in combating increasing antibiotic resistance and coping with this global threat.

Objective: The aim of this study is to examine the effects of climate change on antibiotic resistance and to discuss the roles and responsibilities of healthcare professionals in combating these effects.

Methods: The study was conducted using a literature review method to examine the effects of climate change on antibiotic resistance.

Findings: Increasing temperatures accelerate bacterial growth, triggering pathogen proliferation and facilitating the spread of antibiotic resistance. Extreme weather events and forest fires contribute to the spread of antibiotic resistance genes by deteriorating air quality, while water pollution and sewage overflows increase waterborne infections. Increased bacterial proliferation and strengthened antibiotic resistance have also been observed due to the eutrophication effect of agricultural runoff. In addition, climate change changes the geographical distribution of vectors, causing resistant pathogens to spread to new regions. These findings clearly reveal the threats of climate change to global health and the increase in antibiotic resistance.

Conclusion: The relationship between climate change and antibiotic resistance poses a critical threat to public health and undermines the fundamental foundations of modern medicine. These two global crises feed on each other, posing a major structural risk to health systems.

Keywords: Climate change, antibiotic resistance, microbial resistance, global health

İKLİM DEĞİŞİKLİĞİNİN SAĞLIK ÜZERİNDEKİ YENİ YÜZÜ: ANTİBİYOTİK DİRENCİNİN ARTTIĞI BİR DÖNEM

ÖZET

Giriş: İklim değişikliği, küresel sağlık üzerinde ciddi ve geniş çaplı etkiler yaratmakta ve antibiyotik direnci, bu etkilerin önemli bir boyutunu oluşturmaktadır. Sıcaklık artışı, aşırı hava olayları, orman yangınları ve su kirliliği gibi iklimsel değişiklikler, patojenlerin hızla çoğalmasına olanak tanırken, antibiyotik direncinin yayılmasına da katkıda bulunmaktadır. Bu süreç, enfeksiyon hastalıklarının kontrolünü zorlaştırarak halk sağlığını tehdit etmektedir. Bu bağlamda, sağlık çalışanları, artan antibiyotik direnciyle mücadelede ve bu küresel tehditle başa çıkmakta kritik bir rol üstlenmektedir.

Amaç: Bu çalışmanın amacı, iklim değişikliğinin antibiyotik direnci üzerindeki etkilerini incelemek ve sağlık çalışanlarının bu etkilere karşı mücadeledeki rol ve sorumluluklarını tartışmaktır.

Yöntemler: Çalışma, literatür taraması yöntemi kullanılarak gerçekleştirilmiştir.

Bulgular: Sıcaklık artışı, bakteriyel büyümeyi hızlandırarak patojenlerin çoğalmasını tetiklemekte ve antibiyotik direncinin yayılmasını kolaylaştırmaktadır. Aşırı hava olayları ve orman yangınları, hava kalitesini bozarak antibiyotik dirençli genlerin yayılmasına katkıda bulunmakta, aynı zamanda su kirliliği ve kanalizasyon taşmaları, su kaynaklı enfeksiyonları artırmaktadır. Tarımsal akışların ötrofikasyon etkisiyle bakteri çoğalmasının artması ve antibiyotik direncinin güçlenmesi de gözlemlenmiştir. Ayrıca, iklim değişikliği vektörlerin coğrafi dağılımını değiştirerek yeni bölgelere dirençli patojenlerin yayılmasına neden olmaktadır. Bu bulgular, iklim değişikliğinin küresel sağlık üzerindeki tehditlerini ve antibiyotik direncinin artmasını açıkça ortaya koymaktadır.

Sonuç: İklim değişikliği ve antibiyotik direnci arasındaki ilişki, halk sağlığı açısından kritik bir tehdit oluşturmakta ve modern tıbbın temel dayanaklarını zayıflatmaktadır. Bu iki küresel kriz, birbirini besleyerek sağlık sistemleri üzerinde büyük bir yapısal risk oluşturmaktadır.

Anahtar Kelimeler: İklim değişikliği, antibiyotik direnci, mikrobiyal direnç, küresel sağlık

1. GİRİŞ

İklim krizi, insan faaliyetlerinin sonucunda atmosferde biriken sera gazlarının yol açtığı, uzun vadeli ve geri dönüşü olmayan çevresel bozulmaları tanımlar. Son yıllarda dünya genelinde yaşanan çevresel değişimlerin en dikkat çekici ve endişe verici yönü olan bu kriz, yalnızca hava sıcaklıklarının artışıyla sınırlı kalmayıp, tüm ekosistemleri, su döngülerini ve biyolojik yaşamı derinden etkilemektedir (1,2).

Küresel sıcaklıkların yükselmesiyle birlikte, mikrobiyal yaşamın evrimsel dinamikleri de köklü bir şekilde değişmektedir. Bu değişim, özellikle bakterilerin çoğalma hızını artırmakta, direnç genlerinin yatay gen transferiyle daha hızlı yayılmasına olanak tanımakta ve patojenlerin çevresel toleransını yükselterek antibiyotik direncinin hızını ve yaygınlığını önemli ölçüde artırmaktadır. Dirençli enfeksiyonların artışı, modern tıbbın temel dayanaklarını zayıflatırken, iklim krizi bu süreci daha karmaşık hale getirerek derinleştirmektedir (3). Bu nedenle bu çalışma, iklim değişikliğinin mikrobiyal direnç üzerindeki etkilerini disiplinler arası bir bakış açısıyla inceleyerek, bu iki küresel tehdidin nasıl iç içe geçtiğini ortaya koymayı ve sağlık sistemleri için oluşturduğu yapısal riski görünür kılmayı amaçlamaktadır.

2. İKLİM KRİZİ

İklim krizi, atmosferdeki sera gazı yoğunluğunun artması sonucu, dünya yüzeyinin ortalama sıcaklıklarının sürekli bir şekilde yükselmesi ve bunun sonucunda ekosistemler, biyolojik çeşitlilik, insani yaşam ve ekonomik sistemler üzerinde geniş çaplı ve genellikle olumsuz değişimlere yol açan bir dizi çevresel ve toplumsal sorunun birleşimidir (4). Bu durum, aşırı hava olaylarının artışı, deniz seviyelerinin yükselmesi, su kaynaklarında azalma, orman yangınları, gıda güvenliği sorunları, ekosistem bozulması, hava kalitesinin kötüleşmesi, sağlık problemleri ve küresel göç gibi çeşitli olumsuz sonuçlar doğurmaktadır (5,6).

İklim krizinin ortaya çıkışında insan kaynaklı faaliyetler belirleyici rol oynamaktadır (7,8). Özellikle fosil yakıtların enerji üretiminde yaygın biçimde kullanılması, atmosferdeki sera gazı yoğunluğunu artırmakta ve küresel ısınmayı tetiklemektedir. Ormanların tahrip edilmesiyle karbon yutakları azalmakta, bu da atmosferde tutulan karbon miktarını ciddi biçimde yükseltmektedir (8,9). Sanayi süreçleri ve yoğun tarımsal faaliyetler, karbondioksit ve metan gibi gazların salınımını artırarak sera etkisini derinleştirmektedir (10). Ulaşım sektöründen kaynaklanan emisyonlar, özellikle karayolu, hava ve deniz taşımacılığı yoluyla atmosfere yayılan kirleticilerle bu döngüyü pekiştirmektedir (11). Aynı şekilde, atıkların uygun olmayan biçimde depolanması ve biyolojik bozunma sürecinde açığa çıkan metan gazı da bu sürece katkı sunmaktadır. Tarımsal yayılma, doğal alanların tarım arazisine dönüştürülmesi ve kentleşmeye bağlı olarak artan toprak betonlaşması, hem ekosistemlerin yapısını bozmakta hem de karbon döngüsünü zayıflatmaktadır (10). Endüstriyel tarımda kullanılan sentetik gübreler ve pestisitler, yalnızca toprak sağlığını olumsuz etkilemekle kalmayıp, dolaylı yoldan sera gazı salımını da artırmaktadır (12). Tüm bunlara ek olarak, karbon emisyonlarını azaltmaya yönelik küresel ölçekteki politikaların hem yetersiz kalması hem de uygulamada etkinliğini sağlayamaması, iklim krizini geri döndürülemez bir noktaya taşımaktadır (10).

3. ANTİBİYOTİK DİRENCİ

3.1.Antibiyotiğin Tarihçesi

1928'de Alexander Fleming tarafından penisilinin keşfi, savaşlar, yoksulluk ve kötü hijyen koşulları nedeniyle yaygınlaşan ölümcül bakteriyel enfeksiyonlara karşı modern tıpta devrim niteliğinde bir kırılma noktası olmuştur (13). Antibiyotikler, etkinlikleri, hedefe özgü etkileri ve düşük maliyetleri nedeniyle kısa sürede tıbbın vazgeçilmez araçları hâline gelmiş; bakteriyel hücre yapılarına özgü hedeflere etki ettikleri için insanlar ve hayvanlar üzerinde zararsız kabul edilmişlerdir (14). Ancak zamanla, antibiyotik kullanımının sadece patojenleri değil, konakçının mikrobiyotasını da etkilediği anlaşılmıştır. Güncel araştırmalar, insan, hayvan ve bitki sağlığı için mikrobiyotanın kritik önemde olduğunu ortaya koyarken, bu durum antibiyotiklerin rastgele ve kontrolsüz kullanımının hem direnç gelişimine hem de faydalı mikroorganizmaların kaybına yol açabileceğini göstermektedir. Bu nedenle antibiyotiklerin, yalnızca dirençli patojenleri kontrol altına almak için değil, aynı zamanda ekosistemin dengesi ve konakçı sağlığı açısından da daha bilinçli ve seçici bir şekilde kullanılması gerekmektedir (15,16).

3.2. İklim Değişikliği ve Antibiyotik Direncinin Etkileşimi

Antibiyotikler, modern tıbbın en temel dayanaklarından biridir. Onların etkinliği sayesinde yalnızca basit enfeksiyonlar değil, cerrahi müdahaleler, kanser tedavileri ve organ nakilleri gibi yüksek riskli tıbbi uygulamalar da güvenli biçimde gerçekleştirilebilmektedir. Ayrıca, özellikle çocukluk çağında solunum yolu enfeksiyonlarına bağlı ölümlerin azalmasında da belirleyici bir rol oynamışlardır. Ancak son yıllarda hızla artan antibiyotik direnci, bu kazanımları tehdit eden küresel bir kriz hâline gelmiştir. Dirençli patojenlerin yayılmasıyla birlikte, daha önce tedavi edilebilir olan enfeksiyonlar yeniden ölümcül bir boyuta ulaşmaktadır. Bu tehdit, yalnızca sağlık hizmetlerini değil, toplumun genel dayanıklılığını da sarsma potansiyeline sahiptir (17,18). Üstelik bu kırılgan süreci daha da karmaşıklaştıran, genellikle göz ardı edilen bir etken daha vardır: iklim değişikliği. Artan sıcaklıklar, ekstrem doğa olayları, tarımsal yapıdaki değişimler ve su kaynaklarının kirlenmesi, mikrobiyal yaşamın ekolojik dinamiklerini değiştirerek antibiyotik direncinin yayılımını hızlandırmaktadır (3).

3.3. İklim Krizinin Antibiyotik Direnci Üzerindeki Etkileri

İklim değişikliği, antibiyotik direncini (AMR) doğrudan ve dolaylı yollarla etkilemektedir (18). Aşağıda, bu ilişkinin temel bileşenleri detaylı bir şekilde açıklanmıştır:

3.3.1. Sıcaklık Artışı

Sıcaklık artışı, bakteriyel büyüme hızını artırarak patojenlerin daha hızlı çoğalmasına neden olur ve bu durum enfeksiyonların daha sık görülmesine yol açar. Aynı zamanda, sıcaklığın yükselmesiyle birlikte bakteriler arasında gen transferi hızlanır; bu da antibiyotik direncinin gelişimini kolaylaştıran önemli bir mekanizma olarak öne çıkar. Sıcaklık, nem ve yağış gibi çevresel faktörler, özellikle Gram-negatif bakterilerin neden olduğu enfeksiyon oranlarını artırarak hastaneye yatışları doğrudan etkiler. Ayrıca, sıcaklık artışı cerrahi alan enfeksiyonları ve idrar yolu enfeksiyonlarının da görülme sıklığını artırmaktadır. Tüm bu etkenler, iklim değişikliğiyle birlikte bakteriyel enfeksiyonların yaygınlaşması ve antibiyotik direncinin artmasının, ciddi bir halk sağlığı tehdidine dönüşebileceğini göstermektedir (18,19).

3.3.2. Yangınlar

İklim değişikliğinin neden olduğu orman yangınları, antimikrobiyal direnç artışını destekleyen çevresel faktörlerden biri olarak öne çıkmaktadır. Yangınlar sonucunda atmosfere salınan ince partikül maddeler (özellikle PM2.5), yalnızca solunum sağlığını olumsuz etkilemekle kalmaz, aynı zamanda antibiyotik direnç genlerinin taşınmasına aracılık eden potansiyel vektörlerdir. Bu partiküller, havadaki mikroorganizmalarla etkileşime girerek direnç genlerinin aerosoller yoluyla yayılmasını kolaylaştırabilir. Öte yandan, yangın sonrası oluşan çevresel tahribat, su kaynaklarının kirlenmesine ve atık su sistemlerinin bozulmasına yol açarak su kaynaklı patojenlerin çoğalmasına uygun bir zemin oluşturur. Özellikle yetersiz altyapıya sahip ve aşırı kalabalık bölgelerde bu durum, dirençli mikroorganizmaların toplum içinde daha hızlı yayılmasına neden olarak, AMR'nin halk sağlığı üzerindeki yükünü artırmaktadır. Böylelikle, iklim krizinin yol açtığı orman yangınları, çevresel bulaş yollarını çoğaltarak antimikrobiyal direncin küresel düzeydeki yayılımına katkı sunmaktadır (3,20).

3.3.3. Aşırı Hava Olayları

Şiddetli yağışlar, seller ve fırtınalar; kanalizasyon sistemlerinin taşmasına, temiz ve atık suyun karışmasına ve çevresel kirleticilerin – özellikle direnç genleri taşıyan bakterilerin – yayılmasına yol açmaktadır. Bu durum, su kaynaklı enfeksiyonların artmasına neden olurken, artan enfeksiyon yükü daha fazla antibiyotik kullanımını beraberinde getirerek direnç gelişimini teşvik etmektedir. Aynı zamanda, taşkınlarla birlikte azotlu gübrelerin ve endüstriyel kirleticilerin su kaynaklarına taşınması, ötrofikasyonu artırmakta ve bu da bakteri çoğalmasını kolaylaştırarak direnç genlerinin yatay gen transferiyle yayılımını hızlandırmaktadır. Aşırı hava olayları ayrıca altyapının zarar görmesine ve yerinden edilmiş nüfusun yoğunluğunun artmasına neden olarak, enfeksiyonların yayılmasını kolaylaştırmakta ve sağlık hizmetlerine erişimi zorlaştırarak tedaviye geç yanıt verilmesine yol açmaktadır. Bu çok yönlü etkiler, aşırı hava olaylarının antimikrobiyal direnç dinamikleri üzerindeki etkisini güçlendirmekte ve iklim krizi ile AMR arasındaki ilişkinin ne kadar derin ve karmaşık olduğunu ortaya koymaktadır (3,21).

3.3.4. Hava Kalitesi

Özellikle orman yangınları, fosil yakıt kullanımı ve endüstriyel faaliyetler sonucunda artan ince partikül maddeler (PM2.5 ve PM10), sadece solunum yolu hastalıklarını tetiklemekle kalmaz, aynı zamanda antibiyotik dirençli genlerin çevresel taşınmasında bir vektör görevi görür. Bu partiküller, antibiyotik direnç genlerini taşıyan mikroorganizmaları hem havada askıda tutabilir hem de solunum yoluyla insan vücuduna girmelerine aracılık edebilir. Ayrıca, hava kirliliği bağışıklık sistemini zayıflatarak enfeksiyonlara karşı direnci düşürmekte, bu da antibiyotik kullanımını artırarak direnç gelişimini teşvik etmektedir. Uzun süreli maruziyet, özellikle kronik solunum yolu hastalıklarında enfeksiyon sıklığını ve antibiyotik ihtiyacını artırmakta, bu da dirençli patojenlerin seçilim baskısını güçlendirmektedir (19,22).

3.3.5. Gıda ve Su Kalitesi

Artan sıcaklıklar ve aşırı hava olayları, su kaynaklarının kirlenmesine, su arıtma süreçlerinin yetersizleşmesine ve gıda güvenliğinin tehdit edilmesine neden olabilir. Bu koşullar, özellikle su kaynaklı enfeksiyonların artmasına, dolayısıyla antibiyotik kullanımının yaygınlaşmasına ve sonuç olarak dirençli patojenlerin seçilmesine yol açmaktadır (3,19). İklim değişikliği nedeniyle meydana gelen yağış değişimleri, sel ve kuraklık gibi olaylar,

suyun mikrobiyolojik kalitesini doğrudan etkileyebilir ve kirli suyun insan sağlığını tehdit etmesine yol açabilir. Örneğin, artan su kirliliği, kanalizasyon sularının içme suyu kaynaklarına karışması, su kaynaklı hastalıkların yayılmasına neden olabilir. Bu hastalıkların tedavisinde antibiyotik kullanımı arttıkça, dirençli bakterilerin gelişmesi hızlanmaktadır (23).

Ayrıca, iklim değişikliği gıda üretimini de etkileyerek, tarımda daha fazla antibiyotik kullanımına yol açabilir. Tarımsal üretimde, özellikle hayvancılıkta, antibiyotiklerin fazla ve yanlış kullanımının artması, gıda zincirindeki antibiyotik dirençli bakterilerin yayılmasına neden olabilir. Sıcaklık artışı ve değişen yağış desenleri, bazı bölgelerde gıda üretiminde verimlilik kayıplarına yol açarak daha fazla antibiyotik kullanımını tetikleyebilir. Bu da, tüketiciye ulaşan gıda maddelerinin antibiyotik dirençli patojenler taşıma riskini artırır (24,25).

3.3.6. Vektör ve Patojen Dağılımındaki Değişimler

İklim değişikliği, vektörlerin çoğalması için uygun ortamlara olanak tanır. Özellikle, sıcaklık artışı ve yağış desenlerindeki değişiklikler, sivrisineklerin ve kenelerin üremesi için daha elverişli koşullar yaratır. Bu durum, yeni bölgelere taşınan patojenlerin yerleşmesiyle sonuçlanır ve halk sağlığını tehdit eden yeni enfeksiyonlar doğurur. Bununla birlikte, bu enfeksiyonlar tedavi edilmediğinde, antibiyotiklerin daha fazla kullanılmasına ve antibiyotik direncinin gelişmesine neden olabilir. Ayrıca, iklim değişikliği ile birlikte patojenlerin daha hızlı mutasyona uğraması ve direnç geliştirmesi de mümkündür. Vektörlerin taşıdığı hastalıkların tedavisinde antibiyotiklerin ve diğer antimikrobiyal ajanların yaygın kullanımı, bu patojenlerde direnç gelişimine yol açabilir. Örneğin, vektör kaynaklı hastalıkların tedavisinde kullanılan ilaçların yanlış ve aşırı kullanımı, dirençli bakterilerin seleksiyonunu hızlandırabilir. Bu durum, halk sağlığı açısından ciddi bir tehdit oluşturmakta ve AMR'nin yayılmasını tetiklemektedir. Sonuç olarak, iklim değişikliği, vektör ve patojen dağılımındaki değişimler yoluyla antibiyotik direncinin artmasına ve yeni sağlık tehditlerinin ortaya çıkmasına yol açmaktadır. Bu durum, küresel sağlık için önemli bir meydan okuma teşkil etmekte ve etkili stratejiler geliştirilmesini gerektirmektedir (3,20).

3.3.7. İklim Göçleri

İklim değişikliği, aşırı hava olayları ve çevresel bozulma nedeniyle iklim göçlerini teşvik etmektedir, bu da göçmenlerin sağlık risklerini artırmaktadır (19). Göç eden topluluklar, genellikle düşük sosyo-ekonomik koşullara sahip ve sağlık hizmetlerine sınırlı erişimi olan bölgelere yerleşmektedir. Bu koşullar, aşırı kalabalıklık, hijyen eksiklikleri ve sanitasyon yetersizlikleri gibi sorunları beraberinde getirir, bu da enfeksiyon hastalıklarının yayılma riskini artırır. Su kaynaklarının kirlenmesi ve sağlık altyapısının yetersizliği, mikroorganizmaların hızla yayılmasına yol açar ve antibiyotiklerin aşırı kullanımı, antibiyotik direncinin artmasına zemin hazırlar. Göçmen topluluklar, genellikle tedaviye erişim sıkıntıları ve yanlış tedavi uygulamaları nedeniyle, antibiyotik direnci gelişen bölgelerde daha fazla risk altındadır. Sonuç olarak, iklim göçleri, enfeksiyon hastalıklarının yayılmasını hızlandırarak antibiyotik direncinin küresel bir sağlık sorunu haline gelmesine katkıda bulunur (25).

3.3.8. Toplumsal Cinsiyet Eşitsizliği ve Şiddet

Kadınlar ve kız çocukları, iklim değişikliğinin sağlık etkilerine karşı daha savunmasızdır. Yetersiz beslenme, kalabalıklaşma ve yetersiz sanitasyon, antibiyotik dirençli patojenlerin

yayılma riskini artırır. Bu durum, daha şiddetli ishal, cinsel yolla bulaşan hastalıklar ve yüksek ölüm oranlarına yol açabilir (26).

4. İKLİM KRİZİNİN YOL AÇTIĞI ANTİBİYOTİK DİRENCİYLE MÜCADELEDE SAĞLIK ÇALIŞANLARININ ROLÜ VE SORUMLULUKLARI

Sağlık çalışanları, iklim değişikliğinin yol açtığı antibiyotik direnci (AMR) ile mücadelede önemli bir rol oynamaktadır. İlk olarak, halk arasında antibiyotiklerin doğru kullanımını teşvik ederek, antibiyotiklerin gereksiz yere kullanılmasını engelleyebilir ve bu şekilde direnç gelişimini azaltabilirler. Sağlık çalışanları, erken tanı koyma ve doğru tedavi yöntemlerini uygulayarak, hastaların uygun tedavi almasını sağlayabilir, böylece antibiyotiklerin aşırı kullanımını engelleyebilir. Ayrıca, iklim değişikliği nedeniyle yeni enfeksiyon türlerinin ortaya çıkabileceği göz önüne alındığında, sağlık çalışanları çok disiplinli bir yaklaşım benimseyerek çevre bilimciler ve epidemiyologlarla işbirliği yaparak bu tehditlere karşı daha etkili stratejiler geliştirebilirler. Klinik uygulamalarda ise, biyoteknoloji ve immünoterapi gibi alternatif tedavi yöntemlerini kullanarak, antibiyotik direncine karşı yenilikçi yaklaşımlar geliştirebilirler. Ayrıca, sağlık çalışanları enfeksiyon kontrolü konusunda titizlik göstererek, hastane ortamlarında hijyen ve sterilizasyon önlemlerini arttırabilir ve böylece enfeksiyonların yayılmasını engelleyebilirler. Bu bağlamda, antibiyotik direncinin yayılmasını engellemek için sağlık çalışanları, verilerin toplanması ve analiz edilmesinde de önemli bir rol üstlenebilir, iklim değişikliğinin sağlık üzerindeki etkilerini izlemek için araştırmalara katkıda bulunabilirler. Sağlık çalışanları aynı zamanda, iklim değişikliği ile ilgili sağlık politikaları geliştiren ve savunuculuk yapan gruplara katılarak, bu sorunların çözülmesine yönelik stratejiler oluşturabilirler. Sürdürülebilir sağlık hizmetleri sağlamak adına, çevre dostu uygulamaları benimseyebilir ve toplumda örnek olabilirler. Bunun yanı sıra, afet bölgelerinde ve mülteci kamplarında sağlık çalışanları psikolojik destek sunarak, stresin ve travmanın antibiyotik direncine etkisini azaltabilirler. Bu çabalar, halk sağlığını korumada ve antibiyotik direncinin yayılmasını önlemede sağlık çalışanlarının kritik rolünü pekiştirmektedir (19,27,28).

5. SONUÇ ve ÖNERİLER

İklim değişikliği, antibiyotik direnci üzerindeki etkilerini giderek daha belirgin hale getirmekte ve bu durum, küresel halk sağlığı için büyük bir tehdit oluşturmaktadır. Artan sıcaklıklar, aşırı hava olayları, orman yangınları, su kaynaklarının kirlenmesi, gıda güvenliği ve insan hareketliliği gibi iklimle ilgili faktörler, antibiyotik direncinin yayılmasını hızlandırmakta ve bu sorunu daha da karmaşık hale getirmektedir. İklim krizinin, mikroorganizmaların çoğalma hızını artırması, direnç genlerinin yayılmasını teşvik etmesi ve sağlık altyapısını zayıflatması, toplumları daha savunmasız hale getirmektedir.

Bu bağlamda, antibiyotik direnciyle mücadelede bir dizi önlem ve strateji gereklidir. Öncelikle, toplumlarda antibiyotiklerin doğru kullanımına dair farkındalık arttırılmalı ve sağlık hizmetlerine erişim konusunda eşitsizlikler ortadan kaldırılmalıdır. Ayrıca, sağlık çalışanlarının antibiyotik yönetimi ve enfeksiyon kontrolü konusundaki bilgi ve becerileri güçlendirilmelidir. Sağlık altyapısının güçlendirilmesi, iklim değişikliğinin sağlık üzerindeki etkilerine karşı hazırlıklı olunması ve toplum sağlığını koruyacak önleyici tedbirlerin uygulanması kritik öneme sahiptir. Ayrıca, iklim değişikliği ile mücadelede

küresel işbirliği şarttır. Uluslararası düzeyde etkili politikaların oluşturulması, çevresel sürdürülebilirlik ve sağlık politikalarının entegre edilmesi gerekmektedir. Antibiyotik direncini engellemek için araştırmaların desteklenmesi, alternatif tedavi yöntemlerinin geliştirilmesi ve yeni antibiyotiklerin keşfi için bilimsel araştırmalar teşvik edilmelidir. İklim değişikliği ve sağlık politikalarının uyumlu bir şekilde yönetilmesi, hem çevresel hem de sağlık krizlerinin birlikte ele alınması gerektiğini göstermektedir. Son olarak, tüm toplum kesimlerinin bu soruna karşı bilinçlendirilmesi, savunmasız grupların desteklenmesi ve iklim değişikliğinin sağlık üzerindeki etkileri konusunda güçlü bir dayanışma oluşturulması önemlidir. Bu tür adımlar, antibiyotik direncinin yayılmasını engellemeye ve halk sağlığını korumaya yardımcı olacaktır.

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EFFECTS OF *Punica granatum* FLOWERs EXTRACT ON HEMATOLOGICAL PARAMETERS OF RATS EXPOSED TO CADMIUM CHLORIDE TOXICITY

ABSTRACT

Background: Cadmium (Cd) is a non-essential trace element that poses significant toxic effects on rat. The pomegranate flower extract contains a large number of polyphenols and possesses potent antioxidant. Therefore in the present study, we investigated the role of *Punica granatu*m flowers extract (PGFE) on hematological toxicity in rats treated with cd.

Methods: Control group (G1) received water. PGFE group (G2) received 150 mg/kg PGFE. Toxicity group (G3) received 30 mg/kg Cd orally in a single administration. Cd+ PGFE group (G4) received 30 mg/kg Cd and 150 mg/kg PGFE. Due to their critical role in oxygen transport and their sensitivity to Cd-induced disruptions, which often result in anemia and impaired oxygen delivery to tissues, hematological parameters such as red blood cell (RBC), hemoglobin concentration (HC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were evaluated. Peripheral smear was also performed for morphological evaluation of blood cells.

Results: CD exposure significantly decreased RBC counts, Hb levels, Ht, MCV and MCH, whereas PGFE exposure caused a significant improvement in these values.

Conclusion: As a result, PGFE can be consumed as a protective agent against acute hematological toxicity in rats

Keywords: *Punica granatum* flowers extract, Cadmium chloride, Hematological toxicity

Introduction

Cadmium (Cd), one of the heavy metals, contaminates agricultural soils as a result of human activities such as industrial activities, phosphorus fertilizers, sewage waste and atmospheric deposits (Satarug et al., 2003). Cd in the soil can be easily taken by plants. Cd, which enters the food chain as a result of being taken by plants, can also be washed from the soil by rainwater and reach source waters. For these reasons, Cd creates a significant environmental problem (Wahba et al.,1993). The most important sources of Cd affecting human life are cigarette smoke (1 cigarette contains 1-2 µg Cd), refined food products, water pipes, coffee, tea, coal burning, shellfish, fertilizer use and flue gases formed during industrial production stages. As a result of the long biological half-life of Cd in humans (19-38 years), its accumulation in the human body increases with age (Drasch et al., 2005). Various toxic effects of Cd have been previously reported by many researchers (Choi et al., 2003; Ozdemir & Dursun 2009; Kotyzová et al., 2010). Cd causes changes in blood parameters, enzyme activities and vital organ functions such as the liver (Jamba et al., 2000; Nagaraj et al., 2000; Satoh et al., 2002). It also causes kidney disorders and a bone disease known as itaiitai. Some studies have reported that Cd has mutagenic, carcinogenic and teratogenic effects (Saplakoglu et al., 1997; Waalkes 2003). Studies have shown that Cd-induced reactive oxygen species production is both time- and concentration-dependent, and also affects enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT), as well as the decrease in the amount of glutathione, which has an important role in antioxidant defense (Pappas et al., 2010). For this reason, the idea that antioxidants might be effective against Cd toxicity and the search for a new and effective antioxidant led us to conduct this study. It is reported that the structure of Punica granatum flower contains abundant phenolic compounds (gallic acid, ellagic acid and ethyl brevifolincarboxylate), triterpenes (maslinic, ursolic, oleanolic and asiatic acids), sterols, daucosterol, flavonoids (punicaflavone) and anthocyanins (pelargonidin 5-diglucoside and pelargonidin 3-glucoside). The antioxidant activity of these compounds in vitro and in vivo has also been proven by studies. Therefore, the aim of the present study was to investigate the possible protective effects of PGFE on blood parameters against the harmful effects of Cd, a toxic substance.

Material and Methods

Drugs and Chemicals

Anhydrous cadmium chloride (CdCl2) was supplied from Sigma Chemicals Company and dissolved in bi-distilled water before administration.

Experimental Animals

Water-soluble Cadmium chloride (CdCl2) was used as a source of cadmium (Cd). In this study, 35 male Sprague dawley rats weighing 200-230 g were used. The experiments were designed and conducted according to ethical norms approved by the Local Animal Care Committee of Ataturk University, Erzurum, Turkey (12.05.2014/54826478-217).

Study Plan

Control group (G1) received water. PGFE group (G2) received 150 mg/kg PGFE. Toxicity group (G3) received 30 mg/kg Cd orally in a single administration. Cd+ PGFE group (G4) received 30 mg/kg Cd and 150 mg/kg PGFE. The treatment of all animals was performed by

oral gavage in a volume of 1 mL/kg b.w. Animals were sacrificed 24 h after treatment under anesthesia.

Plant material collection, handling, and extraction process

The leaves of P granatum L. flowers were harvested from Antalya during April-May. The plant material was shade dried, powdered, and extracted at 60°C for 48 hr, with 70% methanol using Soxhlet apparatus.

Blood Sampling

Following the end of the experiment, the rats were fasted for 12 hours and their blood was collected for hematological studies. 1.5 ml of blood was collected from each rat into an anticoagulant tube.

Hematological Analyses

Blood was analyzed with an automatic blood analyzer (Drew Scientific Inc., HEMAVET950, Serial No: HV03409). Analysis of blood indicators were the number of red blood cells (RBC), the hemoglobin concentration (HC), mean corpusular volume (MCV), mean corpusular hemoglobin (MCH), mean corpusular hemoglobin concentration (MCHC). Additionally, blood smears were prepared for erythrocyte morphological studies.

Statistical analysis

Data analysis of biochemical parameters was performed using a one-way analysis of variance (ANOVA) test by Graphpad prism 5.0 statistics software (GraphPad, La Jolla, CA, USA). Tukey's test was used as a post hoc. The non-parametric Kruskal–Wallis test was used to analyze variations among data obtained using the semi-quantitative method at histopathological examination. Analyses between the two groups were performed using the Mann–Whitney U test. $p < 0.05$ was regarded as statistically significant

Results

Effect of Cd and PGFE on the number of red blood cells (RBC)

Compared with the control group, an increase in the number of red blood cells (Figure 1) was observed in the PGFE-only group ($P < 0.05$). On the other hand, when the number of red blood cells in the control group and the Cd-treated mice was compared, a significant decrease was recorded in the cd group ($P < 0.0001$), indicating that Cd has a negative effect on red blood cells.

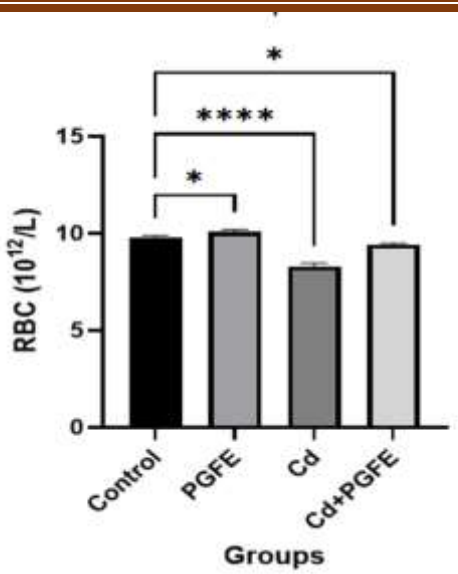


Figure 1. Effect of Cd and PGFE on the number of red blood cells (RBC) in rat (compared with the control group, *P < 0.05, ****P < 0.0001).

Effect of Cd and PGFE on the hemoglobin concentration (HC)

Compared to the control group, no significant difference was observed in the hemoglobin concentration of the PGFE-only group (Figure 2). A significant decrease was noted in the hemoglobin concentration of the Cd-only group compared to the control group (P < 0.0001). Similarly, there was an increase in the hemoglobin concentration of the Cd+PGFE group compared to the Cd-only group (P < 0.05). However, this increase was not enough to bring the hemoglobin concentration exactly close to the control group (P < 0.01).

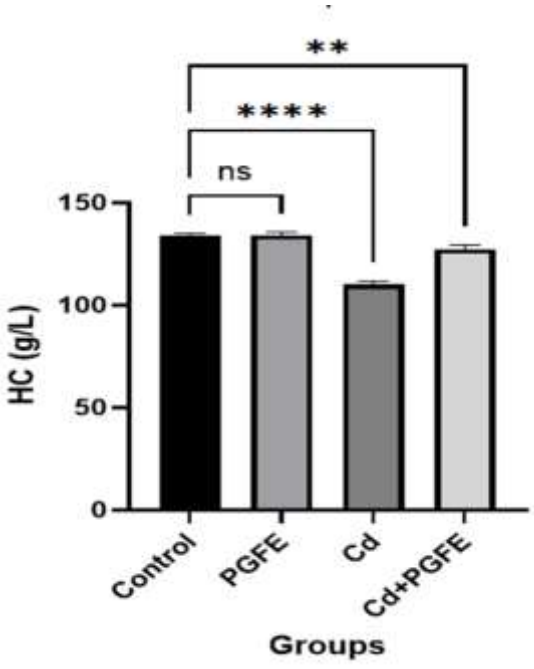


Figure 2. Effect of Cd and PGFE on the hemoglobin concentration (HC) in rat (compared with the control group, *P < 0.05, **P < 0.01, ****P < 0.0001).

Effect of Cd and PGFE on mean corpusular volume (MCV)

Compared to the control group, no significant difference was observed in the mean corpus volume of the PGFE-only group (Figure 3). The mean corpus volume of the Cd-only group decreased significantly compared to the control group ($P < 0.0001$). Similarly, the mean corpus volume of the Cd+PGFE group increased significantly compared to the Cd-only group ($P < 0.05$). The difference in the mean corpus volume of the Cd+PGFE group was significant compared to the control group ($P < 0.05$).

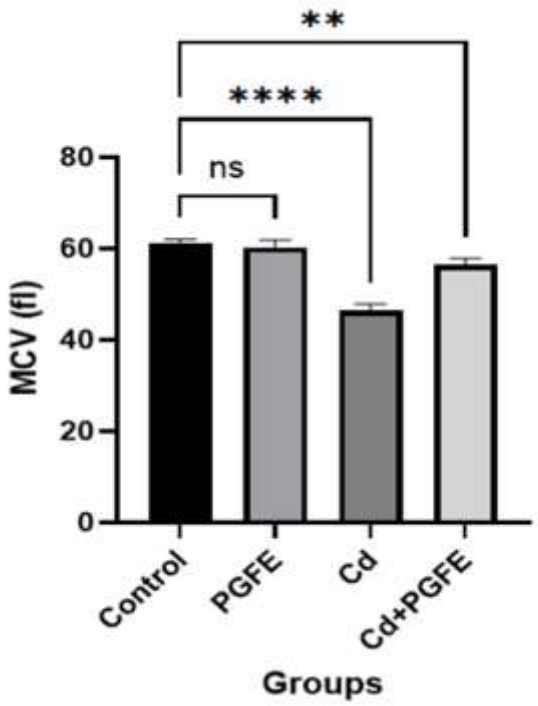


Figure 3. Effect of Cd and PGFE on mean corpusular volume (MCV) in rat (compared with the control group, *$P < 0.05$, **$P < 0.01$, ****$P < 0.0001$).

Effect of Cd and PGFE on mean corpusular hemoglobin (MCH)

Compared to the control group, no significant difference was observed in the mean corpular hemoglobin of the PGFE-only group (Figure 4). A significant decrease was noted in the mean corpular hemoglobin of the Cd-only group compared to the control group ($P < 0.0001$). Similarly, there was a significant increase in the mean corpular hemoglobin of the Cd+PGFE group compared to the Cd-only group ($P < 0.05$). The difference was significant in the mean corpular hemoglobin of the Cd+PGFE group compared to the control group ($P < 0.05$).

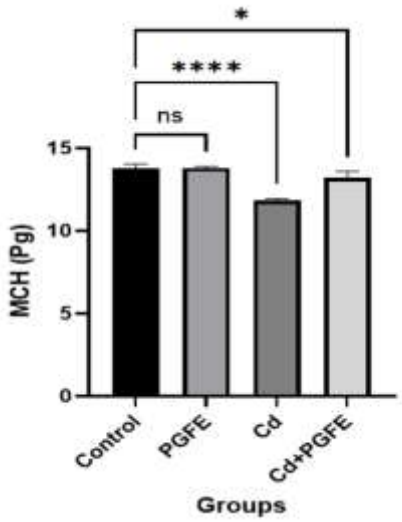


Figure 4. Effect of Cd and PGFE on mean corpusular hemoglobin (MCH) in rat (compared with the control group, *P < 0.05, **P < 0.01, ****P < 0.0001)

Effect of Cd and PGFE on mean corpusular hemoglobin concentration (MCHC)

Compared to the control group, no significant difference was observed in the mean corpuscular hemoglobin concentration of the PGFE-only group (Figure 5). The mean corpuscular hemoglobin concentration of the Cd-only group decreased significantly compared to the control group (P < 0.0001). Similarly, the mean corpuscular hemoglobin concentration of the Cd+PGFE group increased significantly compared to the Cd-only group (P < 0.05). The mean corpuscular hemoglobin concentration of the Cd+PGFE group was significantly different compared to the control group (P < 0.05).

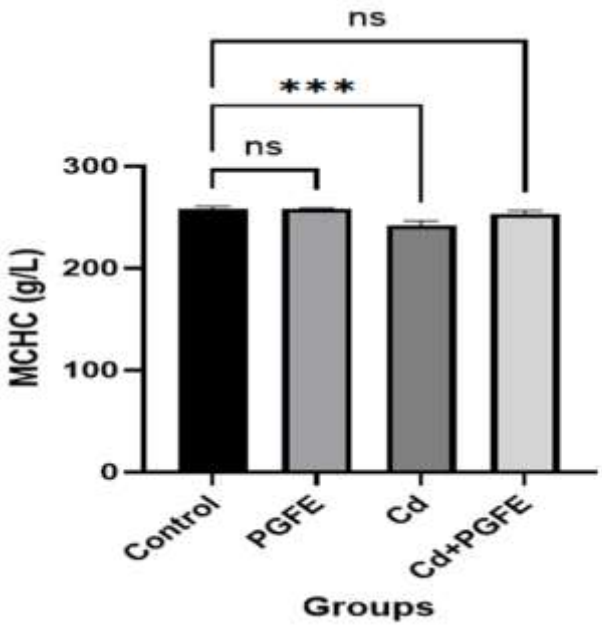


Figure 5. Effect of Cd and PGFE on mean corpusular hemoglobin concentration (MCHC) in rat (compared with the control group, *P < 0.05, **P < 0.01, ****P < 0.0001).

Effects of Cd and PGFE on erythrocyte morphology

Blood smears from the control group (Figure 6A) and the PGFE-only group (Figure 6B) revealed normal histology. Morphological changes in the form of target cells (black arrows), echinocytes (purple arrows) and irregularly contracted cells (white arrows) were evident in the red blood cells of the Cd-treated group (Figure 6C). Cd+PGFE group revealed normal histology like control group (Figure 6D).

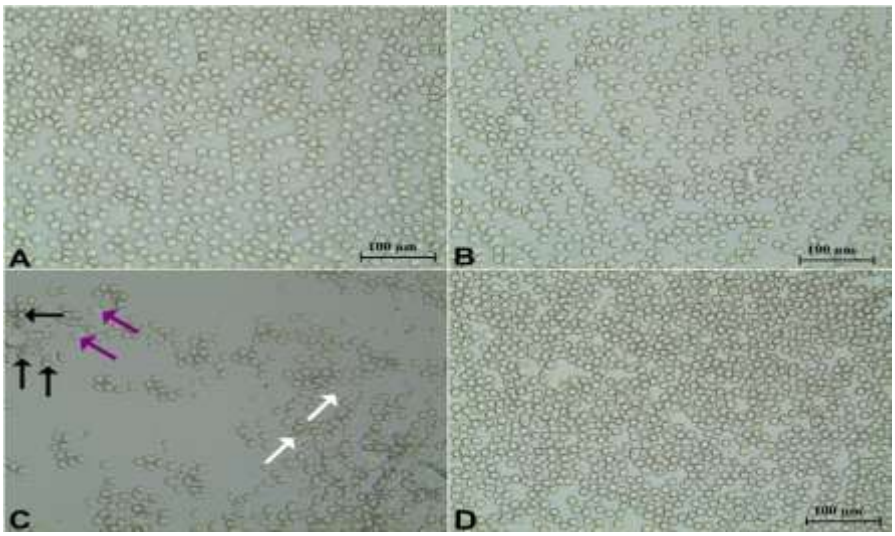


Figure 6. Sprague dawley rat blood smear. (A) Microphotograph of the control group showing normal histoarchitecture. (B) The PGFE group showed similar histoarchitecture to the control. (C) Target cells (black arrows), echinocytes (purple arrows) and irregularly contracted cells (white arrows) are seen in the Cd group. (D) a histoarchitecture almost similar to the control group was observed in the Cd+PGFE group 10x.

Discussion

Cd is a naturally occurring metal. However, chronic cadmium exposure due to industrial and agricultural contamination has become a significant problem, especially in developing countries (Yang et al., 2025). Although the effects of Cd on hematological blood parameters have been reported before, there is no study evaluating the possible therapeutic effects of PGFE extract. Therefore, the present study is the first study on this subject.

In our study, the decrease in the number of red blood cells (RBC) with the application of Cd confirms the toxic effect of Cd especially on red blood cells, while on the other hand, the increase in the number of blood cells with the application of PGFE together with Cd indicates that PGFE eliminates the toxic effect caused by Cd and protects the blood cells from the harmful effects of Cd. Similarly, there are many studies reporting that Cd has negative effects on blood parameters. Again, studies showing the positive effects of antioxidant substances on blood parameters support our current study (Hamada et al., 1998).

In the current study where we evaluated the hemoglobin concentration (HC), we saw that the hemoglobin concentration decreased with the application of Cd and that the application of PGFE together with Cd increased this concentration. Similar values to this result were also observed in previous studies (Khromova & Myshkin 2000).

When we looked at the effects of Cd and PGFE on mean corpuscular volume (MCV) in rats, we observed that Cd also caused a significant toxic effect on mean corpuscular volume (MCV), while PGFE was able to eliminate this toxic effect as expected (Chen et al., 2019). It was observed that mean corpuscular hemoglobin (MCH) was negatively affected by Cd administration in rats. However, PGFE, as a rescuer, was able to eliminate this negative effect. Our literature review found that similar results existed in different studies (Kısadere et al., 2022).

In our study, it was determined that mean corpuscular hemoglobin concentration (MCHC), which was evaluated as the 5th parameter, also received its share of the toxic effect of Cd. It was determined that PGFE caused an improvement in this parameter with its antioxidant effect. (Huang et al., 2021). Finally, we examined red blood cells by peripheral smear and determined that Cd application caused changes in the morphology of red blood cells. The application of PGFE together with Cd succeeded in making the appearance of blood cells similar to the control group. Our literature review found that similar results existed in different studies (Bao et al., 2012).

When all the findings are evaluated together, we can say that Cd has a toxic effect on rats and causes an anemic reaction. In addition, the change in the morphology of blood cells detected by peripheral smear will create an anemic picture, even if there is no decrease in the number of these cells, because they will not be able to carry enough oxygen and nutrients to the tissues.

The improvements in the blood parameters of rats and the normalization of blood cell shapes with PGFE application were made possible by the presence of the therapeutic effect of PGFE on blood parameters. In other words, PGFE can be considered as a therapeutic agent in case of Cd poisoning.

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THE IMPACT OF INNOVATIVE HEALTHCARE TECHNOLOGIES ON MEDICAL LIABILITY

L'IMPACT DES TECHNOLOGIES NOVATRICES DANS LE DOMAINE DE LA SANTE SUR LA RESPONSABILITE MEDICALE

ABSTRACT:

The advent of innovative healthcare technologies, such as telemedicine, connected objects and artificial intelligence, presents promising prospects for the healthcare sector, facilitating access to care and providing support for healthcare professionals. However, the expansion in the use of digital technology raises many questions, as well as significant ethical and legal challenges, particularly with regard to medical liability. It is essential to understand the benefits, such as risk identification, in order to mobilize the legal rules framing the various activities. For example, in the case of current liability regimes, in the event of medical error linked to the use of new technologies, the central issue is the determination of liability. In particular, in the event of damage caused by the use of these new healthcare technologies, liability may lie with the user physician, the software manufacturer or the healthcare establishment.

However, the importance of legal and ethical issues linked to developments in digital medical practice, as well as the major new risks induced by digital tools in healthcare, have led us to examine the question of medical liability in the use of these digital tools and artificial intelligence.

Keywords: Health; innovative technologies; telemedicine, artificial intelligence; medical liability.

INTRODUCTION

L'apparition et le développement des technologies novatrices dans le domaine de la santé, comme la télémédecine, les objets connectés et l'intelligence artificielle, représentent une avancée majeure pour le secteur de la santé. Ces avancées offrent des perspectives prometteuses en facilitant l'accès aux soins pour les patients et en apportant un soutien précieux aux professionnels de santé dans leur pratique quotidienne. Cependant, avec l'avènement croissant de l'utilisation des technologies numériques dans le domaine médical, de nombreuses questions éthiques et juridiques importantes se posent, notamment en ce qui concerne la responsabilité des professionnels de santé.

Il convient de souligner que la responsabilité médicale constitue une forme particulière de responsabilité civile. Par conséquent, elle persiste à assumer la même responsabilité d'indemnisation, sans dévier de cet objectif initial. Cependant, il convient de noter que cette approche diffère du modèle classique de la responsabilité civile, car elle est adaptée à un secteur particulier et sensible, à savoir le domaine de la santé. Cette obligation spécifique consiste à fournir une forme de réparation aux personnes qui ont subi des dommages causés par des professionnels de la santé, tels que les médecins ou tout autre professionnel travaillant dans le domaine médical.

Il est important alors de souligner l'importance des questions juridiques et éthiques qui découlent des avancées de la pratique médicale en lien avec le domaine numérique. En effet, les nouvelles technologies de santé numériques ont introduit des risques majeurs qui nécessitent une réflexion approfondie. C'est pourquoi il est essentiel de se pencher sur la question de la responsabilité médicale dans l'utilisation de ces outils numériques (I), ainsi que dans le recours à l'intelligence artificielle (II).

RESEARCH AND FINDINGS

I. La responsabilité médicale dans l'utilisation des outils numériques

La responsabilité médicale liée à la télémédecine concerne l'ensemble des obligations et des devoirs des professionnels de santé qui utilisent les technologies de l'information et de la communication pour assurer des consultations à distance ou pour échanger des informations médicales. Cette forme de pratique médicale soulève des questions spécifiques en termes de responsabilité, notamment en ce qui concerne la qualité des soins, la protection des données personnelles, la sécurité des échanges, et la traçabilité des décisions prises à distance. La responsabilité est un concept fondamental qui implique qu'une personne soit tenue de répondre de ses actes en raison des fonctions qui lui incombent et des devoirs qui lui sont assignés. Cela signifie qu'elle doit assumer les conséquences de ses décisions et de ses actions, qu'elles soient positives ou négatives. Lorsqu'on aborde le concept de responsabilité, il est primordial de spécifier clairement de quel type de responsabilité il est question. Il peut s'agir de la responsabilité individuelle, professionnelle, sociale, morale, civique, environnementale, financière, familiale, etc. Chaque forme de responsabilité implique des devoirs et des obligations spécifiques qui incombent à la personne concernée. Cela peut impliquer une responsabilité qui peut entraîner des sanctions, telles que la responsabilité pénale en cas d'infraction à la loi ou la responsabilité disciplinaire en cas de non-respect des règles établies, ou une responsabilité qui peut conduire à une indemnisation, comme la responsabilité civile en cas de préjudice causé à autrui ou la responsabilité administrative en cas de faute commise dans le cadre d'une fonction publique.

En vertu du droit marocain, il est important de souligner que le médecin est soumis à une obligation de moyens et non de résultats. Cela signifie que sa responsabilité est engagée en fonction des actions entreprises pour traiter un patient, et non pas en fonction des résultats finaux obtenus. Ainsi, le médecin doit mettre en œuvre tous les moyens nécessaires et appropriés pour soigner son patient, mais il n'est pas garant du succès de ces soins. Cette distinction est fondamentale pour déterminer la responsabilité du praticien en cas de litige médical. Néanmoins, lorsque le numérique intervient directement dans ce type de litige, en jouant un rôle dans un acte défaillant comme la recommandation d'un traitement inapproprié ou d'une intervention chirurgicale non sécurisée, la situation devient plus complexe à traiter.

En télémédecine, les sources de dommages sont variées. Elles peuvent être liées à des problèmes techniques, tels que des erreurs de transmission de données ou des dysfonctionnements des équipements utilisés.

D'autres sources de dommages peuvent également être liées directement à l'acte médical pratiqué à distance, comme des erreurs d'interprétation des symptômes du patient ou des décisions médicales inappropriées. Les responsabilités juridiques des professionnels médicaux restent constantes, car elles reposent sur l'application des principes du droit commun ainsi que de la responsabilité civile professionnelle. Ces obligations légales impliquent que les praticiens de la santé doivent répondre de leurs actes envers leurs patients en cas de faute professionnelle. L'acte de la télémédecine, tout comme tout acte médical, doit impérativement respecter les droits des patients. Cela signifie que les professionnels de santé doivent garantir la confidentialité des informations, obtenir le consentement éclairé des patients, assurer la qualité des soins prodigués, et respecter l'éthique médicale en toutes circonstances. Les professionnels de santé ont l'obligation de fournir à leur patient une information complète concernant les avantages et les risques associés à la pratique de la télémédecine. De plus, ils doivent également expliquer en détail le fonctionnement de la technologie utilisée pour l'acte médical à distance.

La doctrine a examiné diverses pistes de réflexion concernant le régime de responsabilité qui s'applique à la pratique de la télémédecine.

En droit Marocain, il est important de souligner que l’article 11 du code de déontologie Médical ainsi que l’article 446 du code pénal, abordent la question des secrets professionnels. Ces dispositions légales visent à protéger toutes les informations confidentielles concernant le patient qui sont divulguées au professionnel de la santé dans le cadre de l'exercice de sa profession. Le régime de responsabilité applicable aux actes de téléassistance et de télésurveillance est identique à celui qui régit les actes de téléconsultation. Cela signifie que les règles encadrant la responsabilité des professionnels de santé pratiquant la téléassistance et la télé expertise sont les mêmes que celles s'appliquant aux actes de téléconsultation.

En cas de préjudice causé à un patient en raison d'une défaillance de l'équipement de télémédecine, la responsabilité pourrait incomber aux médecins demandeurs, aux médecins sollicités ou aux établissements de santé, même en l'absence de toute négligence de leur part. Cela signifie que ces acteurs pourraient être tenus responsables des conséquences dommageables pour le patient, même s'ils n'ont pas commis d'erreur intentionnelle ou de faute.

Il est important de souligner que dans le cas où le tiers technologique ne respecterait pas les obligations définies dans le contrat qui les lie, ils ont la possibilité d'engager des poursuites légales à son encontre.

II- Les défis éthiques posés par l'intégration de l'intelligence artificielle dans le domaine médical.

En principe, le médecin est tenu à une obligation de moyens dans l'utilisation des outils numériques. Cette situation soulève la question du régime de responsabilité applicable en cas de dommage causé. La responsabilité peut être engagée soit en cas de faute, c'est-à-dire lorsque l'auteur du dommage a commis une erreur, soit sans faute en raison d'un produit défectueux.
Depuis l'arrêt Mercier, rendu par la Cour de cassation en France, il est établi que l'obligation de soins à laquelle est tenu un médecin est une obligation de moyens. Cela signifie que le médecin n'est pas tenu de garantir la guérison du patient, mais il est en revanche engagé à prodiguer des soins de manière consciencieuse, attentive et conformes aux connaissances médicales actuelles.

Les diverses études portant sur les applications de l'intelligence artificielle dans le domaine de la santé mettent en évidence le principe selon lequel la responsabilité en la matière repose sur les épaules du personnel de santé ayant recours à l'IA pour effectuer des actes de prévention, de diagnostic ou de soins. Cette responsabilité implique que le personnel de santé est tenu de répondre de ses actions en cas de faute lors de l'utilisation de l'IA dans le cadre de ses pratiques professionnelles. L'intelligence artificielle est un outil conçu pour faciliter et assister les professionnels de la santé. Il est essentiel de souligner qu'il ne faut pas laisser l'IA prendre des décisions de manière autonome. En effet, l'utilisateur de l'IA doit toujours la superviser et assumer la responsabilité des choix médicaux qui sont faits. Ainsi, il est clair que le professionnel de santé qui utilise l'IA se retrouve dans une position délicate, devant décider s'il suit les recommandations de l'IA ou s'il les rejette. Une question centrale se pose alors : est-ce que le recours à l'IA peut influencer l'appréciation de la responsabilité par le juge ?

En réalité, il est essentiel que le juge fasse preuve de subtilité et de discernement afin de garantir la liberté de choix du professionnel de santé dans le but de protéger les intérêts du patient. De plus, cette approche pourrait également simplifier la réalisation des expertises médicales.
En plus des erreurs techniques liées à l'utilisation de l'intelligence artificielle, il est également important de souligner les lacunes en termes d'informations fournies concernant les risques associés aux traitements médicaux suggérés. En réalité, il est indéniable que le champ d'application de l'information ne cesse de s'agrandir de manière progressive, sous l'influence conjuguée de l'évolution de la jurisprudence et des dispositions légales en vigueur.

L'avancée constante de l'intelligence artificielle dans le domaine médical pourrait inciter les juges à renforcer davantage les exigences en matière d'information que les médecins doivent fournir à leurs patients. Cette information devrait notamment inclure une analyse approfondie des risques potentiels associés à l'utilisation de ces technologies innovantes. La responsabilité pour faute d'information pourrait également être retenue lorsque le médecin, en sa qualité de simple prescripteur, recommande à ses patients l'utilisation d'applications mobiles et d'objets connectés dans le cadre de leur suivi médical. Cette responsabilité

découle du devoir d'informer le patient sur les risques et les bénéfices de ces outils, ainsi que sur la manière de les utiliser de manière adéquate pour garantir leur efficacité et leur sécurité.

En France, le législateur a établi que la responsabilité liée aux dommages causés par un produit de santé est de nature objective, ce qui signifie qu'elle s'applique indépendamment de la recherche d'une faute de la part du responsable, contrairement au principe général de responsabilité pour faute. Une interrogation importante se pose concernant la complexité de l'identification du professionnel de la santé responsable de la prise en charge.

Au Maroc, d'après l'article premier de la loi n° 84-12, tout produit de santé, tel que le logiciel, est catégorisé comme un dispositif médical. Cette classification implique que ces produits sont régis par les réglementations en vigueur pour garantir leur conformité et leur sécurité dans le domaine de la santé. En France, le système d'intelligence artificielle conçu à des fins de diagnostic ou de traitement médical est considéré comme un produit de santé. Ce type de technologie est utilisé pour aider les professionnels de la santé à poser des diagnostics plus précis et à proposer des traitements adaptés aux patients.

CONCLUSION

L'avènement des nouvelles technologies dans le domaine de la santé, telles que la télémédecine et l'intelligence artificielle, soulève des interrogations sur la responsabilité médicale. Cela nous pousse à réexaminer le cadre de la responsabilité médicale, alors que la législation actuelle au Maroc repose encore sur des dispositions générales (notamment les articles 77 et 78 du DOC) ainsi que sur le code pénal (articles 432 et 433). Ainsi, tout manquement à la pratique médicale est considéré comme une transgression à éviter à tout prix. Cette responsabilité médicale se trouve aujourd'hui face à un défi de taille avec l'avènement des technologies de pointe en santé, telles que la télémédecine, les objets connectés et l'intelligence artificielle. Pour y faire face, il est impératif de repenser en profondeur le régime de responsabilité médicale en s'inspirant des meilleures pratiques internationales et en restant à l'affût des dernières avancées dans ce domaine en constante évolution. Pour favoriser l'élan de la créativité tout en veillant à la sécurité des patients et des professionnels de la santé, et garantir des soins de haute qualité.

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PERSONALIZED MEDICINE ON THE RISE – OPPORTUNITY OR RISK FOR WORLDWIDE HEALTHCARE SYSTEMS ?

ABSTRACT

Personalized medicine (PM) technologies are gaining more and more importance in the modern healthcare. As for the last decades PM was dominantly developed for cancer therapy pharmaceutical companies successfully launch PM in non-oncological medical specialties, too. Global market projections indicate that the sector is expected to double in size within the next decade. Notably, the growth rate of PM technologies substantially exceeds that of conventional medicinal products, diagnostics, or pharmaceutical drugs. By definition, personalized medicine aims to match the right patient with the right therapy at the optimal time. Assuming that the diagnostic test is high accuracy, the clinical benefits for the selected patient groups are substantially greater than those observed in the general patients with the disease. The consequence pharmaceutical manufacturers face is a smaller number of patients and a strong justification of a higher price per patient treated. At the extreme end of this spectrum are the gene therapy products which have been approached of 2-4 million USD per patient launched over the recent years.

The objective of this paper is a narrative scoping review based on published scientific evidence on the consequences of the rise of PM for healthcare systems worldwide, and the discussed options to keep the expenses for healthcare systems and patients‘ out-of-pocket costs under control. Among a number of studies, a recent systematic review demonstrated that on average there was zero to negative net monetary benefit of PM. But there was a large heterogeneity of the study results concerning cost-effectiveness.

Healthcare systems all over the world whether in countries with a universal health care or mainly self-paying patients need to find a strategy to govern this trend. It is not be possible or reasonable to stop the trend towards personalized medicine as it is developing exciting break-through innovations for patients. However, the core principle of personalized medicine to “treating the right patient with the right therapy at the right time” must be expanded to include the imperative of delivering care by “at the right costs”.

INTRODUCTION

Personalized medicine (PM) is an evolving field of clinical medicine in which diagnostic tests are used to identify individuals with specific biological markers, often genetic information, to help determine which medical treatments and procedures will work best for the individual patient. By combining this information with individual's medical records, general circumstances such as availability of technologies, and patients' preferences, personalized medicine allows doctors and patients to develop targeted treatment, diagnostic and prevention plans. Alternative terms for personalized medicine include precision medicine, individualized medicine and stratified medicine. PM tries to overcome the dilemma that medical products such as pharmaceuticals and diagnostical tests are standardized due to necessary strict regulations but such a „one size fits all-approach" is leading to an average medical benefit for patients with a specific disease but not to an optimal outcome for every individual patient. An optimization of the selection of better or perfectly fitting patient subgroups approaches the goal of PM to provide the „*The right treatment for the right patient at the right time*" (PMC 2014, Johnson et al. 2021).

The fundamental concept underlying personalized medicine has, in fact, existed for centuries. Biomarkers such as the blood sugar level of diabetics are used since hundreds of years. Further well-known biomarkers such as Hemoglobin A1c or Glycated Hemoglobin (HbA1c) for diabetes or tumor markers such as Cancer Antigen 125 (CA-125) and prostate-specific antigen (PSA) were identified over the years and became standard elements of healthcare. The term „Personalized Medicine" was introduced in an article in *The Wall Street Journal* and shortly later in *The Oncologiest* entitled "New Era of Personalized Medicine: Targeting Drugs for Each Unique Genetic Profile" in 1999 (Langreth et al. 1999). The first targeted therapy of Human Epidermal growth factor Receptor 2 (HER2)-positive breast cancer patients with trastuzumab and the complete decoding of the human genome accompanied the rapid development of PM over the last 25 years (PMC 2017). The reason why it took a quarter of a century might lie in the fact it turned out that with very few exceptions cancer diseases and successful therapeutic approaches are not defined by only one genetic marker but a combination of many (Jorgenson 2019). A selection of the „right patient" by companion diagnostics can massively increases the therapeutic success of the correctly identified patients but due to a limited accuracy of most tests and a not fully perfect fit of tests and therapy there is still a relevant number of non-responders.

Beyond the exclusion of non-responders PM approaches are successfully used in routine care for other purposes, too, such as risk classification of so far asymptomatic individuals, screeing and early diagnosis, as well as prognosis and monitoring of patients currently undergoing treatment. PM was strongly supported by governments and healthcare policy makers. For example Barack Obama, former president of the United States of America, announced in 2015 a new financial support of 215 Mio USD with the words: „Tonight, I'm launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes – and to give all of us access to the personalized information we need to keep ourselves and our families healthier." (Terry 2015, Fox 2015). Over the past, Germany has similarly promoted personalized medicine in both research and clinical application by national initiatives such as the Federal Ministry of Education and Research (BMBF) and the Federal Ministry of Health (BMG) as well as by European partnerships. Personalized Medicine is currently seen as the most important trend in pharma- and medical device industry.

Assuming that the clinical benefits of PM approaches have been demonstrated, the goals of this paper are threefold:

1. How does the market for PM technologies develop?
2. What are the economic consequences of PM technologies? Are PM technologies cost-effective or even cost-saving?
3. How can healthcare systems react to the trend?

RESEARCH AND FINDINGS

The methodological approach of this project can be described as a non-systematic, narrative, scoping review based on published data and scientific evidence. The literature search was performed in digital literature data bases such as pubmed, medline, Google scholar and research gate in April 2024 following standardized search terms without the approach of completeness and without the aim to perform a meta-analysis.

Development of personalized medicine market

After the disturbances of the Covid19 pandemic the worldwide revenue in the PM market was relatively constantly growing by six percent over the last three years (2022-2024) coming close to an overall volume of about 600 million USD. With 297 million USD in 2024 nearly half of the revenues are seen in the sector of personalized nutrition and wellness. The other 316 million USD are shared by PM diagnostics, therapeutics and medical care (Precedence Research 2025). The future prognosis of the PM medicine market size shows about 120% growth over the next 10 years to an overall 1.2 billion USD in 2034 (Towards Healthcare 2025. In comparison, the global pharma market is estimated to grow by about 75% over the same time, as the market for orphan drugs – most of them PM approaches – is increasing by about 145%. It can be summarized that the PM market with an annual rate of about 12% is increasing at a much higher rate as the prognosed increase of about 8% the overall pharma market. The research data underscores the accelerated trajectory of the PM sector, with a compound annual growth rate (CAGR) of roughly 12%, substantially exceeding the anticipated 8% CAGR of the broader pharmaceutical market (Polaris Market Research 2025). This trend reflects not only the increasing adoption of individualized treatment paradigms but also the growing confidence of stakeholders, including investors, healthcare providers, and regulators, in the long-term viability of PM strategies. As such, personalized medicine continues to be recognized as one of the most dynamic and promising domains within the biopharmaceutical and medical technology industries (Hessel 2013). These numbers demonstrate that personalized medicine is continuing to be the most promising strategy in medicinal product industry.

Economic consequences of the use of personalized medicine approaches

A short search in pubmed for „personalized medicine“ and „cost“ shows more than 10,000 hits and a annually, exponentially increasing number of publications to more than 1,500 pubmed-listed publications in 2024. The quality and the results of the studies are very heterogeneous. The vast majority of the studies don’t present health economic studies respectively cost-effectiveness-, budget impact- or costing studies. A recent systematic review (Vellekop et al. 2022) summarizing the results of 128 studies respectively 279 personalized medicine interventions – nutrition and wellness interventions were excluded – shows the following results: Not surprising, most identified PM interventions are for

treatment of cancer patients. The number of PM interventions in other indications in increasing. The results on cost-effectiveness, expressed in average costs per life-year saved or Quality-Adjusted Life Year (QALY) gained in comparison to non-personalized approaches, of the included PM interventions had a very large range. Gene therapy approaches were associated with a high patient benefit (QALY). Cancer therapy approaches showed a higher patient benefit compared to non-cancer treatments, accompanied by higher, often much higher costs. Overall, the net monetary benefit on average for all included PM technologies was 0 to negative on average. In other words: According to the existing study results and assuming that the included studies represent the actual healthcare, there are overall no savings by PM. On average, personalized medicine therapies lead to higher expenses for patients and healthcare systems.

DISCUSSION AND CONCLUSION

In summary personalized medicine approaches show obvious clinical benefits for patients by selecting the right patient for the right therapy at the right time. But often the use of PM leads to higher costs of care for the whole care pathway (Geruso et al. 2018). There are several PM approaches the higher costs for diagnostic tests and high-prized pharmaceuticals are outperformed by the savings due to long-term medical benefits and avoidance of unnecessary treatments of non-responders. Taking in consideration the projected market growth rates of PM technologies above the average pharma market, healthcare systems face an increasing financial problem, not only because of demographic changes. The technological progress in the form of innovative personalized medicine approaches might lead to a higher increase of the treatment costs per patient compared to existing models of health economics.

It will not be possible neither reasonable to stop the ongoing advancement of personalized medicine. For many PM approaches the clinical benefits for patients are without doubt. But healthcare systems will face limits to cover the additional costs of many high-price innovations coming to the market over the next years. There are some personalized medicine technologies which are very cost-effective. It seems to be necessary for high-income countries, in the consequence also for low-income countries to find ways to regulate the market even more. Comparative, real-life studies on medical and financial consequences of personalized medicine should be performed, leading to country and system-specific decisions (Hessel 2013). Regulatory options beyond a restriction are strict regulations of the price of tests and therapy, a selection of patients who benefit most and a limitation of the number of cases. Not only for physicians it seems to be increasingly challenging to choose the right therapy for the right patient at the right time. All patients who would have an additional benefit from an innovative personalized medicine approach should have access to it. To implement a structure and provide financial resources for a universal healthcare is a challenge in real-life in most countries.

The global shift toward personalized medicine offers a transformative opportunity but also poses considerable risks to the financial sustainability of healthcare systems. Pharmaceutical companies and diagnostics manufacturer should consider a fair pricing models to provide access to cost-effective innovative personalized medicine technologies. Moreover, international and national regulatory authorities for pharmaceuticals and medical devices should develop and implement transparent governance rules for approval, pricing and reimbursement of personalized medicine approaches including companion diagnostics.

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IN VITRO STUDY OF PIPERINE'S EFFECTS ON STRUCTURAL, FUNCTIONAL, AND KINETIC PROPERTIES OF BOVINE LIVER CATALASE ENZYME

ABSTRACT

This study examined the impact of piperine (the primary alkaloid in black pepper) on the structural, functional, and kinetic properties of bovine liver catalase. The research methodology employed UV-Vis spectroscopy to analyze enzyme absorption changes at 280 nm and 405 nm wavelengths. Results demonstrated that piperine increased absorption intensity at 280 nm (indicating alterations in the tyrosine and tryptophan amino acid environments), while no significant changes were observed in heme group absorption at 405 nm. Fluorescence spectroscopy studies revealed a concentration-dependent decrease in the enzyme's intrinsic fluorescence intensity, suggesting structural modifications. Calculations of Stern-Volmer constants (Ksv) and quenching constants (Kq) confirmed a static quenching mechanism. Synchronous fluorescence spectroscopy detected an approximately 1 nm blue shift, indicating reduced polarity around tyrosine and tryptophan residues due to piperine interaction. In enzyme kinetics analysis, parameters including IC50 (22.8 μM), inhibition constant (Ki), and α factor demonstrated that piperine reduces catalase activity through a mixed inhibition mechanism. Molecular docking studies verified the existence of a specific piperine binding site on the enzyme. The findings indicate that piperine binding induces significant structural changes in catalase, leading to concentration-dependent enzymatic activity reduction. These alterations involve modifications in key amino acid environments and potential secondary/tertiary structural changes. This research contributes to better understanding food compound effects on antioxidant enzymes and novel drug design. For future studies, we recommend:

1. Surface plasmon resonance (SPR) for detailed binding parameter analysis
2. Circular dichroism techniques to examine secondary structural changes
3. Investigating piperine's effects on other hepatic enzymes
4. Competitive binding assays with markers to validate the molecular docking-identified binding site

These approaches would provide more comprehensive understanding of these molecular interactions.

Keywords: Piperine, Catalase, Enzyme kinetics, UV-Vis spectroscopy, Fluorescence spectroscopy, Molecular docking, Antioxidant enzymes, Liver enzymes.

1- Introduction

The continuous generation of reactive oxygen species (ROS) as by-products of aerobic metabolism represents a critical challenge to cellular homeostasis. These species, which include molecules such as hydrogen peroxide, superoxide anions, and hydroxyl radicals, possess high reactivity that can disrupt cellular components, leading to oxidative stress and associated pathologies such as cancer, neurodegenerative diseases, and inflammatory conditions. Cells rely on antioxidant defense systems to neutralize ROS and preserve functional integrity. Among the key antioxidant enzymes, catalase plays a pivotal role by catalyzing the rapid decomposition of hydrogen peroxide into water and oxygen, thereby mitigating its cytotoxic effects. Catalase is particularly concentrated in the liver, kidneys, and erythrocytes, and its dysfunction or inhibition is closely associated with oxidative damage and disease progression.

Given the centrality of catalase in oxidative balance, there is increasing scientific interest in understanding how dietary and pharmacological compounds affect its function. Natural bioactive substances, particularly those derived from medicinal plants and commonly used spices, have gained attention for their dual roles as antioxidants and modulators of enzyme function. Piperine, the principal alkaloid in black pepper (Piper nigrum), is one such compound that has demonstrated a broad spectrum of pharmacological effects, including antioxidant, anti-inflammatory, and bioavailability-enhancing properties. While piperine has been studied extensively for its therapeutic potential, its direct impact on antioxidant enzymes, particularly catalase, remains poorly defined. Considering its widespread use in the human diet and pharmaceutical formulations, it is imperative to assess whether piperine exerts any modulatory effects on catalase activity or structure.

This study was designed to investigate the effect of piperine on the structure and catalytic function of bovine liver catalase, which is widely used as a model for human catalase due to its high structural and functional similarity. Using a combination of enzymatic kinetics, spectroscopic analyses, and molecular docking simulations, this work seeks to elucidate the nature of the interaction between piperine and catalase. The findings are expected to contribute to a deeper understanding of how common dietary alkaloids influence key antioxidant enzymes and may have broader implications for the safety and efficacy of piperine-containing products.

2- Review of Literature

Reactive oxygen species (ROS), including hydrogen peroxide (H_2O_2), superoxide anion (O_2^-), and hydroxyl radicals (OH•), are generated as by-products of aerobic respiration and various metabolic processes. While these molecules play essential roles in cell signaling and defense against pathogens, their uncontrolled accumulation leads to oxidative stress, which is implicated in the pathogenesis of numerous chronic diseases such as diabetes, atherosclerosis, cancer, and neurodegenerative disorders (Valko et al., 2007). To counterbalance ROS, living organisms rely on an elaborate antioxidant defense system composed of both enzymatic and non-enzymatic components. Among enzymatic antioxidants, catalase is a primary enzyme that rapidly decomposes H_2O_2 into water and oxygen, thus protecting cells from oxidative injury (Chelikani et al., 2004).

Catalase is a heme-containing enzyme with a highly conserved structure across species, and is prominently present in the liver, kidneys, and erythrocytes. Its efficiency and abundance in metabolically active tissues underscore its essential physiological role. The enzyme’s

activity can be influenced by various internal and external factors, including oxidative load, disease states, and exposure to chemicals or bioactive compounds. Studies have shown that reduced catalase activity correlates with higher susceptibility to oxidative damage in conditions such as cancer, Alzheimer's disease, and type 2 diabetes (Reddy et al., 2009). Moreover, catalase deficiency, whether genetic or acquired, has been linked to increased vulnerability to environmental stressors and impaired detoxification capacity.

Piperine, a naturally occurring alkaloid in black pepper (Piper nigrum), has drawn attention for its broad pharmacological profile. In addition to its traditional use as a spice, piperine has been demonstrated to exert anti-inflammatory, antioxidant, anti-tumor, and bioavailability-enhancing effects (Meghwal & Goswami, 2013). It influences various biological pathways and has been reported to modulate the activity of cytochrome P450 enzymes, increase the absorption of nutrients, and enhance the therapeutic index of co-administered drugs. For instance, it improves the bioavailability of curcumin, resveratrol, and several antibiotics by inhibiting their metabolic degradation (Atal et al., 1985; Shoba et al., 1998).

Although piperine is often reported as an antioxidant agent, its interaction with specific antioxidant enzymes such as catalase has not been comprehensively studied. Recent in vitro and in vivo investigations suggest that piperine may influence redox-sensitive enzymes either by direct binding or through modulation of gene expression (Chung et al., 2019). For example, it has been shown to enhance catalase expression under certain oxidative stress conditions, while in other contexts it has been observed to inhibit enzymatic activity depending on dose and exposure time. These dual characteristics necessitate a deeper biochemical examination of its direct effect on catalase activity and structure.

Previous studies on the interaction of plant-derived compounds with catalase indicate diverse mechanisms of action. Compounds such as curcumin, quercetin, and resveratrol have been reported to modulate catalase activity via non-competitive or mixed inhibition mechanisms (Yekta et al., 2017; Rashtbari et al., 2017). Similarly, other dietary alkaloids have shown both inhibitory and enhancing effects depending on concentration and molecular affinity (Samal et al., 2020). Despite the growing body of literature, the specific biochemical impact of piperine on bovine liver catalase, which is structurally homologous to human catalase, remains underexplored. Therefore, the current study aims to fill this gap by characterizing the kinetic and structural interactions between piperine and catalase through spectroscopic analysis and molecular docking simulations.

3- Materials and Methods

To explore the interaction between piperine and catalase, a combination of experimental and computational methods was employed. Bovine liver catalase (BLC), purchased from Sigma-Aldrich, was used as the enzyme model due to its high homology to human catalase. The enzymatic activity was assessed spectrophotometrically by monitoring the decomposition of hydrogen peroxide at 240 nm. A phosphate buffer solution (50 mM, pH 7.0) was used to maintain physiological pH, and hydrogen peroxide (H_2O_2) served as the substrate. Piperine stock solution was prepared by dissolving 1 mg of piperine in 600 µL DMSO and diluting to 1 mL with distilled water, yielding a working solution that allowed a range of final concentrations from 0 to 46.6 µM.

The kinetic measurements involved recording the decrease in absorbance at 240 nm over time to determine initial velocities (Vi) at varying substrate and inhibitor concentrations. The

kinetic parameters, including Michaelis constant (Km) and maximum velocity (Vmax), were calculated using Michaelis–Menten and Lineweaver–Burk plots. The type of inhibition exerted by piperine was inferred from the changes in these parameters at different piperine concentrations, and inhibition constants (Ki and IC50) were also derived.

To study structural changes in catalase, UV-visible and fluorescence spectroscopy were used. Absorbance spectra were recorded to detect alterations in the heme environment of the enzyme, while intrinsic fluorescence measurements focused on tryptophan residues provided insight into tertiary structural perturbations. Synchronous fluorescence was additionally applied to evaluate changes around tyrosine and tryptophan environments. All spectroscopic analyses were performed at two temperatures (25°C and 37°C) to assess temperature-dependent behavior and infer the nature of the quenching interaction, whether static or dynamic.

For computational validation, molecular docking simulations were conducted using AutoDock tools. The three-dimensional structure of catalase was retrieved from the Protein Data Bank, and piperine was docked to identify potential binding sites and calculate binding affinity. The docking results were analyzed to determine the lowest energy conformations and the proximity of binding sites to the enzyme's active center or other functional domains.

All experiments were performed in triplicate to ensure reproducibility, and the results were analyzed statistically. Together, these methodologies provided a comprehensive assessment of the effect of piperine on both the activity and structure of bovine liver catalase.

4- Results and Discussion

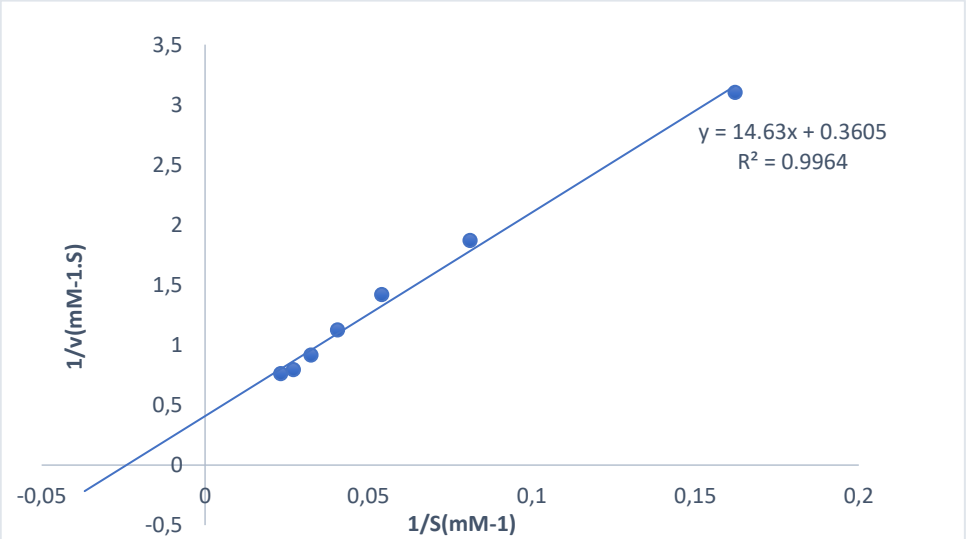
The results of kinetic studies revealed that piperine inhibits catalase activity in a concentration-dependent manner. As the concentration of piperine increased from 0 to 46.6 µM, the relative activity of the enzyme decreased steadily, indicating a dose-responsive inhibition. The value of IC50 was determined to be 22.8 µM, suggesting moderate inhibition strength, while the inhibition constant (Ki) was calculated as 0.14 µM, reflecting high binding affinity.

Table 1. Catalase activity in the presence of increasing piperine concentrations

Piperine Concentration (µM)	Relative Catalase Activity (%)
0.0	100
5.0	92
10.0	78
20.0	55
30.0	38
40.0	24
46.6	18

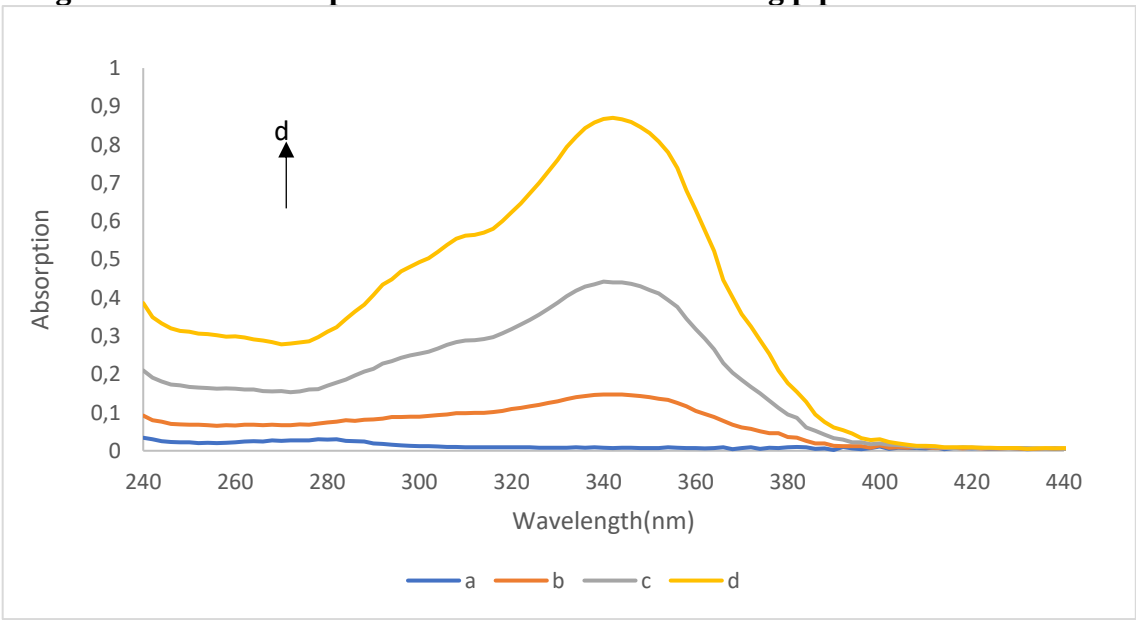
Analysis of the enzyme kinetic parameters through Lineweaver–Burk plots showed that both the apparent Km and Vmax values changed in the presence of piperine, confirming a mixed-type inhibition. This means piperine can bind to both the free enzyme and the enzyme–substrate complex.

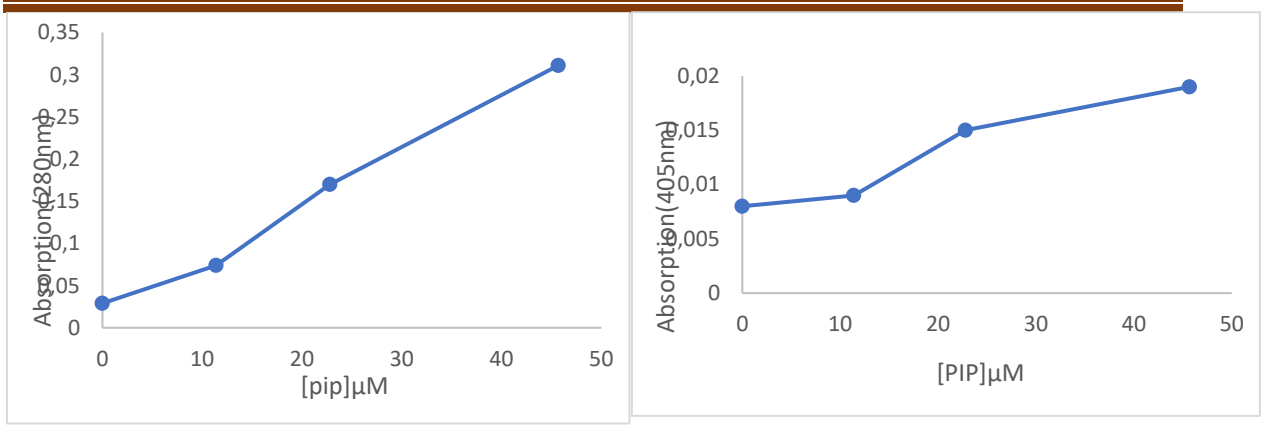
Figure 1. Lineweaver–Burk plots in absence and presence of piperine



Spectroscopic evaluations supported the kinetic data. UV-Visible absorption spectra of catalase showed an increase in absorbance at the Soret band (around 405 nm), indicating an alteration in the heme environment of the enzyme, possibly due to conformational change or perturbation near the active site.

Figure 2. UV-Visible spectra of catalase with increasing piperine concentrations





Fluorescence spectroscopy showed significant quenching of intrinsic tryptophan emission intensity of catalase upon titration with piperine. The quenching followed a static pattern, as demonstrated by temperature-dependent Stern–Volmer plots.

Figure 3. Fluorescence spectra of catalase with and without piperine

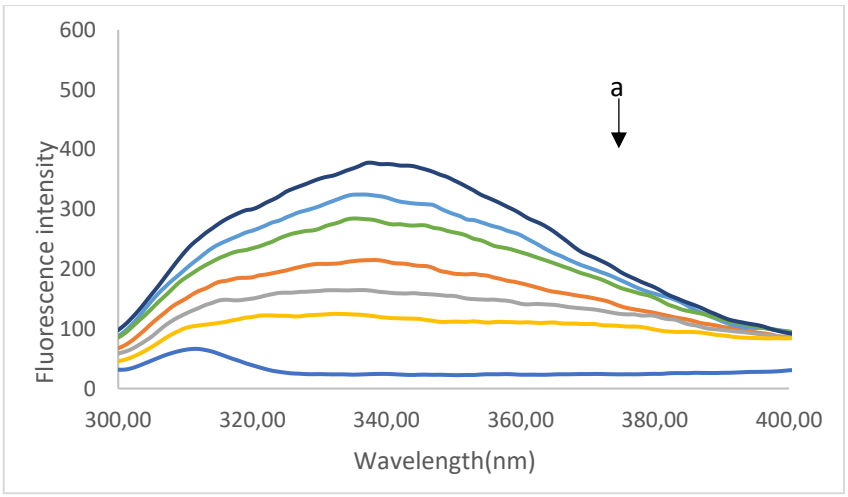
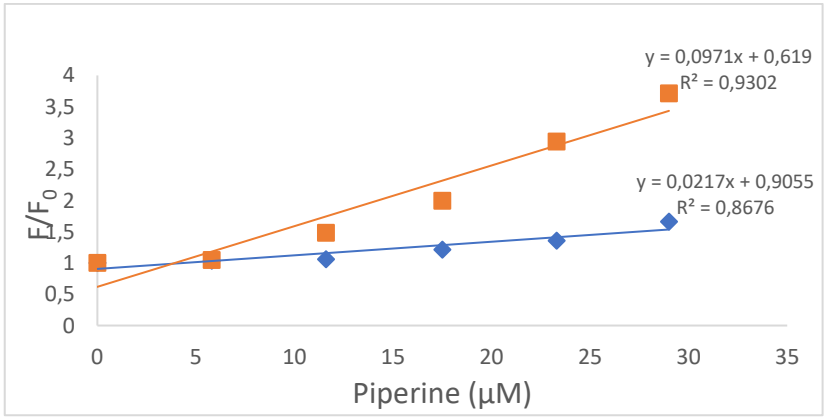


Figure 4. Stern–Volmer plots confirming static quenching mechanism

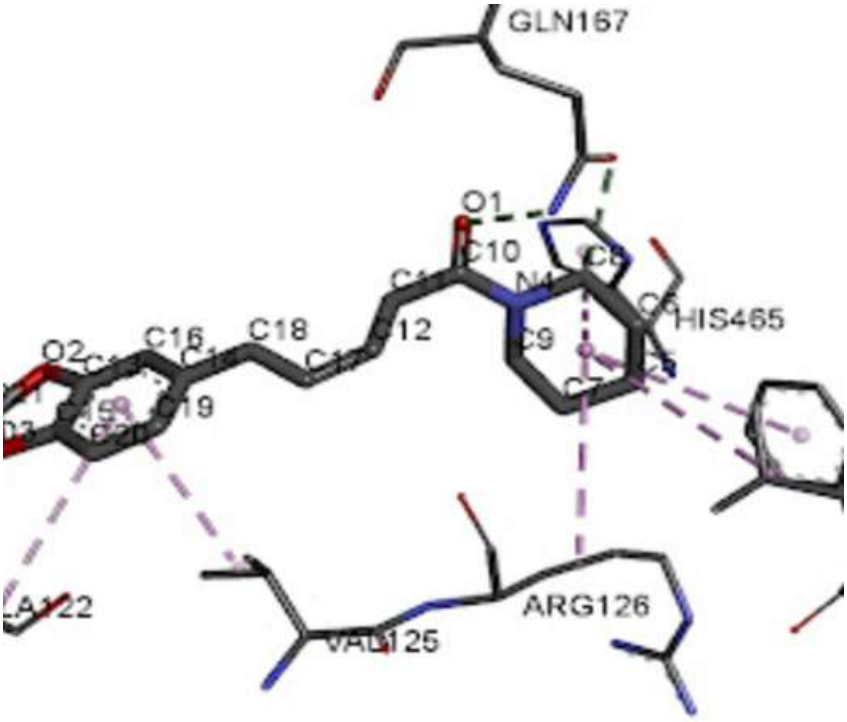


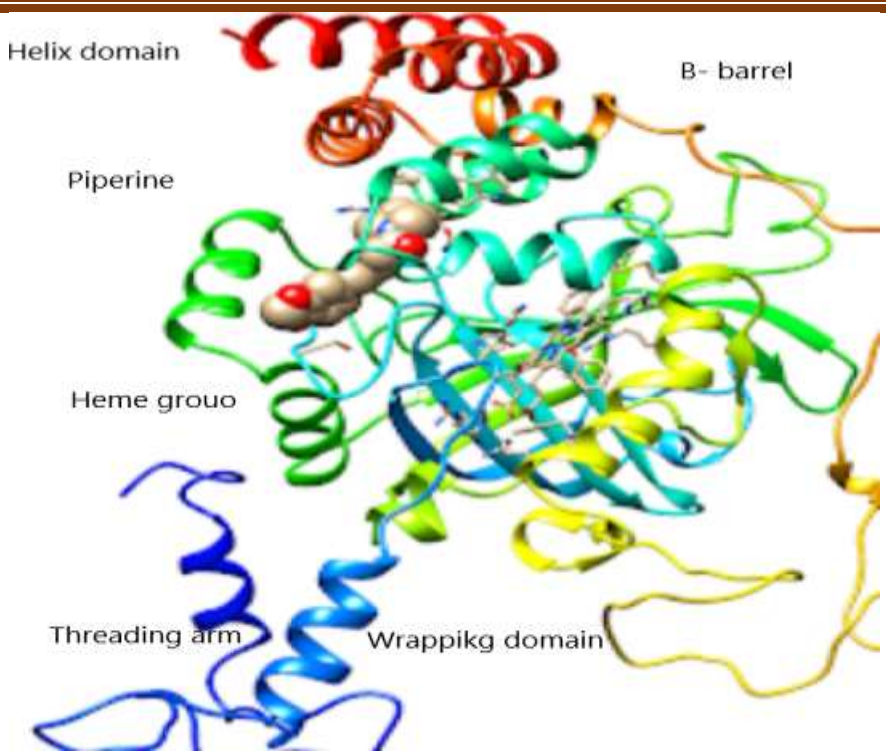
Synchronous fluorescence spectra also indicated minor red or blue shifts in the emission maxima of tyrosine and tryptophan residues, suggesting that the microenvironment of these residues was altered, confirming structural deformation.

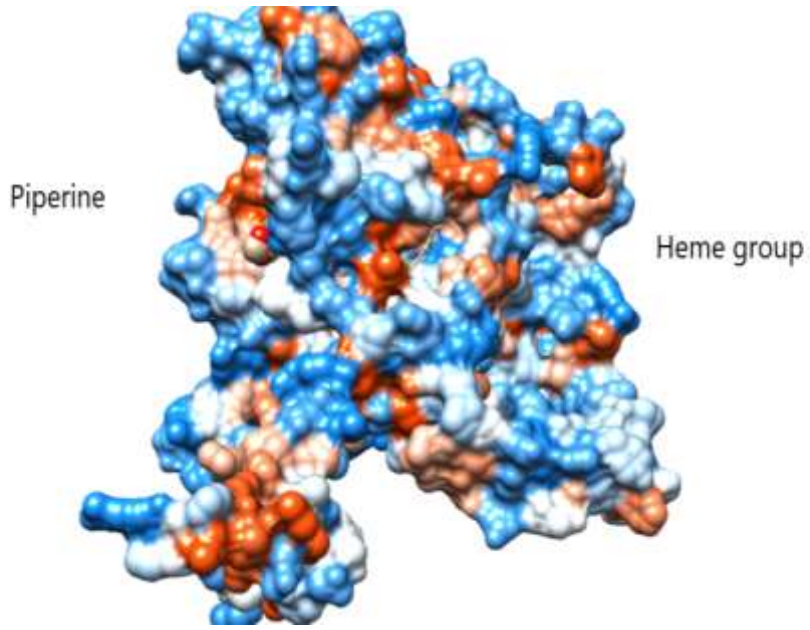
Thermodynamic analyses further supported these findings. The Gibbs free energy change (ΔG) was negative, indicating spontaneity. The positive enthalpy (ΔH) and entropy (ΔS) values suggested that hydrophobic interactions are the dominant forces driving the binding between catalase and piperine.

Molecular docking simulations revealed that piperine binds favorably to a hydrophobic site on the alpha-helix region of catalase, distant from the active site. The minimum binding energy was calculated at –5.27 kcal/mol.

Figure 5. Molecular docking model showing piperine binding site on catalase







These cumulative findings suggest that piperine, despite its known antioxidant potential, can negatively affect catalase function by binding and altering its structure. This may lead to reduced ROS detoxification in cells, especially if piperine is consumed in high doses.

5- Conclusion

This study provides compelling evidence that piperine, a common dietary alkaloid derived from black pepper, can significantly affect the structure and function of catalase, a key antioxidant enzyme. The experimental results demonstrated that piperine inhibits catalase activity in a concentration-dependent manner, with an IC50 value of 22.8 μM and a mixed-

type inhibition mechanism. Spectroscopic analyses confirmed that piperine alters the tertiary structure of the enzyme through static fluorescence quenching and changes in UV-visible absorbance. Thermodynamic parameters indicated that the binding process is spontaneous and primarily driven by hydrophobic interactions.

Molecular docking simulations further corroborated the experimental findings, revealing that piperine binds with high affinity to a site located near the alpha-helix domain of catalase but distant from the active site. This suggests an allosteric inhibition pathway rather than direct interference with substrate binding. Such allosteric modulation may have physiological consequences, particularly under conditions of high dietary intake or supplementation with piperine.

The results underscore the necessity of evaluating natural bioactive compounds not only for their therapeutic potential but also for their possible side effects on critical cellular enzymes. While piperine is widely recognized for its health benefits, this study suggests that excessive consumption could potentially compromise antioxidant defenses by inhibiting catalase function. These findings warrant further investigation, especially in in vivo systems, to assess the broader biological relevance and safety of piperine-containing supplements and diets.

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REGENERATIVE ENDODONTIC TREATMENT: BIOLOGICAL FOUNDATIONS, CLINICAL PROTOCOLS AND FUTURE PERSPECTIVES

ABSTRACT

Regenerative Endodontic Treatment (RET) is an innovative and biologically based approach used in the treatment of necrotic immature permanent teeth. While conventional root canal therapy aims to disinfect the canal system and fill it with inert materials, RET seeks to restore the vitality of the tooth by promoting the regeneration of the pulp-dentin complex. This treatment protocol involves effective canal disinfection using antimicrobial agents such as sodium hypochlorite and EDTA, controlled bleeding induction to allow the influx of stem cells from the apical papilla into the root canal, and the application of biocompatible scaffold materials such as platelet-rich plasma (PRP), calcium hydroxide, and mineral trioxide aggregate (MTA).
Current studies suggest that RET supports root development more effectively than traditional apexification methods, contributes to dentinal wall thickening, and may potentially restore tooth vitality. However, challenges such as standardization of clinical protocols, long-term success rates, and patient-specific variability remain. Advances in stem cell therapy, biomaterial innovations, and tissue engineering hold the potential to further enhance the efficacy of RET. This review comprehensively discusses the biological foundations, clinical applications, advantages, limitations, and possible future developments of regenerative endodontic treatment. RET has demonstrated the potential to enable functional tissue regeneration, especially in immature teeth. Nevertheless, the optimization of standardized protocols and the availability of long-term clinical data are required. RET represents a biologically driven paradigm shift in the future of endodontic practice.

Keywords: immature, necrotic, regenerative endodontic treatment, stem cell therapy

REJENERATİF ENDODONTİK TEDAVİ: BİYOLOJİK TEMELLER, KLİNİK PROTOKOLLER VE GELECEK PERSPEKTİFLER

ÖZET

Rejeneratif Endodontik Tedavi (RET), nekrotik immatür daimi dişlerin tedavisinde kullanılan yenilikçi ve biyolojik temelli bir yaklaşımdır. Geleneksel kök kanal tedavisi, kanal sisteminin dezenfekte edilerek inert materyallerle doldurulmasını amaçlarken, RET ise pulpa-dentin kompleksinin yeniden oluşumunu teşvik ederek dişin canlılığını yeniden kazandırmayı hedefler. Bu tedavi protokolü, sodyum hipoklorit ve EDTA gibi antimikrobiyal ajanlarla etkin kanal dezenfeksiyonu, apeks papilladan kök kanalına kök hücrelerin girişini sağlamak için kontrollü kanama indüksiyonu ve trombositten zengin plazma (PRP), kalsiyum hidroksit ve mineral trioksit agregat (MTA) gibi biyouyumlu iskele materyallerinin uygulanmasını içerir. Güncel araştırmalar, RET'in geleneksel apeksifikasyon yöntemlerine kıyasla kök gelişimini daha iyi desteklediğini, dentin duvarlarının kalınlaşmasını sağladığını ve dişin potansiyel olarak canlılığını yeniden kazanabildiğini göstermektedir. Ancak, klinik protokollerin standardizasyonu, uzun vadeli başarı oranları ve hasta bazlı değişkenlikler gibi bazı zorluklar devam etmektedir. Kök hücre tedavisi, biyomalzeme inovasyonları ve doku mühendisliği alanındaki gelişmeler, RET'in etkinliğini daha da artırma potansiyeline sahiptir. Bu derleme, rejeneratif endodontik tedavinin biyolojik temellerini, klinik uygulamalarını, avantajlarını, sınırlamalarını ve gelecekteki olası gelişmelerini kapsamlı bir şekilde ele almaktadır. RET'in özellikle immatür dişlerde fonksiyonel doku rejenerasyonu sağlayabileceğini göstermektedir. Ancak standart protokollerin optimizasyonu ve uzun dönem klinik veriler gereklidir. RET, endodontik pratiğin geleceğinde biyolojik temelli bir paradigma değişimini temsil etmektedir.

Anahtar kelimeler: İmmatür, nekrotik, rejeneratif endodontik tedavi, kök hücre tedavisi

GİRİŞ

Rejeneratif endodontik prosedürlerin (REP) amacı, daha önce nekroze olmuş veya enfekte olmuş diş pulpasının yapısal ve işlevsel bütünlüğünü rejenere etmektir (1). Bu prosedürü tanımlamak için yıllar içinde rejenerasyon, pulpal revaskülarizasyon ve canlandırma gibi çeşitli terimler kullanılmıştır. Rejeneratif endodonti esas olarak enfekte pulpa dokusunu pulpa ve tam kök gelişimi (apeksogenez) gibi canlı dokularla değiştirmeyi ve olgunlaşmamış apeksin kapanmasını (apikal kapanma) ve kök uzunluğunda ve kalınlığında artış sağlamayı amaçlar (2). Rejenerasyon, dentin ve kök yapısının yanı sıra pulpa-dentin kompleksinin hücrelerini de içeren hem revaskülarizasyonu hem de revitalizasyonu ifade eder .

Rejeneratif endodontinin biyolojik temelleri

Rejeneratif endodontik tedavi, hasar görmüş pulpa dokusunun biyolojik yollarla yeniden oluşturulmasını hedefler. Bu süreç, canlı hücrelerin, büyüme faktörlerinin ve biyomalzemelerin etkileşimine dayanır. Başarılı bir rejenerasyon için steril bir kanal ortamı, uygun hücresel yanıt ve biyouyumlu iskele sistemleri gereklidir. Hücre kaynakları, büyüme faktörleri ve doku mühendisliği yaklaşımları bu sürecin temel yapı taşlarını oluşturur. Biyolojik temellerin iyi anlaşılması, rejeneratif tedavi protokollerinin etkinliğini ve öngörülebilirliğini artırır.

Pulpal rejenerasyon mekenizmaları

Rejeneratif endodontik tedaviye üç yaklaşım vardır (3):

- Hücresiz yaklaşım, hücre bazlı yaklaşım ve hücre yuvalama yaklaşımı.
- Hücresiz yaklaşım, periapikal dokudan yumuşak dokunun çoğalmasını veya kök apeksinden kanamayı indükleyerek kök kanal sisteminin vaskülarizasyonunu indüklemeyi amaçlar, bu işlem aynı zamanda revaskülarizasyon olarak da adlandırılır (4).
- Hücre-yerleşim yaklaşımı, endojen kök hücrelerin fiziksel veya biyolojik uyarılar yoluyla kök kanalına alınarak diş pulpası dokusunun yenilenmesini sağlayan hücresiz bir rejeneratif stratejidir (5). Hücre yerleşiminde, kök kanal sisteminin etkili bir şekilde dezenfeksiyonu ve steril bir ortam elde edilmesi hayati önem taşır.

Doku onarımı ve rejenerasyonu yalnızca konağın savunma mekanizmalarının dokuyu tahrip eden proinflamatuar süreçleri tetiklemediği steril veya oldukça dezenfekte edilmiş bir mikro ortamda gerçekleşebilir (6). Daha etkili bir dezenfeksiyon için, mevcut protokoller önce düşük konsantrasyonda sodyum hipoklorit (%1,5–3) kullanılmasını, ardından tuzlu su veya EDTA ile durulanmasını önerir. Hücre yuvalanmasında, periapikal kaynaklı kanama gibi fiziksel uyarılarla oluşan kan pıhtısı öncelikle bir iskele olarak kullanılır. Bununla birlikte, PRP (trombositten zengin plazma), trombositten zengin fibrin (PRF) ve kolajen membranlar gibi diğer iskeleler de kullanılmıştır (7). Hücre yuvalama tekniğinde ayrıca, antikoagülan veya katkı maddesi içermeyen, %100 hastanın kendisine ait (otolog) bir biyomateryal olan enjekte edilebilir trombositten zengin fibrin (i-PRF) kullanılmıştır.

Kök hücreler

Dolaşımdaki veya çeşitli dokulardaki kök hücreler, yaralanma türüne ve/veya parakrin/endokrin sinyallere bağlı olarak ya hareketsiz kalabilir ya da çoğalıp çeşitli hücrelere farklılaşabilir. Bu hücreler, yaralanmalardan sonra doku yenilenmesi, iyileşme ve rejenerasyondan sorumludur (8). Diş kök hücrelerinin mezenkimal kökenli popülasyonlar olduğu düşünülmektedir. En yaygın diş kök hücreleri arasında dental pulpa kök hücresi (DPSC), insan dökülmüş süt dişlerinden elde edilen kök hücreler, apikal papilla kök hücresinden (SCAP) elde edilen kök hücreler ve periodontal ligament kök hücreleri bulunur (9). DPSC'ler osteoblastlara, yağ hücrelerine ve sinir hücrelerine farklılaşabilen çok potansiyelli hücrelerdir ve endodontik rejenerasyon perspektifinden umut vericidir. SCAP'ler apikal foramenden göç edebilir ve kanal boşluğunda dentin ve kan damarları, kemik, sement ve işlevsel bir periodontal ligament üretebilir (10). Ekzojen büyüme faktörleri olmadan farklılaşabilirler ve diğer mezenkimal kök hücrelere kıyasla daha az telomer kısalması gösterirler. Bu nedenle SCAP'ler doku rejenerasyonu için üstün bir hücre tipi olabilir (11). Özellikle olgunlaşmamış dişlerin apikal papillasından elde edilen SCAP'ler oldukça çoğalır ve "odontoblast benzeri" hücrelere farklılaşabilir, bu nedenle endodontik rejenerasyon vaat eder (12).

Büyüme faktörleri

Büyüme faktörleri, bağlandığında göç, çoğalma, farklılaşma ve olgunlaşma gibi geniş bir hücresel aktivite yelpazesine yol açan polipeptitler veya proteinlerdir. Belirli sinyal yollarını düzenlemek, büyüme faktörlerini doku onarımı ve rejenerasyonunda önemli hale getirir (13). Büyüme faktörleri doğal olarak kan akışından, kalan pulpa parçalarından, kök hücrelerden veya bitişik dentinden oluşabilir. Bununla birlikte, son çalışmalar rejenerasyonun tamamen ekzojen büyüme faktörleri kullanılmadan da meydana geldiğini bulmuştur (14). Dentin duvarında bulunan endojen büyüme faktörleri dezenfeksiyon yaklaşımlarından sonra serbest bırakılabilir ve rejeneratif süreçte kullanılabilir hale gelir (15). İnsan dentininde 300'e yakın protein tanımlanmıştır. Proteinlerin çoğu hücre büyümesi, iletişim, metabolizma ve bağışıklık tepkilerinde rol oynar. Dentin kökenli proteinler kemotaksi ve organize "pulpa benzeri" doku oluşumunu indükleyerek hücresel süreçleri dentin tübüllerine kadar uzatır (16). Dönüştürücü büyüme faktörü Beta 1 (TGF-β1), odontoblastlar tarafından üretilir ve peritübüler dentinde depolanır. Hücre göçü ve proliferasyonunu (çoğalmasını) teşvik ettiği gösterilmiştir. Ancak, olgun ve olgunlaşmamış dişler arasında dağılımında belirgin bir fark gözlenmemiştir. Bu nedenle TGF-β1, rejenerasyon tedavisine ihtiyaç duyan hem genç hem de yaşlı bireylerde doku yenilenmesini destekleyebilir (17). Dentin, anjiyojenik büyüme faktörleri açısından zengin bir doku olarak tanımlanmıştır. Yüksek konsantrasyonlarda trombosit kaynaklı büyüme faktörü (PDGF) ve daha düşük düzeylerde vasküler endotelyal büyüme faktörü (VEGF) ile fibroblast büyüme faktörü (FGF) tespit edilmiştir. PDGF, hücre göçünü doza bağlı olarak teşvik ederken; kök hücre çoğalması, farklılaşması ve miyelin oluşumunu da indüklemektedir. Ayrıca, VEGF'in hayvan modellerinde hücre göçünü uyardığı gösterilmiştir.

Biyomalzemeler/hücre iskeletleri

Hücre dışı matriksler tüm canlı dokuları destekler ve hücrelerin çoğalmasını ve farklılaşmasını sağlar. İskele, doğal hücre dışı matrisi taklit eden mekanik ve kimyasal özelliklere sahip karmaşık üç boyutlu bir malzemedir. Rejeneratif terapi çalışmalarında doğal ve sentetik kökenli çok çeşitli iskele tasarımları test edilmiştir. Başarılı bir iskele, hücrelere yapısal destek sağlamalı, hayatta kalmalarını, çoğalmalarını ve farklılaşmalarını

desteklemeli, ayrıca hücre etkileşimlerini teşvik etmelidir. İskele gözenek boyutu, şekli ve hacmi, oksijen, besin maddeleri ve büyüme faktörlerinin taşınması ve atıkların uzaklaştırılması için önemlidir. Biyouyumlu olması ve yeterli fiziksel ve mekanik mukavemete sahip olması da gereklidir. Bu nedenle, iskele, doku iyileşmesi için uygun bir hızda parçalanmalıdır (18). Fibrin, fibrinojen monomerinin doğal olarak oluşan bir biyopolimeridir. Trombin tarafından parçalanan fibrinojen molekülleri, polimerizasyon reaksiyonlarını başlatır. Çapraz bağlı proteinler, doku desteği ve hücre sağkalımı için uygun bir biyolojik iskele oluşturur. Fibrin ve fibrinojen, kan pıhtılaşması, fibrinoliz, hücresel ve matris etkileşimleri, inflamatuar yanıt ve yara iyileşmesinde kritik bir rol oynar. Fibrin, doku mühendisliğinde yaygın olarak kullanılan bir iskele tasarımıdır ve birçok avantajı vardır. Ayrıca, hastanın kendi kanından elde edilebilir, bu da yabancı cisim reaksiyonu ve enfeksiyon riskini azaltır (19).

Rejeneratif endodontik tedavi protokolü

1. Seans

İlk seansta lokal anestezi uygulanır ve lastik örtü ile izolasyon sağlanır. Giriş kavitesi açıldıktan sonra, periapikal dokulara taşmayı en aza indirecek şekilde 20 ml %1,5'lik sodyum hipoklorit (NaOCl) ile bol irrigasyon yapılmalıdır. Bu işlemde irrigasyon iğneleri veya EndoVac sistemleri kullanılabilir. Kanalların her biri için 20 ml NaOCl ile 5 dakika süreyle irrigasyon yapılması önerilmektedir. Ardından, salin ile 20 ml/kanal süreyle 5 dakika boyunca irrigasyon yapılmalıdır. İrrigasyon iğnesi, apikal dokulardaki kök hücrelere zarar vermemek ve sitotoksisiteyi azaltmak için kök uzunluğundan 1 mm kısa olmalıdır.

İrrigasyon sonrası, kanallar paper point ile kurulanıp, kalsiyum hidroksit veya düşük konsantrasyonda üçlü antibiyotik patı yerleştirilmelidir. Üçlü antibiyotik patı yerleştirilecekse, renklenmeyi en aza indirmek için pulpa odası dentin bonding ajanı ile kaplanmalıdır. Üçlü antibiyotik karışımı, siprofloksasin, metronidazol ve minosiklinin 1:1:1 oranında karıştırılmasıyla hazırlanır. Minosiklinin final konsantrasyonu 0,1 mg/ml olmalıdır. Üçlü antibiyotik patı kanala şırınga ile yerleştirilmelidir. Ayrıca, bu patın, mine-sement sınırının altında kalacak şekilde yerleştirildiğinden emin olunmalıdır. Geçici restorasyon olarak, kavite 3-4 mm derinliğinde Cavit™, IRM™, cam iyonomer siman veya başka bir uygun materyal ile kapatılır ve hastaya 1-4 hafta sonrası için randevu verilmelidir.

2. Seans

İkinci seansta, ilk tedavi gözden geçirilir ve enfeksiyon semptomları devam ediyorsa, alternatif antimikrobiyallerle tedavi yapılabilir. Semptom yoksa, %3'lük mepivakain ile vazokonstriktörsüz anestezi yapılır ve rubber dam ile izolasyon sağlanır. Bol ve nazikçe 20 ml %17'lik EDTA ile irrigasyon yapılmalıdır. Sonrasında, paper point ile kanallar kurutulur. Kanal içine doğru kanama oluşturmak için over instrumentasyon yapılır. Pre-curved K file eğesi kullanılarak, apikal forameni 2 mm geçecek şekilde döndürülerek kanalın tüm boşluğu kanla doldurulur. Pıhtı üzerine, beyaz MTA veya CaOH yerleştirilmesi kolaylaştırmak için CollaPlug™, Collacote™ veya CollaTape™ gibi rezorbe olabilen bir matriks yerleştirilir. Bu kaplama materyalinin üzeri, 3-4 mm kalınlığında cam iyonomer siman ile kapatılıp, 40 saniye ışıklanmalıdır. MTA, renklenmeye neden olabilir, bu nedenle estetik kaygıların olduğu durumlarda alternatif materyaller kullanılabilir.

Anterior ve premolar dişlerde CollaTape/CollaPlug kullanımı önerilmektedir. Restorasyon için, 3 mm rezin modifiye cam iyonomer siman uygulandıktan sonra, mine marjinlerine

bevel yapılır ve kompozit ile restore edilir. Posterior dişler veya prefabrike kron yapılmış dişlerde CollaTape/CollaPlug kullanımı önerilir ve 3 mm MTA uygulandıktan sonra rezin modifiye cam iyonomer siman veya alaşımlar ile restore edilir.

Takip ve değerlendirme

Tedavi sonrası takiplerde, klinik ve radyografik değerlendirmelerde ağrı olmaması, yumuşak dokularda şişlik ve sinüs yolu olmaması gerektiğine dikkat edilmelidir. Genellikle ilk ve ikinci seanslar arasında bu semptomlar gözlemlenebilir. 6-12 ay sonra, apikal radyolusensinin küçülmesi ve iyileşme belirtileri gözlemlenebilir. Kök duvarlarının kalınlaşması, kök uzunluğunun artmasından önce gözlemlenir. 12-24 ay arasında kök uzunluğu ve kalınlığı artarak kök ucunun kapanması sağlanır. Ayrıca, bazı vakalarda pozitif pulpa vitalitesi elde edildiği de bildirilmiştir (20).

Rejeneratif endodontik tedavide kanal içi medikament kulanımı

Bakteriler özellikle alet kullanılmayan bölgelerde ve kök kanal temizliğinden sonra oluşan düzensiz boşluklarda dentin tübülleri içinde kalabilir. Bu mikroorganizmalar çoğalabilir ve kök kanalının yeniden enfekte olmasına neden olarak endodontik tedavinin başarısız olmasına katkıda bulunabilir. Bu nedenle, kök kanal ilaçlarının kök dentininin derinliklerine yerleşmiş bu bakterilere karşı etkili antibakteriyel özelliklere sahip olması ve aynı zamanda periradiküler dokularla uyumlu olması çok önemlidir (21). Kalsiyum hidroksit ($Ca(OH)_2$) ve üçlü antibiyotik patı (TAP), rejeneratif tedavilerde dezenfeksiyon için sıklıkla kullanılan yaygın maddelerdir. TAP, minosiklin, siprofloksasin ve metronidazol gibi antibiyotiklerden oluşur. Minosiklin, kalsiyum şelatlayıcı özelliklere sahip bir antibiyotiktir ve diş sert dokularının demineralizasyonuna yol açarak dentinin mekanik özelliklerini olumsuz etkileyebilir. Araştırmalar, $Ca(OH)_2$'nin yükseltilmiş alkali pH seviyesinin hem kök dayanıklılığını hem de uzun vadeli diş sağlığını (MH) önemli ölçüde azalttığını göstermektedir (22,23). Üçlü antibiyotik patının minosiklin içeriğinden dolayı diş sert dokularında renklenme oluşturmasından dolayı güncel tedavilerde ikili antibiyotik patı önerilmektedir. Üçlü antibiyotik patının $Ca(OH)_2$ ye göre kök hücrelerine daha sitotoksik olması ve seans aralarında kanal içerisinden zor uzaklaştırıldığı için güncel tedavilerde $Ca(OH)_2$ önerilmektedir.

Rejeneratif endodontik tedavide biyomühendislik ve güncel yaklaşımlar

Rejeneratif endododontik tedavide enjekte edilebilir termosensitif antibiyotik yüklü kitosan hidrojeli güncel yaklaşımlarda kullanılmaya başlanmıştır. Enjekte edilebilir jeller, kök kanalı gibi küçük alanlara minimal invaziv uygulama sağlayan akışkanlıkları ile karakterize edilen yenilikçi bir hidrojel ağı türünü temsil eder. Termosensitif enjekte edilebilir hidrojeller, belirli sıcaklıklarda sıvı halde kalır ve vücuda enjeksiyon sırasında jele dönüşür. Bu hidrojeller, fizyolojik koşullar altında (37°C) geri dönüşümlü sol-jel dönüşümlerine uğrayacak şekilde tasarlanmıştır ve canlı dokulara benzer mekanik özelliklere sahiptir(24). Bu termosensitif malzemeler arasında, beta-gliserol fosfat (BGP) ve sodyum hidrojen karbonat (SHC) dahil olmak üzere zayıf bazlarla birleştirildiğinde kitosan (CH), önde gelen bir termosensitif polimer sınıfı olarak ortaya çıkmaktadır. Sıcaklık ve pH değişikliklerine tepki veren kitosan bazlı enjekte edilebilir hidrojeller, birden fazla avantaj sunar: önemli miktarda su emebilirler, minimal invazivdirler ve düzensiz şekilli kusurlara iyi uyum sağlayan gözenekli yapılar oluştururlar. Ek olarak, antibiyotikler ve diğer biyolojik olarak aktif bileşiklerle entegre edilebilir ve bu da terapötik potansiyelini artırır (25,26). Güncel yaklaşımlarda pulpal rejenerasyon ve antibakteriyel özelliği sağlamak için GeIMA hidrojel

kullanılmaktadır. Araştırmacılar, GelMA'ya sarılı DPSC'ler ve endotel hücreleri de dahil olmak üzere mezenkimal kök hücrelerin hem in vivo hem de in vitro olarak kılcal damar benzeri ağlara kendi kendine organize olabileceğini göstermiştir (27,28). Dubey ve ark. antimikrobiyal ve anti-anjiyojenik özelliklere sahip bir hidrojel sistemine öncülük etti. Çözünebilir lifli antibiyotik parçacıklarının GelMA hidrojeline dahil edilmesi üzerine, hücrelere karşı minimum sitotoksisite gözlemlendi. Polimer çözeltisine minosiklin (MINO) veya klindamisin (CLIN) eklenmesi, çözünebilir parçacıkların GelMA içinde değişen konsantrasyonlarda süspansiyon haline getirilmesiyle sonuçlandı ve daha sonra liflere elektroeğrildi. Tasarlanmış hidrojel, antibiyotiğe bağlı şişme ve parçalanabilirlik sergilemiş, bakteri büyümesini engellemiş ve diş pulpası kök hücrelerine karşı minimum toksisite göstermiştir. (29). Bunun yanında, rejeneratif endodonti uygulamalarında organoid teknolojisi de dikkat çeken bir diğer yaklaşımdır. Organoidler kök hücrelerden türetilen, kendi kendini organize edebilen ve organ yapısını taklit eden 3 boyutlu doku modelleridir. Dentin-pulpa kompleksiyle ilişkili organoidler, hücre etkileşimlerini incelemek ve malzeme testleri yapmak için geliştirilmiştir. Örneğin, Li ve arkadaşları tarafından oluşturulan apikal papilla organoidi modeli, SCAP hücrelerinin doku ile etkileşimini ve apikal papillanın in vivo yapısını başarılı bir şekilde taklit etmiştir. Bu organoidler, özellikle inflamatuar ortamlarda hücresel sinyal mekanizmalarını incelemek ve hastalık modelleri oluşturmak amacıyla kullanılmaktadır. Aynı zamanda, in vitro monokültür testleri ile in vivo hayvan deneyleri arasındaki boşluğu doldurabilecek alternatif bir sistem olarak da değerlendirilmektedir (30,31).

SONUÇ

Rejeneratif endodontik tedavi, kök gelişimini tamamlamamış nekrotik dişlerde doku yenilenmesini hedefleyen modern bir yaklaşımdır. Geleneksel tedavilere göre dişin canlılığını ve fonksiyonunu koruma potansiyeli daha yüksektir. Başarı, uygun dezenfeksiyon, biyouyumlu materyaller ve büyüme faktörlerinin doğru kullanımıyla mümkündür. Ancak, uzun dönem sonuçların değerlendirilmesi için daha fazla çalışmaya ihtiyaç vardır.

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BALANCE EVALUATION IN A PEDIATRIC PATIENT WITH MARFAN SYNDROME CASE STUDY

ABSTRACT

Marfan syndrome is an autosomal dominant connective tissue disorder characterized by multisystem involvement, particularly affecting the skeletal, cardiovascular, and ocular systems. Structural abnormalities such as scoliosis, joint hypermobility, and muscle weakness may negatively influence postural control and balance in pediatric patients. The aim of this case study is to evaluate both static and dynamic balance in a pediatric patient diagnosed with Marfan syndrome. A 10-year-old male patient diagnosed with Marfan syndrome presented with complaints of balance difficulty, particularly during walking and stair climbing. Physical examination revealed typical skeletal deformities including increased arm span-height ratio, pectus carinatum, scoliosis, and hypermobile joints. Balance assessment included static tests (Romberg, Tandem Romberg, single-leg stance) and dynamic tests (Timed Up and Go, line walking, Unterberger test), as well as the Pediatric Balance Scale. Results showed decreased balance performance, especially in tasks with reduced visual or proprioceptive input. The findings indicated that proprioceptive deficits, lower limb asymmetry, and trunk muscle weakness contributed to impaired postural stability. These features are commonly observed in Marfan syndrome and may increase the risk of falls in pediatric patients. The current evaluation supports the need for vestibular rehabilitation targeting proprioceptive input and balance strategies. Early and comprehensive balance assessment is essential for pediatric patients with Marfan syndrome to identify risks and improve functional mobility. Vestibular rehabilitation programs tailored to individual needs may enhance postural control and reduce fall risk, ultimately contributing to improved quality of life and independence in daily activities.

Keywords: Marfan syndrome; balance; pediatric; vestibular rehabilitation; proprioception

MARFAN SENDROMLU ÇOCUK HASTADA DENGE DEĞERLENDİRMESİ VAKA ÇALIŞMASI

ÖZET

Marfan sendromu, başta iskelet, kardiyovasküler ve oküler sistemleri etkileyen, multisistemik bulgularla seyreden otozomal dominant bir bağ dokusu hastalığıdır. Skolyoz, eklem hipermobilitesi ve kas zayıflığı gibi yapısal bozukluklar, pediatrik hastalarda postüral kontrol ve dengeyi olumsuz yönde etkileyebilir. Bu vaka çalışmasının amacı, Marfan sendromu tanısı almış bir çocuk hastada statik ve dinamik dengeyi değerlendirmektir. Marfan sendromu tanısı almış 10 yaşındaki erkek çocuk, özellikle yürüme ve merdiven çıkma sırasında denge kaybı şikayetleri ile başvurmuştur. Fizik muayenede artmış kol açıklığı-boy oranı, pektus karinatum, skolyoz ve hipermobil eklemler gibi tipik iskelet deformiteleri gözlemlenmiştir. Statik denge değerlendirmesinde Romberg, Tandem Romberg ve tek ayak üzerinde durma testleri; dinamik denge değerlendirmesinde ise Zamanlı Kalk Yürü Testi, çizgi üzerinde yürüme, Unterberger testi ve Pediatrik Denge Ölçeği kullanılmıştır. Sonuçlar, özellikle görsel ya da propriyoseptif girdinin azaltıldığı durumlarda denge performansının azaldığını göstermiştir. Bulgular, propriyoseptif yetersizlik, alt ekstremite asimetrisi ve gövde kas zayıflığının postüral stabiliteyi bozduğunu ortaya koymuştur. Bu özellikler, Marfan sendromunda sık görülen ve çocuk hastalarda düşme riskini artırabilecek durumlardır. Mevcut değerlendirme, propriyoseptif bilgi ve denge stratejilerini hedefleyen vestibüler rehabilitasyonun gerekliliğini desteklemektedir. Marfan sendromlu çocuk hastalarda erken ve kapsamlı denge değerlendirmesi, risklerin belirlenmesi ve fonksiyonel hareketliliğin artırılması açısından önem taşımaktadır. Bireye özel planlanan vestibüler rehabilitasyon programları, postüral kontrolü geliştirerek düşme riskini azaltabilir ve günlük yaşamda bağımsızlık ile yaşam kalitesini artırabilir.

Anahtar Kelimeler: Marfan sendromu; denge; pediatrik; vestibüler rehabilitasyon; propriosepsiyon

1. GİRİŞ

Marfan sendromu, bağ dokusunun genetik bir bozukluğu olarak birden fazla sistemi etkileyen tipik klinik bulgulara sahip kalıtsal, otozomal dominant bir hastalıktır (Monteleone vd., 2018). Nadir görülen bir durumdur, insidansı 10.000 kişide iki ila üçtür (Ammash vd., 2008; De Paepe vd., 1996) ve erkeklerde ve kadınlarda eşit olarak görülmektedir ("Centers for Disease Control" 2024; Coelho vd. 2020; Connolly vd., 2023; Salik & Rawla, 2023; Wright, 2025). Bağ dokusu proteini fibrilini kodlayan kromozom 15 üzerindeki FBN-1 gen mutasyonlarının bu hastalığa neden olduğu bilinmektedir (Dean, 2007; Dietz vd. 1991; Lidal vd., 2020). Bu proteindeki anormallikler, sayısız farklı klinik soruna neden olur (Lidal vd., 2020).

MFS'li hastalarda genellikle eklem hipermobilitesi, uzun boy, ince vücut habitasyonu, uzun uzuvlar, araknodaktili, skolyoz, lens ektopisi, aort kökü dilatasyonu ve mitral kapak sarkması görülür (Monteleone vd., 2018). MFS tanı kriterleri, klinik bulguları, aile öyküsünü ve moleküler tanıyı birleştiren Ghent nozolojisine dayanmaktadır (Edouard vd., 2024; Loeys vd., 2010). Yetişkin hastalarda MFS tanısı revize edilmiş Ghent kriterlerine göre konur (Loeys vd., 2010), ancak semptomların yaşa bağlı olarak ortaya çıkması nedeniyle çocuk hastalarda tanı koymak o kadar kolay değildir (Mueller vd., 2013). Klasik semptomlar ve bulgular genellikle yaş ilerledikçe gelişir. (Lidal vd., 2020) MFS'li hastaların yaklaşık %75'i etkilenmiş bir ebeveyne sahiptir ve kalan %25'inde de novo mutasyonlar vardır (Dietz, 2001).

Marfan Sendromunda tanı büyük ölçüde kliniktir ve temel olarak üç ana sistemi etkileyen kardinal özelliklerle karakterize edilir. Bunlar:

• İskelet sistemi

• Oküler sistem

• Kardiyovasküler sistemdir

MFS, ince habituslu uzun boy ve uzun ince parmakları (araknodaktili) içeren kardinal iskelet özellikleri ile karakterizedir ve en yaygın iskelet tezahürü, hastaların en az %60'ında görülen skolyozdur (Pyeritz & Francke, 1993). Aksiyel iskelet, MFS'de iskelet sisteminin en sık etkilenen bölümüdür (Harshavardhana & Noordeen, 2016). Diğer yaygın özellikler arasında alışılmadık derecede esnek eklemler, uzun ve dar bir yüz, yüksek kemerli bir ağız çatısı, kalabalık dişler ve çökük (pektus ekskavatum) veya çıkıntılı bir göğüs (pektus karinatum) bulunur. (Parker, 2007)

MFS'de, diğer bağ dokusu hastalıklarında olduğu gibi (Galli vd., 2011), eklem hipermobilitesi ve hafif miyopati (Voermans vd., 2009) hatalı refleks modellerine katkıda bulunabilir (Røgind vd., 2003). Postüral kinematik zincirdeki gevşekliğe ek olarak eklem reseptörlerinden gelen hatalı proprioseptif bilgi, postüral kontrolde bozulmaya neden olabilir (Monteleone vd., 2018). Bunlar, postüral kontrol ve denge üzerinde direkt etkili olabilecek unsurladır. Çocuklarda bu yapısal değişiklikler, özellikle denge ve hareket kontrolünü olumsuz etkileyerek vestibüler sistemle ilişkili işlevleri zayıflatabilir. Vestibüler sistemin temel görevi, denge, göz hareketleri ve baş pozisyonunun kontrolünü sağlamaktır. Marfan sendromlu çocuklarda sık gözlenen skolyoz, kas zayıflığı ve proprioseptif bozulmalar vestibüler sistemin refleks kontrol mekanizmaları üzerinde dolaylı etkilere yol açabilir.

Vestibülo-oküler refleks (VOR) bozulduğunda sabit görme zorlaşır; vestibülo-spinal refleks zayıfladığında ise düşme riski artar (Herdman & Clendaniel, 2014).

Bu nedenle, genetik olarak tanısı konmuş Marfan Sendromlu 10 yaşında erkek hastada hem statik hem de dinamik denge analiz edilmiştir. MFS'li hastanın hem sakin duruşta hem de yetersiz bir destek tabanının yarattığı zor koşullarda ayakta denge kontrolünün düşük olacağı düşünülmüştür. Gözlerin kapalı olduğu testlerde, yetersiz propriyoseptif bilgi sebebiyle ayakta durma kapasitesini daha da düşüreceği beklenmiştir.

2. VAKA RAPORU

10 yaşında bir erkek çocuk hastanın, erken çocukluğundan beri yürüme ve dengeyi korumada zorluk şikayetleriyle birlikte anormal derecede eğri bir omurga ve çeşitli kardiyovasküler sistem problemleri 2 yıl önce tanısı konulmuş Marfan Sendromu ile ilişkilendirilmiştir. Hastanın tıbbi öyküsünde çarpıntı, göğüste ağrı veya solunum sıkıntısı, otonomik disfonksiyon belirtisi yoktur. Aile öyküsünde benzer belirtiler ve genetik bozukluk yoktur. Fiziki muayenede, hastada uzun/ince vücut yapısı, uzun kollar ve bacaklar, vücut boyunu aşan kol açıklığı, uzun parmaklar, esnek eklemler, uzun/dar yüz, çıkıntılı yapıda göğüs kemiği ve omurga eğriliği gibi kas-iskelet sistemi deformiteleri olan bir yapı vardır.

Mevcut hastalığın öyküsünde hastanın ailesi çıkıntılı göğüs kemiğinin çok belirgin olmadığını, nefes darlığı veya çarpıntı gibi şikayetlerin yaşanmadığını belirtmiş ancak yürüyüş veya merdiven çıkma esnasında denge kaybı yaşadığı ve bazı sportif faaliyetlerde zorlandığı için vestibüler değerlendirmeyi uygun gördüklerini belirtmiştir.

Fiziksel muayenede genel durumu iyi gözlemlenmiştir. Kol açıklığı/boy oranı: 1.08, bacak uzunluğu farkı 1,3 cm (sağ>sol), vücut kitle indeksi: 17,4 tespit edilen hastanın hareketliliği dinamik denge testlerini uygulamaya elverişlidir.

2.1. Değerlendirme Parametreleri ve Bulgular

Marfan sendromlu çocuklar için özel olarak geliştirilmiş bir denge değerlendirme aracı bulunmamaktadır. Bu nedenle hasta, vestibüler değerlendirmede yaygın olarak kullanılan statik ve dinamik denge testleri ile Pediatrik Denge Ölçeği kullanılarak değerlendirilmiştir. Ancak bu testlerin Marfan sendromlu çocuklar için geçerliliği veya güvenilirliği üzerine herhangi bir çalışma bulunmamaktadır. Testlere başlamadan önce hastanın düz bir zeminde, normal yürüme hızı ile 10 m mesafeyi yürüme süresi sn cinsinden belirlenmiştir.

Statik denge testleri: Romberg testi, Tandem Romberg testi ve Tek ayak üzerinde durma testi.

Romberg testinde hastadan düz zeminde kolları her iki yanda serbest, ayakları omuz hizasınca açılmış dik bir duruşla ayakta durması istenmiştir. Desteksiz hastanın, gözler açık ve kapalı pozisyonda Romberg testi pozitif (+) gözlemlenmiştir. Tandem Romberg testinde hastadan bir ayak topuğu diğer ayak parmaklarına değecek biçimde 60 sn tandem duruşta gözler açık pozisyonda 25 sn ve gözler kapalı pozisyonda 23 sn ayakta durduğu gözlemlenmiştir. Tek ayak üstünde durma testinde hastadan bir dizini diz kapağından 90° içe bükerek tek ayağı üzerinde durması istenmiştir. Hastanın her iyi ayağı için de ayrı ayrı ölçüm yapılmış, gözler açık pozisyonda süre her iki ayak için de 30 sn ve gözler kapalı

pozisyonda süre sağ ayak üzerinde durma testinde 18 sn, sol ayak üzerinde durma testinde 20 sn olarak kaydedilmiştir.

Dinamik denge testleri: Zamanlı kalk yürü testi, Tek çizgi üzerinde yürüme testi, Unterberger testi.

Zamanlı kalk yürü testinde hastanın oturacağı banka 3 m uzaklıkta bir hedef belirlenmiştir. Hastadan, banktan kalkıp 3 m yürümesi ve geri dönüp tekrar banka oturması istenmiş ve testi tamamlama süresi 9 sn olarak kaydedilmiştir. Tek çizgi üzerinde yürüme testinde hastanın normal yürüme hızının belirlendiği 10 m mesafede, önce gözleri açık sonra gözleri kapalı pozisyonda yürümesi belirtilmiş ve hasta tek çizgi üzerinde yürürken izlenerek, sağ ve sol yöne sapmaları tespit edilmiştir. Unterberger testinde ise hastadan gözleri kapalı pozisyonda kollarını öne doğru uzatarak bulunduğu yerde adım atması istenmiş ve herhangi bir yöne sapma gözlenmemiştir.

Fonksiyonel Değerlendirme: Pediatrik Denge Ölçeği

Son olarak dengeyi değerlendirmek ve düşme riskini belirlemek için hastaya Pediatrik Denge Ölçeği uygulanmıştır. Ölçek toplamda 14 bölümden oluşan ve dengeyi fonksiyonel olarak değerlendiren bir ölçektir (Franjoine vd., 2003). Bu ölçek günlük hareketler esnasında sabit durumdan farklı pozisyona geçme ve dik durma durumunda dengeyi zorlayabilecek manevraları içeren fonksiyonel bir değerlendirmedir. Her bir soru için 0-4 arası puan verilmektedir. Test sonunda hastanın aldığı toplam puan hesaplanmaktadır (Franjoine vd., 2003; Horak, 1987). Testin toplam puanı 56 ve test süresi 20 dakikadır (Usta, 2011). Hastanın ölçek değerlendirmesi sonucu, skoru 44 olarak kaydedilmiştir.

2.2. Değerlendirme ve Yorum

Hastanın dinamik denge testlerinde yaşına göre düşük performans sergilediği görülmüştür. Özellikle hastanın iki bacak uzunlukları arasındaki fark alt ekstremite denge kontrolü açısından önemli bir risktir. Hipermobilite ve gövde kaslarındaki zayıflık, özellikle yürüyüş esnasında dengesizliğe sebep olmaktadır. Elde edilen bulgular, gövde ve alt ekstremite stabilitesindeki zayıflıkla birlikte proprioseptif farkındalığın azaldığını ve hipermobilitenin de bu tabloyu derinleştirdiğini göstermektedir.

2.3. Müdahale Önerileri

Marfan sendromlu çocuk hastalarda sendromun denge ve propriosepsiyon üzerindeki olumsuz etkilerini en aza indirmekle beraber, vücut koordinasyonunu düzenlemek ve günlük yaşamda daha güvenli hareket etmeyi sağlamak için vestibüler rehabilitasyon önerilmektedir. Vestibüler rehabilitasyonun temel hedefleri şunlardır:

• Vestibülo-oküler refleksin iyileştirilmesi

• Postüral stabilitenin artırılması

• Propriosepsiyon ve denge stratejilerinin güçlendirilmesi

• Fonksiyonel mobilite ve güvenli hareket kapasitesinin artırılması

2.3.1. Rehabilitasyon Yaklaşımları

a. Göz-Baş Koordinasyonu Egzersizleri

• VOR x1 ve x2 egzersizleri: Sabit hedefe odaklanarak baş hareket ettirme

• Takip ve sakkadik göz hareketleri: Gözle hedef takibi, hızlı odak değiştirme

b. Postüral Denge Egzersizleri

• Köpük yüzey üzerinde durma

• Tek ayak ve tandem duruş

• Gözler kapalı denge egzersizleri

c. Fonksiyonel Vestibülo-Spinal Aktiviteler

• Baş hareketleri eşliğinde yürüyüş

• Engel aşmalı denge yürüyüşleri

• Dairesel yön değiştirmelerle dur-kalk çalışmaları

d. Oyun Temelli Vestibüler Uyarım

• Salıncak, top oyunları, göz kapalı yön bulma aktiviteleri

• Sanal gerçeklik tabanlı denge uygulamaları (eğer olanak varsa)

Bu egzersizler, haftada 2–3 kez, bireyin toleransına uygun şekilde 6–8 haftalık bir program dahilinde uygulanabilir.

3. TARTIŞMA

Marfan sendromu, yalnızca sistemik semptomları olmayan, aynı zamanda bireyin görünümünü ve hayat kalitesini de etkileyen bir durumdur (Rudagi vd., 2020). Bugüne kadar daha az dikkat çekmiş olan MFS'nin kas-iskelet belirtileri de hayat kalitesi üzerinde önemli bir etkiye sahip olabilir ve MFS popülasyonunun yaşı arttıkça daha önemli hale gelmesi muhtemeldir. MFS'nin kas-iskelet sistemi komplikasyonlarının göz ardı edilen ancak önemli bir etkisi de günlük işlevselliktir (Lidal vd., 2020).

Literatürde, Marfan sendromlu bireylerde denge bozuklukları üzerine doğrudan odaklanan sınırlı sayıda çalışma bulunmaktadır. Özellikle çocuk hasta grubunu değerlendiren nicel çalışmalara pek rastlanmamıştır. Bu durum, çocuk hastaların denge problemlerinin değerlendirilmesinde klinik karar vermeyi zorlaştırmaktadır. Bozok Üniversitesi'nde yapılan bir vaka sunumunda, Marfan sendromlu bir bireyde denge, yürüme ve düşme korkusu değerlendirilmiş, bireyin düşme riski taşıdığı ve yürüme performansının kısıtlı olduğu belirtilmiştir (Çopur & Yıldız, 2022). Benzer şekilde, Hacettepe Üniversitesi kaynaklı bir başka çalışmada, benzer bulgulara yer verilmiş ve fizyoterapi uygulamaları ile sürecin yönetimi anlatılmıştır (İnce & Aras, 2023). Bir diğer çalışmada, postürografi kullanılarak Marfan sendromlu bir basketbol oyuncusunun postüral stabilitesi

değerlendirilmiş ve bireyin yüksek düşme riski taşıdığı tespit edilmiştir. Çalışmada, bağ dokusu zayıflığının dengeyi olumsuz etkileyebileceği vurgulanmıştır (Bozgeyikli, 2021).

Yadao ve arkadaşları (2024) tarafından yapılan bir çalışmada, Marfan sendromunun klinik özelliklerini ve çocuklarda ortaya çıkan iskelet anormalliklerinin denge üzerindeki etkilerini incelemiştir. Bu çalışma, Marfan sendromlu çocukların denge değerlendirmesinde dikkate alınması gereken önemli bulgular ile birlikte rehabilitasyon, egzersiz ve ortopedik müdahaleleri kapsayan kas-iskelet sistemi yönetiminin Marfan sendromlu çocuk hastalar için oldukça gerekli olduğunu gözler önüne sermektedir. Bir başka çalışmada ise Severijns ve arkadaşları (2019), dinamik denge kontrolünün 3D spinal hizalanma ile ilişkisini araştırmış ve Marfan sendromu gibi spinal deformitelerin denge kapasitesi üzerindeki etkilerini değerlendirmiştir. Ancak mevcut değerlendirme yöntemlerinin yetersizlikleri olabileceğinden Marfan sendromlu hastalar gibi kas-iskelet deformitesi olan bireylere özgü bir denge ölçeği geliştirmeye olan ihtiyacı gündeme getirmektedir.

Marfan sendromunun yönetimi karmaşıktır ve birden fazla organ sistemini etkileyen çeşitli klinik belirtileri ele almak için multidisipliner bir yaklaşım gerektirir (Yadao vd., 2024). Kas-iskelet yönetimi, Marfan sendromunda yaygın olan skolyoz, eklem hipermobilitesi ve pektus deformiteleri gibi ortopedik komplikasyonların yönetilmesini içerir. Fizik tedavi ve düzenli egzersiz, kas-iskelet sistemi fonksiyonunu iyileştirmek ve komplikasyonları önlemek için çok önemlidir. İskelet gelişimini izlemek ve gerektiğinde müdahale etmek için düzenli ortopedik takip esastır (Yadao vd., 2024).

4. SONUÇ

Marfan sendromlu çocuk hastalarda postüral instabilite ve düşme riski gibi önemli sorunlarla beraber vestibüler sistemin de etkilenmesi sık görülebilir. Bu nedenle, bu hasta grubuna özel denge değerlendirme çalışmalarının yapılması hem tanı hem de rehabilitasyon süreci açısından büyük önem taşımaktadır. Bu hastalarda, dinamik denge testleri aracılığıyla denge bozukluklarının erken dönemde tespiti mümkündür. Dinamik denge değerlendirmeleri, bu popülasyonda standart bir yaklaşım haline getirilmelidir. Bu bireylerde vestibüler rehabilitasyon hem denge kontrolünü iyileştirmek hem de düşme riskini azaltmak için önemli bir terapi yöntemidir. Marfan sendromlu çocuk hastalarda denge değerlendirmesi rutine alınmalı, bireye özel rehabilitasyon planları oluşturulmalıdır. Bu popülasyonda fonksiyonel ve oyun temelli yaklaşımlar ile desteklenen bireysel programlar, çocuk hastanın yaşam kalitesini ve bağımsızlığını artırabilir.

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ANTIFUNGAL PROPERTIES OF *Eruca vesicaria* FLOWER ESSENTIAL OIL AGAINST NON-*albicans Candida* SPECIES USING RESAZURIN-BASED DILUTION METHOD

ABSTRACT

Aim: Infection caused by *Candida* species affects the cutaneous layer and mucous membrane, causing infections in the mouth, skin, vagina, and intestines. Non-*albicans Candida* species account for 35-65% of all fungal diseases, and this rate is increasing year by year. In addition, treating diseases caused by *Candida* is complex and time-consuming, and creates a severe economic burden. Therefore, there has been an increase in the tendency towards natural alternative sources that can be used to treat fungal diseases. *Eruca vesicaria* belongs to the Brassicaceae family and is used as a part of the human diet in the Mediterranean region. Its pharmacological properties have attracted the attention of scientists. Therefore, this study examined the antifungal activity of *E. vesicaria* against non-*albicans Candida* species.

Material and Method: In this study, the essential oil of *E. vesicaria* flowers was obtained by the hydrodistillation method. The antifungal activity of the essential oil of *E. vesicaria* flowers against non-*albicans Candida* species was tested using the resazurin-based broth microdilution method. Minimum inhibitory concentrations (MICs) of *E. vesicaria* against the tested strains (*Candida parapsilosis, Candida krusei* and *Candida glabrata*) were determined separately.

Results: Due to the hydrodistillation, 4.5 µl of essential oil was obtained, and the essential oil yield was determined as 9.76% µL/g. The antifungal activity test showed that the flower essential oil had an MIC value of 0.187 µL/mL against *C. parapsilosis* and *C. glabrata* and 0.375 µL/mL against *C. krusei*.

Conclusion: This preliminary study with the essential oil of *E. vesicaria* flowers has proven that the essential oil is effective against some important non-*albicans Candida* species. These species are difficult to treat in the clinic and have recently developed serious drug resistance. Therefore, it will be useful from a pharmaceutical point of view to examine this essential oil obtained from the plant flower in more detail and in advance as an important antifungal agent in future studies.

Keywords: *Eruca vesicaria,* non-*albicans Candida* species, antifungal activity, broth dilution

INTRODUCTION

Infections caused by *Candida* species affect the cutaneous layer and mucous membranes that provide suitable conditions for growth and cause infections in the mouth, skin, vagina and intestines. Non-*albicans Candida* species account for 35-65% of all fungal diseases. They are more common in cancer patients, patients with hematological malignancies and bone marrow transplant patients with a rate of 40-70%, while they are less common in intensive care and surgical patients with a rate of 35-55%, in children with a rate of 1-35% and in HIV-positive patients with a rate of 0-33% (Krcmery & Barnes, 2002). The rate of non-*albicans Candida* species among *Candida* species causing fungal diseases is increasing yearly. In the two decades up to 1990, non-*albicans Candida* species caused 10-40% of all fungal diseases, while between 1991 and 1998, non-*albicans Candida* species caused 35-65% of all fungal diseases. The most common non-*albicans Candida* species are *Candida parapsilosis* with 20-40%, *Candida tropicalis* with 10-30%, *Candida krusei* with 10-35%, and *Candida glabrata* with 5-40%. Other non-*albicans Candida* species cause less than 1% of fungal diseases in humans (Pappas et al., 2016; Pappas et al., 2009). The mortality rate due to non-*albicans Candida* species is between 15% and 35%, which is close to the mortality rate (20-40%) due to *Candida albicans* (Krcmery & Barnes, 2002).

Candidal infection causes include broad-spectrum antibiotic use, birth control pills and oral corticosteroids, cancer treatments, diabetes, and a weak immune system. A cohort study found that non-*albicans Candida* infections were unaffected by recent antibiotic use, diabetes, and probiotic use (Tressler et al., 2018). In addition, vaginal candidiasis caused by non-*albicans Candida* can be more challenging to treat and usually requires more aggressive treatment (Fong, 1996; Deorukhkar et al., 2014).

For all the reasons listed above, scientists are investigating the use of natural resources in the treatment of infections caused by nan-*albican Candida*. *Eruca vesicaria* is a plant that detailed pharmacological studies have evaluated, and its effectiveness has been proven (Hichri et al., 2019; Omri Hichri et al., 2016). *E. vesicaria* flower essential oil, which was observed as an effective pharmacological compound in this study, has been proven to have antifungal activity against non-*albicans Candida* species that are difficult to treat in the clinic. At the same time, the MIC values of the flower essential oil were determined separately for each *Candida* species.

MATERIAL AND METHOD

Extraction of the Plant Flowers' Essential Oil

The flowers of the *E. vesicaria* were cultivated and collected in Malatya (Turkiye) (38°19'00.3" N 38°16'58.9" E), dried in a cool place in the shade, and cut into small pieces for essential oil extraction (Figure 1). The hydrodistillation method was used to obtain the essential oil. Essential oil was obtained from a 46.1100 g sample by hydrodistillation using a Clevenger apparatus for at least three hours. The essential oil yield was calculated volumetrically by Clevenger's graduated column.



Figure 1. *Eruca vesicaria* flowers

Media and Strains

Sabouraud dextrose agar was used for subculture of *Candida* strains, and Sabouraud dextrose broth (Merck K GaA- Germany) was used for resazurin-based broth microdilution method to observe the inhibitory effect of *E. vesicaria* flower essential oil against non-*albicans Candida* strains. *Candida parapsilosis* ATCC 22019, *Candida krusei* ATCC 14243, and *Candida glabrata* ATCC 90030 were purchased from the American Type Culture Collection.

Antifungal activity assay against non-*albicans Candida*

The antifungal activity of *E. vesicaria* flower essential oil against non-*albicans Candida* species was tested using the resazurin-based broth microdilution method (Unver & Gurhan 2024a and 2024b). For this purpose, 96-well microplates were used. 4.5 µL of essential oil obtained from plant flowers was dissolved in 150 µL of Dimethyl Sulfoxide (DMSO). Then, 50 µL of DMSO suspension containing plant essential oil was added to the first wells of the microplate to complete the first well to 200 µL. 100 µL of Sabouraud broth was added to the subsequent microplate wells to make a two-fold dilution starting from the first well. Therefore, the concentration of flower essential oil from the first well to the tenth well varied between 0.75 µL and 0.001 µL. Standard inocula were created for each *Candida* species, and their turbidities were adjusted to 0.5 McFarland standard ($1x10^6$ cfu/mL). Then, 1 µl of *Candida parapsilosis, Candida krusei,* and *Candida glabrata* were inoculated into rows A, B, and C of the microplates, respectively. Then, the microplate was left for overnight incubation at 37°C. The next day, 15 µl of 0.15% Resazurin was added to each well. It was kept in the oven at 37°C for 3 hours, and the growth of *Candida* species was evaluated by observing the color change.

RESULTS

Yield of Essential Oil

Hydrodistillation yielded 4.5 µl of turbid white essential oil. Essential oil yield was determined to be 9.76% µL/g.

Results of Antifungal Activity against non-*albicans Candida*

The MIC values are determined as the essential oil concentration at which the lowest amount of plant essential oil is used, which does not show any color change on the microplate. Resazurin was added after 24 hours of incubation. Pink indicates growth, while blue indicates inhibition of growth. As a result of this study, the minimum inhibitory concentration (MIC) value of flower essential oil was determined as 0.187 µL/mL against *C. parapsilosis* and *C. glabrata*, and 0.375 µL/mL against *C. krusei* (Figure 2, Table 1). 11A, B, and C are controls expressing the viability of non-*albicans Candida* yeast species used in antifungal activity. 12A, B, and C are controls confirming the absence of any contamination during microplate preparation.



Figure 2. Microplate image of Antifungal activity test of *Eruca vesicaria* flower essential oil using resazurin-based broth microdilution. The flower essential oil concentrations in wells A3 (0.187 µL/mL), B2 (0.375 µL/mL) and C3 (0.187 µL/mL), which did not show any color change, were accepted as MIC values for *C. parapsilosis*, *C. krusei* and *C. glabrata* in these wells, respectively.

Table 1. Minimum Inhibitory Concentrations (MIC) of *Eruca vesicaria* flower essential oil

Microorganisms	**MICs (µL/mL**
C. parapsilosis	0.187
C. krusei	0.375
C. glabrata	0.187

DISCUSSION AND CONCLUSION

The mortality rate of non-*albicans Candida* species is highest in intensive care and surgical patients; it is lower in children, cancer patients, and HIV positive patients. There are several risk factors for non-*albicans Candida* species to cause infection. These risk factors are related to foreign body placement, neonates and hyperalimentation for *C. parapsilosis*, azole prophylaxis for *C. krusei*, neutropenia and bone marrow transplantation for *C. tropicalis*, and azole prophylaxis, surgery, vascular and urinary catheters for *C. glabrata*. Some non-*albicans Candida* species are naturally or secondarily resistant to fluconazole. 75% of *C. krusei* strains, 35% of *C. glabrata*, and 10-25% of *C. tropicalis* strains resist this resistance. Amphotericin B resistance is also seen in 10-15% of *C. krusei*. Other non-*albicans Candida* species, *C. parapsilosis* and *C. tropicalis*, are sensitive to both azoles and polyenes, like *C. albicans*. Therefore, antifungal treatment specific to the species detected for fungal infections is applied (Krcmery & Barnes, 2002). This situation shows that over the years, *Candida* species can develop resistance to the antifungal chemicals used in infections caused by *Candida* species. This is where the use of herbal sources that are found in nature and are easily accessible is of vital importance as side-effect-free and natural agents.

In this study, the most sensitive yeast species to *E. vesicaria* flower essential oil were found to be *C. parapsilosis* and *C. glabrata* with MIC value of 0.187 mg/mL. These two species were followed by *C. krusei* with the MIC value of 0.375 mg/mL. *C. parapsilosis* is associated with endocarditis in intravenous narcotic addicts. In studies, *C. parapsilosis* has been observed as an important hospital pathogen with clinical symptoms such as fungemia, endocarditis, endophthalmitis, and septic arthritis, all of which usually occur in association with invasive procedures or prosthetic devices. Therefore, *C. parapsilosis* infection outbreaks have occurred as a result of contamination of intravascular pressure monitoring devices and routine solutions administered to patients in the clinic. Although experimental studies generally show that *C. parapsilosis* is less lethal than *C. albicans* or *C. tropicalis*, the rapid spread of *C. parapsilosis* in hospital environments, its frequent colonization of the skin, its ability to grow especially in solutions containing glucose, and its ability to adhere to synthetic materials increase the intensity of *C. parapsilosis* infections (Weems Jr, 1992). This study found that the inhibitory effect of *E. vesicaria* flower essential oil was most effective on *C. parapsilosis* and *C. glabrata*. Therefore, it can be considered that the plant flower oil can be used as a potential agent, especially in preventing hospital-acquired infections.

C. krusei is well known as a fungal pathogen that causes infections in patients with hematological malignancies and transplant recipients. Several studies have reported *C. krusei* as a potentially multidrug-resistant fungal pathogen due to reduced susceptibility to both flucytosine and amphotericin B, as well as resistance to fluconazole (Drago et al., 2004; Abbas et al., 2000; Abi-Said et al., 1997). Some studies reported superinfections due to *C. krusei* in patients receiving fluconazole or amphotericin B (Abbas et al., 2000; Majoros et al., 2006). In addition, amphotericin B exhibits significantly delayed killing kinetics against *C. krusei* compared to *C. albicans* (Majoros et al., 2006). The multidrug resistance phenotype exhibited by *C. krusei* poses a therapeutic dilemma, especially when considering treatment options for neutropenic and critically ill patients, especially for patients previously exposed to fluconazole (Pfaller et al., 2008). In addition, the high efficacy of *E. vesicaria* flower essential oil against *C. krusei* in our study can be detailed in future studies as a factor that may facilitate the treatment of the infection caused by this multidrug-resistant microorganism.

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EXAMINATION OF POTENTIAL HEALTH RISKS OF SOCIAL MEDIA USE IN CHILDREN AND ADOLESCENTS

ABSTRACT

Objective: This review study was conducted to examine the potential health risks of social media use in children and adolescents.

Materials and Methods: In this study, a literature review was conducted using the keywords "children, adolescent, social media use, sleep, loneliness, depression, mental health" and their Turkish equivalents. The databases searched included Google Scholar, PubMed, ScienceDirect, Web of Science, Wiley, Taylor & Francis and JMIR Publications. Articles published between 2020 and 2025, written in English or Turkish, and available in full text, were included.

Results: Research has shown that social media use is significantly associated with psychological issues such as difficulty falling asleep, loneliness, depression, and anxiety in adolescents. Problematic social media use, in particular, negatively affects sleep quality and increases feelings of loneliness in both male and female adolescents. The effects of different social media platforms vary; for instance, prolonged use of Instagram has been linked to increased loneliness, while Twitter has been associated with lower levels of loneliness but higher levels of anger. Moreover, self-compassion has been found to mitigate the negative effects of social media use, and physical activity has been shown to play a mediating role in reducing symptoms of depression and anxiety. These findings indicate that the psychosocial outcomes of social media use may vary depending on the platform, duration of use, individual characteristics, and gender.

Conclusion: In conclusion, the study findings reveal that social media use in children and adolescents has significant effects on psychosocial variables such as sleep quality, loneliness, depression, and anxiety, depending on the platform and manner of use. Particularly, problematic and intensive social media use is strongly associated with difficulty falling asleep and feelings of loneliness. Accordingly, it is recommended to develop psycho-educational programs that raise awareness about social media use at an early age and to enhance digital literacy.

Keywords: Children, Adolescent, Social Media Use, Sleep, Depression, Nursing

1. INTRODUCTION

Over the past decade, social media usage has had a profound impact on individuals' daily lives and social behaviors. Initially limited to content sharing, social media platforms have gradually become more interactive, offering users opportunities to receive feedback, join online communities, and present their digital identities.[1] The global prevalence of social media, particularly among children and adolescents, has raised concerns about potential health risks. As of 2022, there were 4.59 billion social media users worldwide, and individuals reportedly spent an average of 151 minutes per day on these platforms.[2] This level of usage has heightened international concerns regarding negative effects such as social media addiction and social isolation.[3]

Adolescence is a critical phase in individuals' psychological and social development, during which the risks associated with social media usage are strongly felt. According to a report by the World Health Organization (2020),[4] 7% of adolescents reported problematic social media use, while 35% were classified as heavy online users. A study conducted in Europe found that more than 80% of European youth actively used the internet daily to access social networks.[5] Similarly, a study in North America revealed that more than 35% of young people consistently used at least one social media platform, 36% believed they spent too much time on social media, and 54% stated that it would be difficult for them to give it up.[6]

Children and adolescents, in particular, are a vulnerable group to the mental, physical, and social effects of social media.[7] Adolescence is a developmental period during which individuals are more prone to psychological disorders. Social media content has the potential to trigger this vulnerability. Among adolescent girls especially, psychological concepts such as body image, appearance-related self-esteem, and self-worth may be negatively affected by social media interactions.[8–9] The idealized body image promoted by social media influencers can lead to psychosocial problems such as low self-esteem, eating disorders, and anxiety.[10] Additionally, frequent use of digital devices has been associated with negative effects like attention deficit and decreased academic performance.[11–12]

One of the most commonly reported risks of social media use is psychological problems. These include factors such as depression, anxiety, addiction, sleep disorders, cyberbullying, and social isolation.[13] Furthermore, the spread of unhealthy eating habits through social media can pose a threat to adolescents' physical health.[14] These effects develop in interaction with individuals' neurobiological structures and social environments, making the impact of social media multidimensional.[1]

In this context, multi-layered interventions are recommended to mitigate the potential health risks associated with social media use. Strategies such as parental supervision, digital literacy education, screen time guidelines, and age-appropriate platform usage can help children and adolescents maintain a safer presence in digital environments.[3,11,15] Therefore, identifying the negative effects of social media use and developing effective strategies to mitigate these effects is essential for protecting and promoting the health of children and adolescents. For these reasons, the aim of this study is to systematically evaluate the potential health risks of social media use among children and adolescents and to examine the mental, physical, and social effects that may arise from such use.

2. MATERIALS AND METHODS

In this study, a literature review was conducted using the keywords “children, adolescent, social media use, sleep, loneliness, depression, mental health” and their Turkish equivalents. The databases searched included Google Scholar, PubMed, ScienceDirect, Web of Science, Wiley, Taylor & Francis and JMIR Publications. Articles published between 2020 and 2025, written in English or Turkish, and available in full text, were included.

3. RESULTS

A study aimed to examine the relationship between technology and social media use—including platforms like Facebook and YouTube—and difficulties in falling asleep among adolescents aged 11–15. Overall, 34.3% (1081/3151) of adolescents reported having trouble falling asleep, with this rate being 29.7% (483/1625) in boys and 39.2% (598/1526) in girls. Difficulties in falling asleep were reported by 30.3% (356/1176) of 11-year-olds, 36.2% (389/1074) of 13-year-olds, and 37.3% (336/901) of 15-year-olds. Sleep difficulties were more frequently observed in adolescents who used electronic devices more intensively. The study found a significant association between screen-based device use and online social media exposure with sleep onset problems in adolescents.[16]

In another study investigating the use of different social media platforms among female adolescents (16–19 years) and its relation to anxiety, sleep, and loneliness, it was found that users with Social Media Disorder (SMD) reported higher levels of loneliness and, on average, slept less, especially on weekdays, compared to those without SMD. Unlike general usage, the frequency of posting on Facebook was associated with poorer sleep quality. These preliminary findings suggest that SMD may relate to mental health and sleep differently depending on the platform and type of use.[17]

A study conducted among Malaysian adolescents (aged 13–21) examining the level of social media addiction and its relationship with depression found that 72.0% of the 384 participants had high levels of social media addiction, and 33.0% had depression. A significant but weak positive correlation was identified between social media addiction and depression. The levels of addiction and depression were found to vary by age group, gender, ethnicity, and time spent on social media. These findings reflect the need to take measures against excessive social media use among adolescents.[18]

Another study involving children (average age: 9.83±1.23) showed that self-esteem mediated the relationship between the use of social networking sites (Facebook, Instagram, Twitter, WeChat Moments, Qzone, Sina Microblogs) and depression, while self-compassion played a moderating role in this process. It was reported that high self-compassion reduced the negative effects of social media use, whereas low self-compassion increased them.[19]

A large-scale study involving 212,613 adolescents (aged 11–15) from 40 countries in Europe and North America examined the relationship between intense and problematic social media use (SMU) and difficulties in falling asleep. Sleep onset difficulties were more prevalent among girls (27.1%) compared to boys (20.8%). Intense SMU was significantly associated with sleep problems in boys from 17 countries and in girls from 25 countries. Overall, only problematic SMU exposure was strongly associated with difficulties in falling asleep in both girls (OR 2.20, 2.04–2.38) and boys (OR 1.88, 1.73–2.04). The intensity of social media use was found to be similar between genders (Girls: OR 1.27, 1.23–1.31; Boys: OR 1.22, 1.18–1.27).[20]

In a study assessing the relationship between the use of social media platforms and sleep quality, the most commonly used platforms were reported to be TikTok (80%), Snapchat (77.9%), Instagram (63.8%), and YouTube (58.8%). In terms of sleep quality, 34.7% (333/961) of students were classified as poor sleepers. TikTok use, hours spent on social media, and the presence of moderate to severe depressive symptoms were identified as significant and independent predictors of poor sleep.[21]

Another study examining the relationship between social media use and symptoms of depression and anxiety in adolescents (aged 12–17), with physical activity considered as a mediator, found that social media use was associated with more depressive symptoms, anxiety, and loneliness, even when age and gender were controlled. After controlling for social media use and other extracurricular activities, physical activity was found to reduce symptoms of depression and anxiety. Additionally, significant gender differences in symptoms were observed; girls reported higher social media use, while boys had higher rates of depression. Nonbinary and transgender individuals showed higher levels of depression, anxiety, and loneliness compared to male and female adolescents in the sample.[22]

A school-based study examining the prospective relationships between adolescents' (average age: 14.3) emotional responses to social media experiences and depressive symptoms, also considered gender differences in these processes. High levels of depressive symptoms were associated with more frequent negative emotional responses to social media experiences one year later. Conversely, more positive emotional responses were linked to lower levels of depressive symptoms in the future. Overall, girls reported more intense emotional reactions to social media experiences, but gender did not moderate the relationship between emotional responses and depressive symptoms.[23]

According to a study conducted with adolescents (aged 13–18) living in Turkey, which aimed to determine the relationship between social media use and levels of loneliness and anger, no significant relationship was found between Facebook use or duration and loneliness scores. However, adolescents who used Instagram for extended periods had statistically higher loneliness scores, although their anger scores remained similar. Twitter users were found to have lower loneliness scores but higher anger scores. No significant relationship was found between TikTok use and loneliness scores.[24]

4. CONCLUSION

In conclusion, the study findings reveal that social media use among adolescents has significant effects on psychosocial variables such as sleep quality, loneliness, depression, and anxiety, depending on the platform and type of usage. In particular, problematic and intensive social media use is strongly associated with difficulties in falling asleep and feelings of loneliness. In this context, it is recommended to develop psycho-educational programs that raise awareness about social media use from an early age and to enhance digital literacy. Within this framework, nurses working in primary healthcare services can play a guiding role in promoting healthy digital media habits by providing social media awareness education to adolescents in school health, community health, and clinical practice settings as part of preventive mental health care. Additionally, it is of great importance that nurses identify early signs of sleep disorders, loneliness, anxiety, and depression, and provide appropriate referrals and counseling services as part of preventive mental health efforts. Structuring health and education policies in a way that ensures healthier and more controlled interactions between young people and digital media will contribute to protecting adolescents from digital risks.

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EVALUATION OF INTERVENTION PROGRAMS ON HEALTH-RELATED QUALITY OF LIFE AND GLYCEMIC CONTROL IN INDIVIDUALS WITH TYPE 2 DIABETES

ABSTRACT

Objective: This study aims to examine the effectiveness of intervention programs implemented to improve health-related quality of life and glycemic control levels in individuals with type 2 diabetes.

Materials and Methods: In this study, a literature review was conducted using the keywords 'Type 2 diabetes, quality of life, glycemic control, treatment adherence' and their Turkish equivalents in databases such as Google Scholar, PubMed, Science Direct, Web of Science, and Scopus. Full-text articles published between 2020 and 2025 in English and Turkish were included.

Results: The reviewed studies show that intervention programs applied to individuals with type 2 diabetes (including web-based transitional care, cognitive behavioral therapy, online counseling, telephone-based health coaching, and lifestyle counseling) significantly improve glycemic control and quality of life. Nurse-led web-based transitional care programs have been reported to reduce HbA1c levels and increase quality of life. Cognitive behavioral therapy has been shown to have a positive impact on treatment adherence and quality of life by reducing psychological symptoms in individuals with type 2 diabetes. Online diabetes education and counseling were found to enhance treatment adherence scores and lead to significant improvements in clinical parameters such as HbA1c and blood pressure. Diabetes health coaching delivered via telephone has been reported to be more effective in improving glycemic control and quality of life than standard education. A holistic program based on lifestyle interventions has shown positive results in both biochemical parameters and in quality of life and healthcare costs. Overall, the findings suggest that personalized,technology-supported,and psychosocially oriented interventions improve glycemic control, enhance quality of life, and strengthen treatment adherence in individuals with type 2 diabetes.

Conclusion: In conclusion, interventions such as nurse-led web-based transitional care programs, online counseling services, cognitive behavioral therapy applications, and telephone-delivered health coaching have shown significant improvements in glycemic control, treatment adherence, and quality of life.

Keywords: Type 2 diabetes, Quality of life, Glycemic control, Treatment adherence, Nursing

1. INTRODUCTION

Diabetes mellitus is a chronic syndrome characterized by hyperglycemia and elevated glucagon levels, resulting from inadequate insulin secretion, insulin resistance, or structural abnormalities of the insulin molecule. This condition affects carbohydrate, protein, and lipid metabolism and has become a major global public health concern because to its rising prevalence and negative impact on health, particularly through the possibility of acute and chronic consequences.In particular, the prevalence of type 2 diabetes is rising steadily in line with changes in lifestyle behaviors (3). According to the International Diabetes Federation (IDF), the number of individuals with diabetes globally, which was 537 million in 2021, is expected to reach 643 million by 2030 and 783 million by 2045 (1). It is further estimated that Turkey will rank 10th globally by 2045, with approximately 10.4 million individuals living with diabetes (2).

Type 2 diabetes is not limited to its physiological effects; it can also adversely affect individuals' daily lives in multiple ways, thereby reducing their quality of life. Consequently, the concept of health-related quality of life (HRQoL), which serves as an important indicator in assessing the overall impact of the disease on the individual, has gained prominence (4). HRQoL comprehensively addresses an individual's physical, psychological, and social conditions, and supports a patient-centered approach to care by promoting the inclusion of patients in medical decision-making processes (5). Therefore, in diabetes management, it is essential to consider not only biochemical indicators such as glycemic control but also subjective evaluations like quality of life, in order to enhance treatment effectiveness (6). Another critical factor influencing quality of life is the psychological burden associated with diabetes. Anxiety, depression, fear of hypoglycemia, and the perception of living with a chronic illness can disrupt the individual's psychosocial balance and negatively affect their quality of life (7). In this context, it is believed that interventions addressing psychosocial components can contribute to improving the overall well-being of individuals.

In recent years, advances in digital health technologies have introduced innovative approaches aimed at improving the quality of life for individuals managing type 2 diabetes. In this context, nursing-based technological interventions such as smartphone applications have been shown to support individuals in managing their condition more effectively, leading to significant improvements in their quality of life (8). Furthermore, the existing literature indicates that various interventions implemented in the management of type 2 diabetes have demonstrated positive effects on both quality of life and glycemic control (9). Interventions delivered through diverse methods, including web-based transitional care programs, online counseling services, cognitive behavioral therapy, telephone-based health coaching, and lifestyle modification strategies based on holistic approaches, have shown meaningful improvements not only in biochemical markers but also in psychosocial well-being, treatment adherence, and health-related quality of life (13). By means of these initiatives, nurses can improve patients' quality of life by promoting treatment compliance, bolstering their self-efficacy, and reducing their psychological burden. In addition, these interventions have been found to contribute positively to psychosocial factors such as depression, anxiety, and loneliness, alongside clinical indicators such as glycemic control. Therefore, nurses can play a critical role in the diabetes care process by collaborating with multidisciplinary teams to develop and implement such interventions. Given this, the present study aims to examine the effects of intervention programs designed to improve health-related quality of life and glycemic control in individuals with type 2 diabetes.

2. MATERIALS AND METHODS

In this study, a literature review was conducted using the keywords "Tip 2 diyabet, yaşam kalitesi, glisemik kontrol, tedaviye uyum" and "Type 2 diabetes, quality of life, glycaemic control, treatment adherence" across the databases Google Scholar, PubMed, ScienceDirect, Web of Science, and Scopus. English and Turkish full-text articles published between 2020 and 2025 were reviewed.

3. RESULTS

In Guangzhou, China, a randomized controlled trial assessed how a web-based transitional care program directed by a nurse affected the quality of life and glycemic control of people with type 2 diabetes after they were discharged from the hospital. A total of 116 patients diagnosed with type 2 diabetes and residing in Guangzhou participated in the study. Participants were randomly allocated to the intervention group (n = 58) or the control group (n = 58). Participants in the intervention group took part in a web-based transitional care program over a three-month period, which included individualized treatment plans, online educational modules, group sessions, remote counseling, and continuous data monitoring. Participants in the control group received only standard pre-discharge education along with an informational brochure. After three months, the intervention group exhibited a statistically significant reduction in HbA1c levels ($\beta = 2.87$; $p < 0.01$) and a substantial improvement in quality of life ($\beta = 7.69$; $p < 0.01$) when compared to the control group. Additionally, it was found that these benefits were indirectly mediated by treatment adherence ($\beta = 0.17$; $p < 0.05$) and self-efficacy ($\beta = 0.18$; $p < 0.05$). These findings demonstrate that transitional care contributes positively to both glycemic control and quality of life, suggesting its potential value in community-based healthcare practices (10).

A randomized controlled trial conducted in Faisalabad, Pakistan assessed the effects of cognitive behavioral therapy (CBT) on diabetes distress, depression, health anxiety, quality of life, and treatment adherence in individuals with type 2 diabetes. The study comprised 90 individuals aged 23 to 50 who used outpatient services and had been diagnosed with type 2 diabetes for at least 6 months. Participants were randomly allocated to one of two groups: intervention (n=45) or control (n=45). The individuals in the intervention group received 8-10 sessions of individually structured CBT over a 16-week period. The intervention included components such as psychoeducation, cognitive restructuring, problem-solving, relaxation techniques, activity planning, and relapse prevention. During this time, no psychological interventions were administered to the control group. At the end of the intervention, the experimental group showed a significant reduction in diabetes distress ($p<0.001$, $\eta^2 = .788$), depression ($p<0.001$, $\eta^2 = .611$), health anxiety ($p<0.001$, $\eta^2 = .771$), and treatment non-adherence levels, while significant increases were observed in quality of life ($p<0.001$, $\eta^2 = .581$), treatment adherence ($p<0.001$, $\eta^2 = .566$), and physical activity levels ($p<0.001$, $\eta^2 = .74$). In comparison, there were no significant changes observed in the control group. These findings indicate that CBT is an effective intervention in reducing psychological symptoms and improving quality of life and treatment adherence (11).

In Mardan, Pakistan, a quasi-experimental study was carried out to assess the effectiveness of online diabetes education and counseling in improving treatment adherence and quality of life in patients with type 2 diabetes. The study involved 196 individuals with type 2 diabetes who received regular online follow-up and counseling services over a six-month period. As part of the intervention, participants were informed about topics such as diet, medication use, and lifestyle changes through biweekly phone calls by educators.

Additionally, measurements of HbA1c, RBS, blood pressure, and BMI were monitored at three-month intervals. At the end of six months, a significant increase was observed in treatment adherence, as measured by the Morisky Medication Adherence Scale (MMAS) ($p < 0.001$); the low adherence rate decreased from 66.3% to 50%, while the high adherence rate increased from 1% to 4%. Statistically significant reductions in HbA1c, RBS, BMI, and systolic blood pressure were also found ($p < 0.001$). Particularly in areas like sexuality, disease-related worries, and nutritional flexibility, improvements in quality of life scores were noted. These findings demonstrate that online education is an effective method for improving treatment adherence and glycemic control (12).

A community-based randomized controlled trial conducted in Ontario, Canada, assessed the effects of diabetes health coaching (DHC) delivered via telephone on glycemic control and quality of life in individuals with type 2 diabetes. The study included 365 adults with an HbA1c level of ≥7.5% and access to a telephone. Participants were randomized into two groups: a control group (n=177) receiving standard diabetes education (DE) only, and an intervention group (n=188) receiving both DHC and DE. The intervention group received regular health coaching sessions via telephone for 12 months. The primary outcome measure was the change in HbA1c levels after one year. Secondary outcomes included the Diabetes-Related Quality of Life (ADDQoL-19) scores and self-care behaviors. The results showed that the intervention group experienced an average 1.8% reduction in HbA1c, compared to a 1.3% reduction in the control group, which was 0.49% greater. Furthermore, the intervention group's quality of life scores significantly improved (mean weighted score difference: 0.28; 95% CI: 0.04 to 0.52; p=0.02). There were no significant differences between the groups in terms of emergency department visits or hospitalization rates. These findings suggest that telephone-based health coaching is an effective intervention for improving glycemic control and quality of life in individuals with type 2 diabetes (13).

A quasi-experimental study conducted in New Delhi, India, assessed the effects of a lifestyle intervention-based holistic approach (LIH model) on blood glucose levels, health-related quality of life (HRQoL), and medical treatment costs in individuals with type 2 diabetes. The study included 224 individuals with type 2 diabetes, who were divided into two groups: the intervention group (n=112) receiving lifestyle intervention counseling (LIC) and the control group (n=112) receiving only standard treatment. The intervention group received comprehensive lifestyle counseling based on the LIH model, developed by dietitians, endocrinologists, yoga, and meditation instructors. The counseling covered topics such as diet, physical activity, stress management, medication adherence, and regular medical check-ups. This counseling was repeated monthly for the first six months. The control group received only standard pharmacological treatment. At the one-year follow-up, the intervention group showed significant reductions in fasting blood glucose levels (0.26 mg/dL), postprandial blood glucose levels (-70.16 mg/dL), and HbA1c levels (-2.82%) ($p<0.001$). Additionally, significant improvements in quality of life assessments (SF-36 and ADS scales) were observed in the intervention group. The intervention group demonstrated significant reductions in costs related to medications, hospitalizations, and surgical procedures ($p<0.005$). These findings indicate that a holistic approach grounded in lifestyle interventions contributes to improved glycemic control, enhanced quality of life, and reduced medical treatment costs among individuals with type 2 diabetes (14).

4. CONCLUSION AND RECOMMENDATIONS

The studies conducted have demonstrated that intervention programs aimed at improving glycemic control and enhancing quality of life in individuals with type 2 diabetes are effective. Interventions such as nurse-led web-based transition care programs, online counseling services, cognitive-behavioral therapy applications, and telephone-based health coaching have resulted in significant improvements in glycemic control, treatment adherence, and quality of life. Based on these findings, it is recommended to expand the use of digital health technologies and psychosocial support-oriented interventions in type 2 diabetes management. Furthermore, these interventions should be integrated into healthcare systems as part of a person-centered care model.

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CONVENTIONAL AND POTENTIAL NATURAL THERAPEUTIC DRESSING MATERIALS IN ENDODONTICS: CURRENT APPROACHES

ABSTRACT

Dressing materials used in endodontics are applied during root canal treatment or between treatment sessions to control intracanal infections, eliminate bacteria, reduce inflammation, and seal the dentinal tubules. These materials, placed inside the canal between appointments, enhance the success of the treatment by eliminating microorganisms. Among many intracanal medicaments such as antibiotic-containing dressings, chlorhexidine (CHX), formocresol, phenol derivatives (e.g., para-chlorophenol), and corticosteroids, calcium hydroxide ($Ca(OH)_2$) remains the most widely used material. However, in resistant cases, alternative agents like antibiotic pastes or chlorhexidine are often preferred. Additionally, in certain cases, corticosteroid-containing dressings are used to alleviate postoperative pain and inflammation.

In recent years, naturally derived materials have gained popularity in endodontic dressing procedures due to their potential contribution to sustainability. Natural component-based dressings have been proposed to minimize tissue irritation, promote healing, and provide alternatives to synthetic agents, particularly in situations involving allergies or toxicity. Plant-based substances such as propolis, aloe vera, curcumin, ginger extract, neem, and tea tree oil have demonstrated antimicrobial, anti-inflammatory, and regenerative effects, making them promising candidates for intracanal disinfection.

This review provides an up-to-date evaluation of both conventional dressing materials and recently developed natural alternatives that contribute to sustainable endodontic practices. It also highlights the growing body of literature supporting the efficacy and biological compatibility of natural compounds.The combined use of conventional and natural materials may form the foundation for future personalized endodontic treatment strategies. This integrative approach could increase treatment success while promoting the use of more biologically compatible materials.

Keywords: Endodontic treatment, dressing materials, natural compounds

ENDODONTİDE KONVANSİYONEL VE POTANSİYEL DOĞAL TERAPÖTİK PANSUMAN MATERYALLERİ: GÜNCEL YAKLAŞIMLAR

ÖZET

Endodontide kullanılan pansuman materyalleri, kök kanalı tedavisi sırasında veya seanslar arasında kanal içi enfeksiyonları kontrol altına almak, bakterileri yok etmek, inflamasyonu azaltmak ve dentin tübüllerini kapatmak amacıyla uygulanır. Seanslar arasında kanal içine yerleştirilen bu materyaller, bakterileri elimine ederek tedavinin başarısını artırır. Antibiyotik İçeren Pansumanlar, Klorheksidin (CHX), Formokrezol, Fenol Türevleri (Örn: Paraklorofenol), Kortikosteroidler gibi bir çok kök kanal materyali bulunmakla birlikte Kalsiyum Hidroksit ($Ca(OH)_2$), **en yaygın kullanılan materyaldir,** ancak dirençli vakalarda **antibiyotik patları veya klorheksidin gibi alternatifler de tercih edilir.** Bunun yanısıra bazı vakalarda, postoperatif ağrı ve inflamasyonu azaltmak amacıyla kortikosteroid içeren pansumanlar da kullanılabilir.

Son yıllarda doğal bileşenli materyallerin sürdürebilirlik acısından endodontik pansuman işlemlerinde popülerliği artmaktadır. Doku irritasyonunu en aza indirerek iyileşmeyi teşvik etmek ve sentetik ajanlara alternatif doğal çözümler sunmak (özellikle alerji/toksisite durumlarında) için doğal bileşenli pansuman materyalleri öne sürülmüştür. Propolis, aloe vera, kurkumin, zencefil özü, neem ve çay ağacı yağı gibi bitkisel kökenli maddelerin antimikrobiyal, antiinflamatuar ve rejeneratif etkileri sayesinde kanal içi dezenfeksiyonda etkin olabileceği bildirilmektedir.Bu açıdan bu derleme güncel pansuman materyallerini ve yeni geliştirilen ve sürdürebilirliğie katkı sunan son çıkan materyalleri ele alarak güncel bir değerlendirme sunmaktadır. Konvansiyonel ve doğal materyallerin kombine kullanımı ise gelecekte kişiselleştirilmiş endodontik tedavi yaklaşımlarının temelini oluşturabilir. Bu sayede hem tedavi başarısı artırılabilir hem de biyolojik uyumluluğu yüksek materyallerin kullanımı teşvik edilebilir.

Anahtar Kelimeler: Endodontik tedavi,pansuman materyalleri,doğal bileşenler

GİRİŞ

Kanal tedavisinin başarısı, pulpa dokularının, dentine kalıntılarının ve mikroorganizmaların ortadan kaldırılmasıyla tam pulpa boşluğu debridmanına dayanır (1). Kök kanal sisteminin karmaşıklığı nedeniyle tek başına mekanik enstrümantasyonla intra-radiküler enfeksiyonların tamamen yok edilmesi imkansızdır (2). Bu nedenle kimyasal ve mekanik preparatlar birlikte yapılmalıdır (3). Ayrıca, iyileşmeye izin vermek için, mikro organizmaların yok edilmesinden sonra kanalda bırakılabilecek herhangi bir antijenin etkisiz hale getirilmesi gerekir. Şekillendirme ve dezenfeksiyonun ardından kanal içerisinde sağ kalan bakteriler, randevular arasında sayıca artış gösterebilmektedir (4). Bu nedenle, kombine kemo-mekanik tedaviyi enfekte kanallarda kullanılacak uygun bir pansuman materyali takip etmelidir (5).

Tedavi planlaması tek veya çok seans yaklaşımının dikkatle değerlendirilmesini içerir. Kök sayısı, kanal anatomisi, mevcut zaman ve klinisyenin becerileri dikkate alınması gereken etkenler arasında bulunmaktadır. Örneğin şişlik olsun ya da olmasın şiddetli ağrısı olan bir hasta, tek seans endodontik tedavi için öncelikli aday değildir. Devital ve apikal periodontitisli dişler mikrobiyolojik bir problem teşkil ederler. Bakteriyel debrisin periapikal dokuların içine doğru itilmesinden kaçınmak önemlidir. Kök kanal tedavisinin tek seansta tamamlanamadığı durumlarda kanal içi pansuman materyalleri kullanılır. Kök kanal tedavisinde kullanılan pansuman materyalleri, kanalın iyileşmesi ve enfeksiyonların kontrol altına alınması için kritik bir rol oynar. Hangi pansuman materyalinin kullanılacağı, tedavi sürecine, dişin durumuna ve kullanılan materyallerin özelliklerine bağlıdır. Bu pansuman materyallerinin etkili bir şekilde kullanılması, tedavi başarısını artırır ve dişin sağlıklı bir şekilde iyileşmesini sağlar.

Kanal içi pansuman materyallerinin kullanım amaçları

Endodontide kullanılan pansuman materyalleri, enfeksiyon kontrolü, inflamasyonun azaltılması ve dentin dokusunun iyileştirilmesini sağlamak ya da bazen kök kanal sistemi içindeki kalan mikrobiyotanın yeniden büyümesini önlemek ve dezenfeksiyon seviyesini artırmak için seanslar arasında uygulanır.

*Kök kanalının dezenfeksiyonunu sağlamak

*Kanaldaki mikroorganizma sayısını azaltmak

*Bakterilerin tekrar büyümesini önlemek

*Periapikal dokulardaki inflamatuar cevabı ve seanslar arası ağrıyı azaltmak

*Vital ve nekrotik kanal içeriğini fikse etmek

Kanal içi pansuman materyallerinin taşıması beklenen özellikleri

Endodontik pansuman materyalleri, enfeksiyon kontrolü, doku iyileşmesi ve başarılı bir tedavi için antibakteriyel, biyouyumlu, radyoopak, stabil ve dentin penetrasyonu yüksek olmalıdır. Dentin yapısı gereği pansuman materyallerinin difüzyonunu sınırlar, içindeki hidroksiapatit ilaçları tamponlar ve nemliliği hidroliz için kısıtlıdır. Dolayısıyla etkinliklerini azaltır. Pansuman materyallerinin tam etkinliklerini göstermeleri için uzun süre dentinle temasta kalmaları gerekir. Bu nedenle ilacın akışkanlığını ve penetrasyonunu belirleyen yüzey gerilimi ve temas açısı önemlidir. Ayrıca kanal içi pansuman materyallerin

kullanımında seanslar arasında sızıntıya dikkat edilmeli ve sızdırmaz geçici restorasyonlar yapılmalıdır.

Kanal içi pansuman materyallerinin taşıması beklenen özellikleri aşağıda sıralanmıştır:

*Antibakteriyel etkisi yüksek olmalı

*Etkili germisit ve fungusit olmalı. Kanalda bulunabilen bütün mikroorganizma türlerini ortadan kaldırabilmelidir. Özellikle kök kanalı patojenlerine etkili olabilecek anaerobik spektrumu bulunmalıdır.

*Çabuk etki göstermeli ve etkisini uzun süre devam ettirmelidir.

*Mikroorganizmalara bakterisid veya en azından bakteriyostatik etki gösterirken, canlı konak dokulara toksik olmamalıdır.

*Hücresel immün cevabı tetiklememelidir.

*Yumuşak doku ve dişlerde renklenmeye neden olmamalıdır.

*Kanala uygulanması ve uzaklaştırılması kolay olmalıdır.

Kanal içi pansuman materyallerinin sınıflandırılması

Kanal içi pansuman materyalleri, enfeksiyon kontrolü sağlamak, mikrobiyal yükü azaltmak ve iyileşme sürecini desteklemek amacıyla kullanılan geçici medikal ajanlardır. Bu materyaller, sahip oldukları antimikrobiyal özellikler, toksisite düzeyleri ve doku uyumluluklarına göre sınıflandırılmaktadır. Tablo 1'de, klinik kullanımda yer bulmuş başlıca kanal içi pansuman materyalleri; içerikleri, toksisiteleri ve klinik özellikleri doğrultusunda özetlenmiştir.

Tablo 1. Konvansiyonel olarak kullanılan kanal içi pansuman materyalleri

Materyal	Konsantrasyon	Toksisite Düzeyi	Açıklama
Kalsiyum Hidroksit ($Ca(OH)_2$)	%100 (saf) veya sulu süspansiyon	Düşük	Antibakteriyel, doku dostu, sert doku oluşumunu destekler
Klorheksidin (CHX)	%0.2 - %2(solüsyon) %2(jel)	Orta	Antibakteriyel, kalıcı etki, doku iritasyonu yapabilir
İyodoform	%100 veya $Ca(OH)_2$ ile karışım içinde	Düşük-Orta	Antibakteriyel, yavaş salınım
Formokrezol	%19 formaldehit, %35 trikresol	Yüksek	Antiseptik ama toksik; özellikle pedodontide tartışmalı kullanımı vardır
Fenol ve türevleri (Kresatin, Krezol, Kamporofenol	%2-%5(solüsyon formu)	Yüksek	Güçlü antiseptik, çevre dokular için toksik
Triple antibiyotik patı (TAP)	%1:1:1 (Metronidazol, Siprofloksasin, Minosiklin)	Orta-Yüksek	Rejeneratif endodontide kullanılır, yüksek konsantrasyonda sitotoksik olabilir
Kortikosteroidler(Lederm ix,Deksametazon)	Hazır form	Orta	Antibakteriyel + antiinflamatuvar, doku rejenerasyonunu etkileyebilir

Kalsiyum hidroksit

1920'de piyasaya sürülmesinden bu yana kalsiyum hidroksit ($Ca(OH)_2$) pansuman materyali endodontide yaygın olarak kullanılmaktadır. Güçlü bir alkali maddedir (pH = 12,5). Sulu bir çözeltide kalsiyum ve hidroksil iyonlarına ayrışır. Antimikrobiyal aktivite, doku çözme yeteneği, diş rezorpsiyonunun inhibisyonu ve sert doku oluşumu ile onarımın indüksiyonu gibi çeşitli biyolojik özellikler bu maddeye atfedilmiştir. $Ca(OH)_2$ yavaş etkili bir antiseptiktir; in vitro doğrudan temas deneylerinde enterokokların tamamen öldürülebilmesi için 24 saatlik bir temas periyodunun gerekli olduğu gözlemlenmiştir (6). Bakterileri öldürmeye ek olarak $Ca(OH)_2$, bakteriyel lipopolisakkaritlerin lipid bileşenini hidrolize ederek lipopolisakkaritin biyolojik aktivitesini inaktive eder ve etkisini azaltır (7). Şu anda endodontik tedavi sırasında en etkili antimikrobiyal pansumanlardan biri olarak kabul edilmektedir (8). $Ca(OH)_2$ in bir hafta boyunca uygulanmasının mikroorganizmaları azalttığı gösterilmiştir (9). En çok tercih edilen ilaç olmasına rağmen, kök kanal sistemindeki tüm bakteri türlerine karşı eşit bir etki göstermez (10, 11). $Ca(OH)_2$ in etkisini gösterebilmesi için doku ile direkt temas halinde olması gerekir. $Ca(OH)_2$ tozu; steril su veya serum fizyolojik ile karıştırılabilir ve bir lentulo yardımıyla kök kanallarına yerleştirilebilir (12).

Klorheksidin

1970'lerden beri diş hekimliğinde yaygın olarak kullanılan klorheksidin (CHX), endodontide irrigasyon ve kanal içi dezenfektan olarak önerilmiştir. Klorheksidin geniş spektrumlu bir antimikrobiyal ajandır ve endodontide etkili bir kanal içi pansuman materyali olarak savunulmuştur (13). Klorheksidinin avantajları, diş kökü dentinindeki tutucu karakteri (14) ve nispeten düşük toksisitesidir (15). Ek olarak, kalsiyum hidroksite dirençli suşlara karşı da etkilidir (16). In vitro çalışmalarda, kanal içi pansuman materyali olarak uygulanan CHX'in en az $Ca(OH)_2$ kadar ve hatta yer yer daha iyi antimikrobiyal etkinlik gösterdiği bildirilmiştir (17). Ancak, klorheksidin tek başına fiziksel bir bariyer oluşturamaz ve radyoopaklık sağlayamaz (18); bu nedenle, kalsiyum hidroksit ile kombine kullanımı bu özellikleri sunabilir. Bir çalışmada, çözeltilerinin, jellerinin ve kontrollü salım preparatlarının Enterococcus faecalis ve Candida albicans gibi dirençli mikroorganizmalara karşı etkili olduğu bulunmuştur (19). Viskozitesi nedeniyle klorheksidin jelinin, sıvı karşılığına göre mekanik temizlikte daha iyi olduğu bulunmuştur (20).

İyodoform

İyodoform, endodontide antibakteriyel, antiseptik ve biyouyumlu özellikleri nedeniyle kanal içi pansuman materyali olarak kullanılan sarı renkli, kristal yapılı bir bileşiktir. Tek başına veya kalsiyum hidroksit, öjenol, metilselüloz gibi diğer maddelerle kombinasyon halinde uygulanabilir. İyot salınımı sayesinde bakterisidal etki gösterir.

Formokrezol

Formokrezol olarak kullanılan formaldehit, yüksek derecede toksik, mutajenik ve kanserojen bir materyaldir; ancak tarihsel süreçte endodontik tedavide yaygın olarak kullanılmıştır (21).

Formokrezolün formaldehit bileşeni %19 ile %37 arasında değişiklik gösterir.

Fenol ve türevleri

Fenol (C_6H_5OH) ve fenolik preparatlar endodontide yaygın olarak kullanılmış pansuman materyalleridir. Ancak sonrasında uçucukları sebebiyle geçici dolgulardan sızabildiği ve periapikal doku yoluyla yayılarak toksisiteye neden olabileceği gösterilmiştir. Fenolik preparatların şiddetli toksisitelerine rağmen piyasada hala paramonoklorofenol (C_6H_4OHCL), timol ($C_6H_3OHCH_3C_3H_7$) ve kresol ($C_6H_4OHCH_3$) gibi fenol türevleri mevcuttur.

Halojenler

Halojenler olarak klorlu solüsyonlar kök kanallarının irrigasyonu için uzun yıllardır kullanılmaktadır. Ayrıca N-kloro-tosilamid sodyum tuzu olan Kloramin-T formunda kanal içi pansuman materyali olarak da kullanılırlar.IKI (iyodin potasyum iyodid) enfekte dentinde etkili bir dezenfektandır; in vitro olarak enfekte dentindeki bakterileri 5 dakikada öldürebildiği bildirilmiştir (22).

Antibiyotik patları

Siprofloksasin, metronidazol ve minosiklin karışımı olan üçlü antibiyotik macunu (TAP), belirli konsantrasyonlarda kök kanal sisteminin dezenfeksiyonunda etkinlik göstermiştir (23). TAP, odontojenik enfeksiyonlarda gram-negatif, gram-pozitif ve anaerobik bakterilere karşı etkilidir (24). TAP'ın en büyük dezavantajlarından biri, tetrasiklin türevi olan minosiklin bileşeninin neden olduğu diş renklenmesidir (25). Bu sorunun üstesinden gelmek için, ikili antibiyotik macunu (DAP) üretmek üzere minosiklin formülasyondan atıldı.

Kortikosteroidler

Kortikosteroidler immün cevabı baskılarlar bu nedenle ağrı ve inflamasyonun giderilmesinde kullanılırlar. Steroidler, ağrı ve enflamasyonu azaltmak için kök kanal sistemi içinde lokal olarak kullanılmaktadır. Ledermix, 1960'lı yıllarda Prof. Andre Schroeder tarafından geliştirlmiştir, piyasada hala bulunan bir üründür. Aktif bileşenleri, geniş spektrumlu bir antibiyotik olan demoklosiklin ve güçlü bir antienflamatuar kortikosteroid olan triamsinolon asetoniddir. Ledermix'in etki mekanizması, bakterilerde ribozomal protein sentezinin inhibisyonuna dayanmaktadır.

Güncel Pansuman Materyalleri

Son zamanlarda, kalsiyum hidroksit parçacık boyutunu değiştirerek nano-kalsiyum hidroksitte nanoteknoloji kullanımı gibi bakterilerin antibiyotiklere karşı direncinin üstesinden gelebilecek daha iyi özelliklere sahip bir malzemeyi tanıtmak için bir çalışma yapılmıştır (26). Geleneksel kalsiyum hidroksit parçacıklarının boyutu 1 ila 10 µm arasında değişir (27), oysa dentinal tübüllerin çapı pulpaya yaklaşık 2 –2,5 µm'dir. Sonuç olarak, daha büyük olan geleneksel kalsiyum hidroksit parçacıkları dentinal tübüllere kolayca nüfuz edemez (28). Parçacıkların yüzey-hacim oranındaki artış, kök kanalındaki antibakteriyel ajanların çözünürlüğünü, kimyasal ve antibakteriyel aktivitelerini artırır (29). Araştırmalar, nanopartiküller ne kadar küçük ve konsantrasyonları ne kadar yüksek olursa, antibakteriyel aktivitelerinin o kadar yüksek olacağını göstermiştir (30).

Biyoaktif katkılarla zenginleştirilmiş pansuman materyalleri

Gümüş, biyoaktif cam, kitosan , seryum oksit ve polilaktik-ko-glikolik asit (PLGA) dahil olmak üzere nanopartiküller, antimikrobiyal özelliklere ve endodontik pansuman materyallerinin performansını iyileştirme potansiyeline sahiptir. Biyoaktif camların kök kanallarında antibakteriyel özellikleri vardır ancak pH'a bağlı değildir.Dentinden etkilenmedikleri gösterilmiştir. Biyoaktif cam mükemmel rejeneratif ve antimikrobiyal özelliklere sahiptir. Gümüş (Ag) esas olarak antimikrobiyal özellikleri için kullanılır.

Alternative inflamatuar ve/veya antinflamatuar potansiyel medikamentler

Doğal ürünler, eski çağlardan beri alternatif tıpta kullanılmaktadır. Diş hekimliğinde ise fitoterapötik ilaçlar yaygın olarak kullanılmıştır. Tıbbi özelliklere sahip bitkiler, çeşitli hastalık süreçlerinin tedavisi için faydalı ve etkili bir kaynaktır. Kök kanalının kemo-mekanik preparasyonu bakteri sayısını azaltabilse de, kök kanal sisteminin dezenfeksiyonunu en üst düzeye çıkarmak için antibakteriyel etkili kanal içi bir pansuman materyali gereklidir (31). Endodontide, kullanılan kanal içi pansuman materyallerinin çoğunun sitotoksik reaksiyonları ve dentin tübüllerinden bakterileri uzaklaştıramamaları nedeniyle, son zamanlardaki tıbbın eğilimi doğal bitkilerden elde edilen biyolojik medikamanları kullanmaktır (32). Bitkisel ürünler ayrıca giderek artan bir şekilde sedatif, plak azaltıcı ve sağlıklı diş etleri için kullanılmaktadır.

Tablo 2. Endodontik Uygulamalarda Potansiyel Taşıyan Fitoterapötik Ajanların Biyolojik Özellikleri

Bitki Adı	Antibakteriyel	Antienflamatuar	Antioksidan
Hint zamkı (Acacia nilotica)	+		
Aloe vera	+	+	
Dulavrat otu (Arctium lappa)	+	+	+
Neem (Azadirachta indica)	+	+	
Karvakrol	+	+	
Casearia sylvestris	+	+	
Sarımsak (Allium sativum)	+	+	
Alman papatyası	+	+	
Yeşil çay (Camellia sinensis)	+		+
Limon (Citrus limonum)	+		
Hint dutu (Morinda citrifolia)	+	+	+
Propolis	+		+
Guava (Psidium guajava)	+		
Psoralea tohumu	+		
Afrika sumak (Rhus lancia)	+		
Misvak (Salvadora persica)	+		
Karanfil (Syzygium aromaticum)	+		
Çay ağacı yağı (Tea tree oil)	+		
Triphala	+		+
Zerdeçal (Curcuma longa)	+	+	+
Meyan kökü (Glycyrrhiza glabra)	+		+

Kitosan

Kitosan nanopartikülleri, gelişmiş antimikrobiyal etkileri nedeniyle kanal içi pansuman materyali olarak kullanılmıştır (33,34). Bu nanopartiküller, geleneksel $Ca(OH)_2$ tedavilerinin eksikliklerinin potansiyel olarak üstesinden gelerek daha iyi penetrasyon, gelişmiş antimikrobiyal aktivite ve biyofilmlerin daha iyi bozulmasını sağlayabilir.

Kitosan, kabukluların kabuklarında bulunan kitinin deasetilasyon işlemiyle elde edilen doğal bir polisakkarittir. Chitosan'ın yüksek biyouyumluluk ve düşük toksisite de dahil olmak üzere özellikleri, onu endodontik tedavide uygulanabilir bir alternatif pansuman materyali olarak konumlandırır.

Propilen glikol (PG), kitosan bazlı kanal içi pansuman materyali vermek için uygun bir araç olarak hizmet edebilir ve dentinal tübüllerden ve apikal foramenden geçişini kolaylaştırabilir (35,36). Bu nedenle, ilacın antimikrobiyal aktivitesine de katkıda bulunabilir.

Propolis

Propolis, doğal biyouyumlu reçineli bir malzemedir. Bal arıları (Apis mellifera L.) tarafından bitkilerin farklı kısımlarından toplanan ve bir arı kovanına bırakılan maddelerden hazırlanır (37). Propoliste bulunan flavonoidlerin varlığı nedeniyle antimikrobiyal ve antienflamatuar özelliklere sahiptir. Sonuç olarak, diş çürüğü yönetimi için uygulanmadan önce oral ve boğaz enfeksiyonu tedavisi için kullanılmıştır (38). Ayrıca, kanal içi medikament olarak önerilmiştir (39). Propolisin antienflamatuar ve analjezik etkisini indüklediği mekanizma, anahtar hücrelerin lipopolisakkarit kaynaklı enflamatuar tepkisinin baskılanmasıdır (40). Güçlü antimikrobiyal ve antienflamatuar özellikleri nedeniyle, propolisin randevular arası ağrı oluşumunu ve yoğunluğunu azaltması bekleniyordu. Antimikrobiyal, anti-inflamatuar, antioksidan, anestezik ve sitotoksik özellikler de dahil olmak üzere çeşitli biyolojik aktiviteler sergiler (41). Propolisin anti-inflamatuar özelliği, propolisteki kafeik asit ve fenetil esterin varlığından kaynaklanmaktadır.

Diş hekimliğinde pulpa kaplama ajanı, kanal içi irrigasyon solüsyonu, ağız gargarası, kariostatik ajan, periodontitis ve protez stomatiti tedavisi vb. olarak kullanılır (42). Propolisin $Ca(OH)_2$ ile kanal içi medikaman olarak E. faecalis'e karşı antimikrobiyal aktivitesi, propolisin mikroorganizmaları elimine etmede etkili olduğunu göstermiştir (43).

Kurkumin

Hint mutfağında yaygın olarak bulunan bir bileşen olan kurkumin (Curcuma longa veya zerdeçal), çok yıllık bir bitkidir ve Zingiberaceae ailesinin bir üyesidir (44). Kurkumin, zerdeçal köklerinden elde edilen ve anti-inflamatuar, antibakteriyel ve antioksidan etkiler gösteren ana bileşendir (45). ABD Gıda ve İlaç Dairesi, kurkumin molekülünü “Genel Olarak Güvenli Kabul Edilen (GRAS)” olarak sınıflandırmıştır (46). Laboratuvar, hayvan ve insan çalışmalarını içeren sistematik bir inceleme, kurkuminin yüksek dozlarda bile mutajenik olmadığını, toksik olmadığını ve biyouyumlu olduğunu bulmuştur (47). Endodontide, farklı yazarlar kurkumini kanal içi medikament (48) olarak kullanmış ve umut verici sonuçlar göstermiştir.

SONUÇ

Kanal tedavisinin başarılı olması için pulpa dokularının, dentin kalıntılarının ve mikroorganizmaların ortadan kaldırılmasıyla kök kanal temizliği sağlanmalıdır. Kök kanal sisteminin karmaşık yapısı nedeniyle sadece mekanik enstrümantasyonla mikroorganizmaların tamamen kanaldan uzaklaştırılması çok zordur. Bu yüzden antimikrobiyal özellikte bir pansuman materyali kök kanallarını dezenfekte etmek için seanslar arası uygulanmalıdır.

Bu pansuman materyalleri, patojen bakterileri ortadan kaldırmak için dentin tübüllerine nüfuz edebilmelidir. Ayrıca kullanılacak pansuman materyalinin kalan bakterileri yok etmek için belirli bir süre boyunca kanal içinde bekletilmelidir. Doğal içerikli pansuman materyalleri, antimikrobiyal, antiinflamatuar, antioksidan ve rejeneratif özellikleri sayesinde endodontik tedavilerde terapötik potansiyel taşımaktadır. Bu materyaller, özellikle alternatif tedavi yaklaşımlarında, biyouyumluluğun ve doku dostu uygulamaların ön plana çıktığı durumlarda tercih edilebilecek önemli seçenekler sunmaktadır. Doğal pansuman materyalleri genel olarak yenilenebilir, biyobozunur ve düşük çevresel etkiye sahip olmaları nedeniyle sürdürülebilirlik açısından avantajlıdır. Ancak bu avantajların korunması için, üretim ve tedarik süreçlerinin doğa dostu tekniklerle yürütülmesi**,** biyolojik çeşitliliğin gözetilmesi ve etik ilkelere uygunluk sağlanması büyük önem taşır. Bu nedenle, endodontik uygulamalarda doğal materyal tercihi yapılırken yalnızca klinik etkinlik değil, sürdürülebilir kaynak kullanımı da göz önünde bulundurulmalıdır.

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AN EXAMINATION OF NURSING INTERVENTIONS IN PROMOTING CARDIOVASCULAR HEALTH BEHAVIORS AMONG ADOLESCENTS

ABSTRACT

Objective: This review study was conducted to examine intervention programs implemented to improve cardiovascular health behaviors in adolescents.

Material and Method: In this study, a literature review was conducted using the keywords 'adolescent, health promotion, cardiovascular health, cardiovascular health behaviors, nursing, nursing interventions' in both Turkish and English. The databases Google Scholar, PubMed, Science Direct, Web of Science, and Springer Nature were searched. Articles published between 2020 and 2025, written in English and Turkish, and with full-text access were included.

Results: Studies on the subject indicate that community- and school-based nursing interventions generally create positive effects on cardiovascular health indicators among adolescents. The interventions contribute to favorable improvements in body mass index, blood pressure, nutritional habits, and physical activity levels. Furthermore, the studies revealed that innovative approaches such as digital health applications and multi-component educational programs support adolescents in adopting healthy lifestyle habits.

Conclusion: In conclusion, community/school-based interventions and digital applications provide significant improvements in cardiovascular health indicators such as body mass index, blood pressure, nutritional habits, and physical activity levels in adolescents. It is recommended that future studies focus on developing and disseminating comprehensive, culturally sensitive, nurse-led intervention programs supported by school-family-community collaboration and technology, to enhance adolescents' healthy lifestyle behaviors.

Keywords: Adolescent, Cardiovascular Health Behaviors, Health Promotion, Nursing

1. INTRODUCTION

According to the World Health Organization (WHO), the period between the ages of 10 and 19 is defined as adolescence [1] Adolescents constitute 16% (13.4 million) of the population in Türkiye [2] and one-sixth (1.2 billion) of the global population. This number is expected to reach approximately 1.13 billion by 2025 [3]. The adolescent period stands out as a time of rapid physical, cognitive, and psychological development. During this period, individuals begin to gain independence, and their social skills and learning behaviors increase. Moreover, it is a critical time for the development of future lifestyle behaviors and serves as a transitional phase between childhood and adulthood [3,4]. Failure to adequately understand the changes and problems experienced during adolescence and the lack of timely and appropriate interventions may lead young individuals to adopt many risky behaviors that can negatively affect their entire lives [5]. The continuation of these behaviors into adulthood increases morbidity and mortality rates [6].

In recent years, there has been a noticeable increase in cardiovascular risk factors and risky behavioral tendencies, particularly among young people. Globally, there are at least 107.7 million individuals under the age of 18 who are classified as obese [7]. It has been reported that approximately 8% to 10% of adolescents worldwide are affected by hypertension [8]. The literature indicates that the age of smoking initiation has decreased to the adolescent period, and exposure to tobacco products at an early age has increased [9,10]. Furthermore, with technology becoming the most common source of entertainment for children and adolescents, physical inactivity rates are increasing, accompanied by a rise in sleep disorders and unhealthy dietary behaviors among school-aged individuals. These factors, in combination with risk factors such as a family history of cardiovascular disease, are considered significant threats to adolescent cardiovascular health [11-15]. Reducing these modifiable risk factors is reported to significantly decrease the prevalence of cardiovascular disease and, consequently, reduce mortality rates associated with the disease [16,17].

A review of the literature also highlights the effectiveness of community and school-based interventions aimed at improving cardiovascular health behaviors [18-22]. The effective implementation of these interventions requires the active involvement of healthcare professionals, particularly nurses, working in the field. It is of great importance that nurses working in primary healthcare services support the development of healthy habits in adolescents through health education, counseling, and behavioral interventions [23-25]. The current literature demonstrates the effectiveness of community- and school-based interventions [18-22] and strengthens the necessity of implementing evidence-based programs targeting cardiovascular health behaviors in this field. Accordingly, integrating evidence-based cardiovascular health behavior intervention programs for adolescents into nursing practices should be considered a critical measure for both individual and public health. For these reasons, this study aims to examine intervention programs implemented to improve cardiovascular health behaviors among adolescents.

2. METHOD

In this study, a literature review was conducted using the keywords “adolescents, health promotion, cardiovascular health, cardiovascular health behaviors, nursing, nursing interventions” in both Turkish and English through the databases Google Scholar, PubMed, ScienceDirect, Web of Science, and Springer Nature. Articles published between 2020 and 2025, written in English and Turkish, and with accessible full texts were reviewed.

3. FINDINGS

Community-based nursing interventions have been found to yield positive outcomes for individuals with cardiovascular disease risk factors. According to a systematic review of 46 studies, such interventions led to improvements in self-care, health status, healthcare utilization, and quality of care. Specifically, reductions in HbA1c levels in diabetic patients, blood pressure control in individuals with hypertension, and improved dietary habits in those with dyslipidemia were observed. Additionally, decreases in hospital admissions and emergency room visits, along with increased satisfaction with healthcare services, were reported. It was indicated that the effectiveness of interventions could be enhanced through strategies such as patient empowerment, targeted approaches, and home visits. The study noted that interventions should be supported by appropriate resources, planning, and nurse training [26].

In a study that examined adolescents' cardiovascular health trends using the American Heart Association's (AHA) "Life's Essential 8" (LE8) metrics, data from 6,999 adolescents aged 12 to 19 between 2007 and 2018 were analyzed based on eight components: diet, physical activity, nicotine exposure, sleep health, body mass index (BMI), blood lipids, blood glucose, and blood pressure. The results showed that the cardiovascular health score increased from 72.8 in 2007–2008 to 77.3 in 2017–2018. The most notable improvements were observed in nicotine exposure, sleep health, blood lipids, and blood pressure. However, no significant improvements were seen in lifestyle factors such as diet and physical activity, and only a decrease in BMI was reported. These findings suggest that while adolescents' overall cardiovascular health status has improved, more interventions and policies are needed specifically in the areas of diet and physical activity [27].

In a cluster-randomized controlled trial conducted between 2017 and 2021 in Madrid and Barcelona, Spain, the effect of a school-based cardiovascular health promotion program on adolescents was evaluated. The study included 1,326 adolescents aged 12 to 16 who were middle school students with at least one cardiovascular risk factor. Participants were divided into three groups: a long-term intervention group lasting four years (n=412), a short-term intervention group lasting two years (n=504), and a control group (n=441). Students in the intervention groups received a multi-component educational program covering topics such as healthy eating, physical activity, and prevention of tobacco and substance use. Classroom activities through teachers, family newsletters, and school-wide health recommendations were implemented. Students in the control group received only the standard curriculum. Although a statistically significant increase in cardiovascular health scores was observed in the long-term intervention group compared to the control group by the second year of the intervention, this difference was not sustained by the fourth year. Additionally, small positive changes were observed in cardiovascular health components (e.g., diet, physical activity, blood pressure, glucose levels) in both intervention groups, but most of these changes were not statistically significant. The cancellation of certain activities and the transition to online education during the COVID-19 pandemic negatively impacted the implementation of the third and fourth years of the long-term intervention group. By the end of the study, students in the control group showed a more pronounced trend toward smoking, low physical activity, and deterioration in general health status compared to the intervention groups [22].

In a mixed-method study conducted in the León region of Spain, the effectiveness of the digital health application (eHealth app) "SanoYFeliz," developed to promote healthy lifestyle habits among adolescents, was evaluated. A total of 301 adolescents from first- and

second-year high school students participated in the study. Students in the intervention group (n=210) actively used the app for 14 weeks, which offered features such as social networking, personalized health recommendations, and virtual rewards. Students in the control group (n=91) were only able to access the app's limited public section. The use of the app was encouraged by physical education teachers, and the involvement of students' families was also recommended. Measures assessed included age- and gender-adjusted body mass index (BMI) percentiles, adherence to the Mediterranean diet (KIDMED score), and physical activity level (PAQ-A). Students in the intervention group showed a statistically significant trend toward BMI levels closer to the ideal 50th percentile. Additionally, a significant improvement in dietary habits and a lesser decline in physical activity levels compared to the control group were observed. According to social network analysis (SNA), mutual friendship ties among students in the intervention group increased. Moreover, students identified as "leaders" in the social network were found to be more physically active and more frequent users of the app. It was concluded that these leaders positively influenced their peers by promoting physical activity behaviors [19].

A cluster randomized controlled trial conducted in Seremban, Malaysia, aimed to evaluate the effectiveness of a school-based intervention program in reducing body mass index (BMI) and age-related z-score (BAZ) among overweight and obese adolescents. A total of 400 overweight/obese adolescents participated and were randomly assigned to an intervention group (n=200) and a control group (n=200). The intervention group received a five-session lifestyle modification program based on social cognitive theory over 10 weeks, with one session every two weeks. The control group received no intervention. Primary outcome measures were BMI and BAZ, while secondary outcomes included breakfast frequency, physical activity level, self-efficacy in nutrition and weight control, self-efficacy in physical activity, and body satisfaction. In the intervention group, BMI decreased from 28.10 kg/m² to 27.93 kg/m² post-intervention and to 27.80 kg/m² during follow-up. BAZ decreased from 2.19 to 2.12 and then to 2.07. Significant improvements were also found in secondary measures such as breakfast frequency, physical activity level, healthy eating habits, and body satisfaction [21].

In a cluster randomized controlled study conducted in the Brong Ahafo region of Ghana, 732 public high school students aged 14–19 participated, with four schools randomly assigned to intervention and control groups. During the six-month intervention period, students in the intervention group received a program that included health education and physical activity modules, while the control group received no intervention. The program aimed to encourage the adoption of healthy lifestyle behaviors, focusing on healthy dietary habits and physical activity levels. In the intervention group, significant increases were observed in overall physical activity levels and consumption of fruits, vegetables, seafood, and water. There were also notable reductions in the consumption of carbohydrates, fried foods, sugary snacks, and soft drinks. Statistically significant decreases in body weight, BMI, and diastolic blood pressure were recorded in the intervention group. The findings suggest that school-based health education and physical activity programs can be effective in reducing cardiovascular disease risk factors among adolescents. However, no significant effects were found on smoking behavior or systolic blood pressure [18].

In a multicenter cluster randomized controlled trial conducted in China, 57,210 students aged 7 to 17 participated, with 30,629 in the intervention group and 26,581 in the control group. The intervention included educational programs focusing on healthy eating and physical activity. The primary outcome was the cardiovascular health (CVH) score based on the

American Heart Association's "Life's Essential 8" framework, which includes four health behaviors (diet, physical activity, nicotine exposure, and body mass index) and three health factors (blood lipids, glucose, and blood pressure). Secondary outcomes included health behavior score, health factor score, and the proportion of students achieving high CVH (CVH score ≥80). After nine months of follow-up, 22.0% of students in the intervention group met the ideal CVH criteria compared to 17.5% in the control group. The intervention was associated with an increase of 0.89 points in CVH score and a 14% higher likelihood of achieving high CVH. Subgroup analyses revealed more pronounced positive effects of the intervention among primary (grades 1–6) and lower secondary school students (grades 7–9) [20].

4. CONCLUSION AND RECOMMENDATIONS

The literature review indicates that community- and school-based interventions, as well as digital applications, have shown varying degrees of effectiveness in reducing cardiovascular risk factors among adolescents. These nurse-led interventions have resulted in significant improvements in self-care habits, nutritional and physical activity levels, body mass index (BMI), metabolic indicators, and health literacy. However, the long-term sustainability of these interventions and their lasting impact on lifestyle changes may remain limited.

It is recommended that future studies focus on developing and disseminating comprehensive, culturally sensitive, technology-supported intervention programs led by nurses. These programs should be designed to promote healthy lifestyle behaviors in adolescents through collaboration between schools, families, and communities.

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KIDNEY MORPHOLOGY IN TORTOISE (*TESTUDO GRAECA, LINNAEUS, 1758*)

ABSTRACT

Testudo graeca (Linnaeus, 1758) is a reptile species that has adapted to a terrestrial lifestyle and is widely distributed. The morphological and histological characteristics of excretory system structures play a significant role in the species' ability to withstand environmental conditions. In particular, structural analysis of the kidneys is valuable for understanding homeostatic regulation. This study aimed to describe the anatomical location and basic morphological and histological features of the kidneys in a T. graeca specimen. The study was conducted on a tortoise that was brought to Siirt University due to a carapace fracture and died during treatment. The animal was rapidly dissected, and the carapace was opened along the midline to access the internal organs. The kidneys were carefully isolated, and morphometric measurements (length, width) were recorded and photographed. Kidney tissues were fixed in 10% formaldehyde solution for microscopic analysis, passed through a graded series of alcohol and xylene, and embedded in paraffin. Sections of 5 µm thickness were stained using Crossman's trichrome method and examined under a light microscope with a digital camera. The kidneys of T. graeca are located in the posterior-dorsal region of the body cavity, symmetrically aligned on either side of the vertebral column. These organs are firmly attached beneath the carapace and are characterized by a long, broad, and dorsoventrally flattened structure. Although a distinct cortex-medulla separation is not apparent, glomerular and tubular regions are partially distinguishable. Nephrons consist of a Malpighian corpuscle, tubular segments, and collecting ducts, but notably lack the loop of Henle found in mammals. These structural features represent important adaptations for terrestrial life in this species.

Keywords: Kidney histology, kidney morphometry, spur-thighed tortoise

KARA KAPLUMBAĞASINDA (*TESTUDO GRAECA, LİNNAEUS, 1758*) BÖBREK MORFOLOJİSİ

ÖZET

Testudo graeca (Linnaeus, 1758), karasal yaşama uyum sağlamış, geniş yayılıma sahip bir sürüngendir. Bu türün çevresel koşullara direnç göstermesinde, boşaltım sistemine ait yapıların morfolojik ve histolojik özellikleri önemli rol oynamaktadır. Özellikle böbreklerin yapısal analizi, homeostatik dengenin anlaşılması açısından değerlidir. Bu çalışmada, *T. graeca* bireyine ait böbreklerin vücut içindeki anatomik konumları ile temel morfolojik ve histolojik özelliklerinin tanımlanması amaçlanmıştır. Çalışmada, karapaks kırığı nedeniyle Siirt Üniversitesi'ne getirilen ve tedavi sırasında ölen bir kaplumbağa kullanılmıştır. Hayvan hızlıca diseke edilmiş, karapaks orta hattan açılarak iç organlara ulaşılmıştır. Böbrekler dikkatlice izole edilmiş, morfometrik ölçümler (uzunluk, genişlik) yapılmış ve fotoğraflanmıştır. Mikroskobik inceleme için böbrek dokuları %10'luk formaldehit ile tespit edilmiş, alkol ve ksilen serilerinden geçirilerek parafine gömülmüş, 5 µm kalınlığında kesitler alınarak Crossman'ın trikrom yöntemiyle boyanmıştır. Kesitler dijital kameralı ışık mikroskobu ile incelenmiştir. Kaplumbağa böbrekleri, vücut boşluğunun arka-dorsalinde, omurganın her iki yanında simetrik yerleşim göstermektedir. Kabuk altına sıkıca tutunmuş, uzun, yassı ve geniş yapıda organlardır. Korteks-medulla ayrımı net olmamakla birlikte, glomerüler ve tübüler bölgeler kısmen ayrışmıştır. Nefronlar Malpighi cisimciği, tübül sistemleri ve toplayıcı kanalcıklardan oluşmakta; memelilerdeki Henle kulpu ise bulunmamaktadır. Bu yapısal özellikler, türün karasal çevreye uyumuna katkı sağlayan önemli adaptasyonlar arasında yer almaktadır.

Anahtar kelimeler: Böbrek histolojisi, böbrek morfometrisi, kara kaplumbağası

INTRODUCTION

The spur-thighed tortoise (Testudo graeca) is a small to medium-sized terrestrial tortoise species widely distributed across the Mediterranean basin, North Africa, Southern Europe, and Western Asia (Anadon et al., 2012). In Turkey, it is commonly found in the Aegean, Mediterranean, and Southeastern Anatolia regions, reaching a maximum straight carapace length of approximately 25 cm (Baran & Atatür, 1998). Typically inhabiting semi-arid and low-humidity environments, this species remains active during the day, retreating to shaded areas or underground burrows during extreme heat and dry periods to minimize water loss (El Mouden et al., 2006). Reptilian kidneys exhibit a simpler anatomical structure compared to those of mammals and birds, characterized by fewer functional units and limited capacity for urine concentration (Holz, 2020). Notably, reptilian nephrons lack the loop of Henle, resulting in an inability to produce hypertonic urine or to extensively reabsorb water (Innis, 1997). Consequently, these limitations impose significant physiological constraints on kidney function in terrestrial tortoises. Nevertheless, T. graeca compensates through alternative adaptive mechanisms, primarily adopting a uricotelic excretion strategy, which effectively minimizes water loss during nitrogenous waste elimination (Johnson et al., 2016). Thus, by excreting uric acid, T. graeca effectively conserves water while safely eliminating nitrogenous wastes (Wright, 2018). Moreover, given their limited renal water retention capacity, tortoises rely on extra-renal structures, notably an extensive urinary bladder, for water balance regulation. Many tortoise species possess considerable bladder storage capacity, enabling them to fill their bladder during wet periods and subsequently reabsorb this stored water when facing prolonged drought conditions (Johnson et al., 2016). Collectively, these adaptations form an effective water conservation strategy, facilitating survival in arid habitats. Kidney morphology fundamentally supports these physiological adaptations. Anatomical and histological features of T. graeca kidneys reflect adaptations crucial for terrestrial life. In chelonians, kidneys are flat, highly lobulated organs firmly attached to the posterior body wall (Solomon, 1985). The number of nephrons in tortoises is significantly lower compared to mammals, with approximately one thousand times fewer nephrons for a given body mass (Wright, 2018). Accordingly, tortoise glomeruli tend to be smaller and less vascularized compared to those of mammals and birds, representing a morphological adaptation aimed at conserving water. While literature on the renal histology of T. graeca is limited, ultrastructural studies conducted in the 1980s provide valuable insights. Zuasti et al. (1986) reported significant ultrastructural differences in the glomerular structure of T. graeca between active and hibernation periods through electron microscopy. In this study, detailed histological examinations and morphometric measurements of kidney tissue obtained from an injured T. graeca individual are presented. The objective was to characterize the kidney morphology of T. graeca at both macroscopic and microscopic levels, comparing findings with existing literature and evaluating adaptations related to terrestrial life. Thus, this study aims to contribute to the limited body of literature concerning tortoise renal morphology and function.

MATERIAL and METHODS

In our study, a turtle brought to Siirt University Animal Health Practice and Research Hospital with a carapace fracture and which subsequently died during treatment was used. The deceased turtle was dissected immediately. For this purpose, the shell structure known as the carapace was carefully opened from the midline and laterally removed. The kidney tissues located dorsally within the body cavity were carefully dissected and isolated. Morphometric parameters such as kidney length, width, and thickness were recorded.

At the microscopic stage of the study, tissue samples taken from the kidneys were fixed in a 10% formaldehyde solution pH 7.0 for 24 hours at room temperature. The tissues underwent dehydration through a graded alcohol series and clearing with xylol before being embedded in paraffin wax. The paraffin blocks were sectioned at a thickness of 5 µm. Sections were stained using Crossman's trikrome for histological examination. The sections were examined under a light microscope (DM750, Leica) equipped with a digital camera (MC170, Leica), and representative sections were photographed.

RESULTS

According to the macroscopic findings, the kidneys of *Testudo graeca* were located in the caudodorsal part of the abdominal cavity, near the pelvic region (Figure 1). Each kidney exhibited a triangular, pyramid-like shape rather than the typical bean-shaped form and extended in a roughly parallel orientation. In freshly dissected specimens, the kidneys appeared dark reddish-brown, with a smooth surface covered by a thin fibrous capsule. The sizes of the right and left kidneys were similar, with average dimensions of approximately 25.18 mm in length and 22.48 mm in width (Figure 2). Considering the carapace length of the specimen, these values indicate relatively small kidneys in proportion to the overall body size.



Figure 1. Dorsal and lateral views of the dissected *Testudo graeca*.
(A) Lateral view of the dissected body cavity of *Testudo graeca*. The kidney is marked with an asterisk (*).
(B) Dorsal view of the dissected specimen. The kidney is indicated by an asterisk (*).

The medial margin of each kidney displayed the entry points of the renal artery and vein. A distinct renal hilum was not observed; instead, blood vessels branched diffusely throughout the kidney parenchyma. The testes were noted immediately medial to the kidneys. The ureters originated from the posteroventral pole of each kidney and extended caudally over a short distance. No renal pelvis or collecting reservoir, as typically seen in mammals, was identified macroscopically. It was assumed that the collecting ducts connect directly to the ureters. Additionally, pyramidal medullary structures commonly observed in mammalian kidneys were absent in this specimen. Cross-sectional examination confirmed the lack of a distinct separation between the cortex and medulla.



Figure 2. Macroscopic view of the *Testudo graeca* kidney with morphometric measurements. The length and width were recorded using a millimetric ruler for scale.

Histological examinations revealed that the kidney of *Testudo graeca* is composed of the fundamental nephron components. These structures include the renal corpuscle (Malpighian corpuscle), proximal tubule, intermediate segment, distal tubule, and collecting ducts. The renal corpuscle consists of a glomerulus surrounded by Bowman's capsule. The glomerulus is formed by a tuft of capillaries, and its visceral layer is covered by specialized cells known as podocytes. Bowman's capsule comprises two layers: an inner visceral layer (podosyte-lined) and an outer parietal layer composed of simple squamous epithelium (Figure 3).

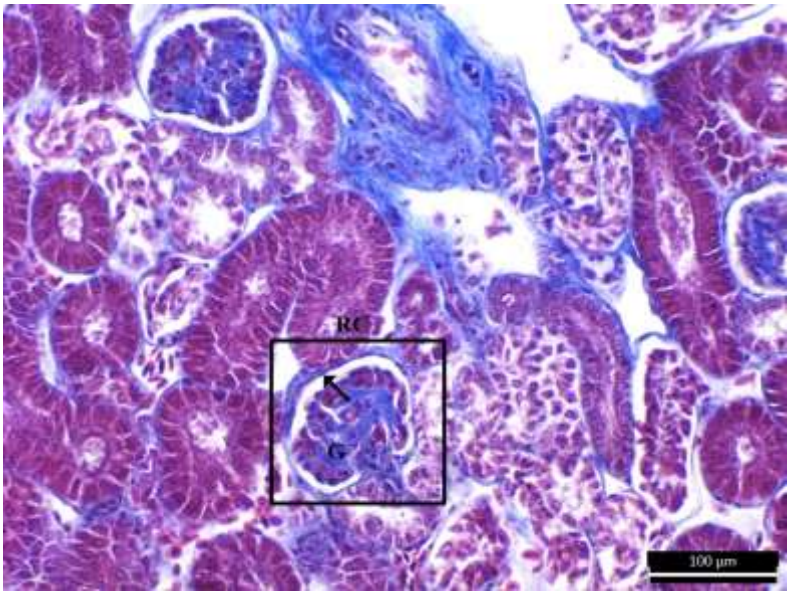


Figure 3. Light microscopic image of renal corpuscle (RC). G: glomerulus; arrow: parietal layer. Crossmon's triple staining. Bar: 100 µm.

The proximal tubules are lined by low columnar epithelial cells with a narrow lumen and weakly eosinophilic cytoplasm. In histological sections, proximal tubules were observed more frequently than distal tubules. The intermediate segments are composed of simple cuboidal epithelial cells. Distal tubules, in contrast, have a wider lumen and are lined with low columnar epithelial cells with less eosinophilic cytoplasm (Figure 4).

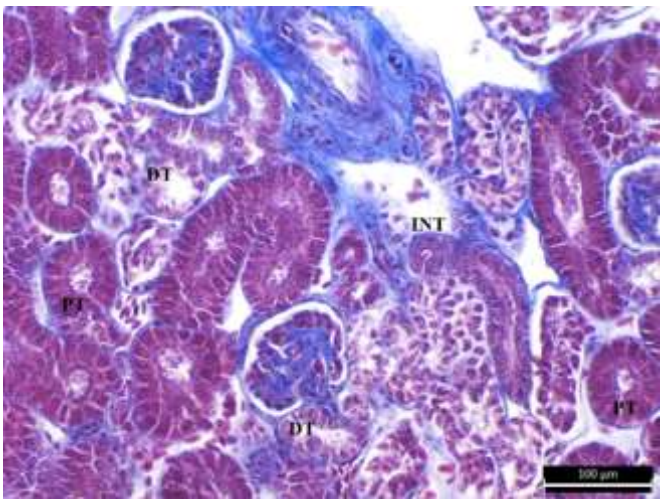


Figure 4. Light microscopic image of proximal (PT), intermediate (INT), and distal (DT) tubule segments. Crossmon's triple staining. Bar: 100 µm.

The collecting ducts are distinctly visible and widely distributed within the renal parenchyma. These ducts are lined by tall columnar epithelium and possess a wide lumen (Figure 5).

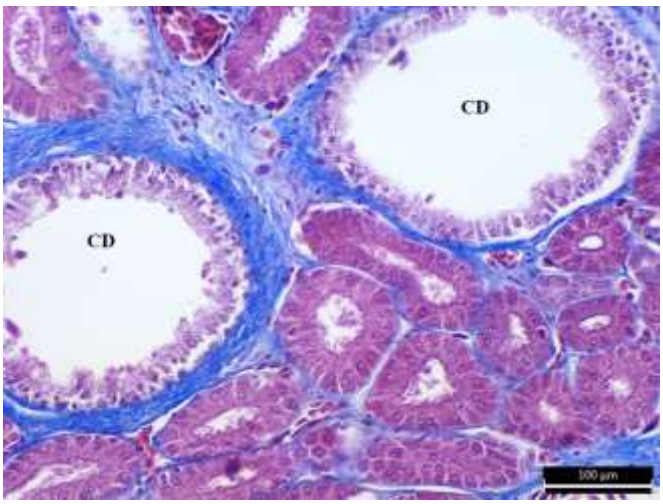


Figure 5. Light microscopic image of collecting ducts (CD). Crossmon's triple staining. Bar: 100 µm.

Among all nephron structures, no formation resembling a loop of Henle was observed. This finding indicates that Testudo graeca lacks the mechanism for producing concentrated urine as seen in mammals, and instead maintains water balance primarily through restricted glomerular filtration and fluid reabsorption via the cloaca and urinary bladder. Additionally, no structure resembling a loop of Henle was observed in the histological sections.

DISCUSSION

In this study, the histological structure of the kidney in Testudo graeca was comprehensively evaluated, revealing morphological features associated with terrestrial adaptation. The findings were largely consistent with data from previous studies. Macroscopic examination demonstrated that the kidneys are dorsally located near the pelvic region, exhibiting a lobulated, triangular-pyramidal shape. This morphology aligns with the general renal structure previously described in Chelonia (Solomon, 1985). The kidneys of T. graeca were found to be small, flat, and lobulated macroscopically. With average dimensions of 2.5 × 2.2 cm, these kidneys are proportionally much smaller than those of similarly sized mammals, a phenomenon attributed to the notably lower total nephron count in turtles (Wright, 2018).

Furthermore, the absence of a renal pelvis and direct connection of the collecting ducts to the ureter represent significant differences compared to mammalian anatomy, reflecting typical turtle kidney structure; indeed, literature indicates that turtle kidneys lack renal pelvis and renal pyramids (Paries et al., 2019). This distinct organization of the collecting system shifts the responsibility of urine storage from the kidneys to the bladder. In turtles, urine accumulates in the bladder where additional water reabsorption occurs (Holz, 2020). This adaptation is crucial due to the limited concentrating capacity of turtle kidneys. In our case, a notably large bladder was observed during dissection. It is likely that the animal fills its bladder during periods when water is available and utilizes this reserve during drought conditions. It is known that large terrestrial tortoises, such as Galapagos tortoises, fill their bladders with fresh water following rainfall and reabsorb this stored water during prolonged dry periods (Johnson et al., 2016).

Due to their positioning in the posterior abdominal cavity, kidneys of Testudo graeca are closely associated with surrounding organs. In male individuals, the testes are located immediately cranial and slightly ventral to each kidney (Kirchgessner and Mitchell, 2009). Epididymides are situated behind each testis and adjacent to the anterior margin of the kidneys. The ductus deferens extends from the testis alongside the ureter toward the cloaca (Kirchgessner and Mitchell, 2009).

The kidney structure of Testudo graeca exhibits significant differences compared to mammalian and avian kidneys but shares general similarities with other reptilian kidneys. These similarities and differences reflect evolutionary adaptations and environmental adaptation strategies. Mammalian kidneys classically exhibit two distinct regions: an outer cortex and an inner medulla. The cortex densely contains glomeruli and proximal and distal tubule segments, whereas the medulla houses Henle loops and collecting ducts, forming macroscopic renal pyramids that drain into a renal pelvis. The Henle loop is a distinctive nephron segment in mammals that enables urine concentration significantly above plasma osmolarity through a countercurrent multiplier mechanism. Birds represent an intermediate form with two nephron types: reptilian-type nephrons (lacking Henle loops, short and cortical) and mammalian-type nephrons (possessing Henle loops extending into the medulla) (Morit et al., 1985).

Reptilian kidneys generally show a more primitive structural plan compared to mammals and birds. Most reptiles, with few exceptions such as crocodilians, lack Henle loops, leading to indistinct cortical-medullary differentiation (Yari and Gharzi, 2013). Our findings confirm this literature, indicating the absence of renal pelvis and direct connections of collecting ducts to the ureter, consistent with typical turtle kidney anatomy as described by Zwart (2006). One of the most significant findings in our study was the notably small and sparsely

capillarized glomeruli, indicative of a limited glomerular filtration surface. Small and simple glomerular structures in T. graeca and other terrestrial turtles have been documented previously (Zuasti et al., 1986). Researchers such as Peek and McMillan (1979) suggest that reptilian glomeruli might have evolved for reduced filtration pressures and rates.

CONCLUSION

In conclusion, the renal morphology of *Testudo graeca* possesses a set of features that optimize the balance between water retention and waste excretion. These characteristics form the foundation of the tortoise's ability to withstand environmental stressors such as dehydration and seasonal changes. Our study provides original insights into these adaptive strategies at the histological level, contributing novel data to the existing literature. In future studies, examining *T. graeca* kidneys across different seasons or within various age and sex groups may help to better understand the dynamics of these adaptations. Furthermore, since a thorough understanding of normal histology is essential for diagnosing renal diseases in tortoises, this study lays a foundation for distinguishing between normal and pathological conditions. By shedding light on the kidney structure of *T. graeca*, a species commonly found in our region, this research offers fundamental information relevant to reptile physiology and pathology. Particularly in the fields of exotic animal veterinary medicine and comparative renal research, the findings presented here provide valuable data for understanding normal tortoise kidney histology.

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BIG DATA-BASED EPIDEMIOLOGICAL SURVEILLANCE APPLICATIONS

ABSTRACT

Aim: This review study aims to reveal the role of big data, which is becoming increasingly widespread in the field of health, especially in epidemiological monitoring processes, and to examine the current practices, contributions, and challenges in this field from a holistic perspective.

Method: In this review study, a literature review was conducted. Web of Science, PubMed, Scopus databases were used in the search process and keywords such as “big data”, “epidemiological surveillance”, “public health”, “health informatics” and “real-time data analysis” and their combinations were used. No date limitation was made in the selection of studies, and current and basic sources directly related to epidemiologic surveillance were taken into consideration. The review included systematic reviews, original studies and case reports.

Results: The potential of big data-based systems to contribute to public health is evaluated in the context of technological developments and digital transformation. Big data is reshaping the processing and interpretation of health data in terms of volume, variety, veracity, velocity, and value. Data from various sources, such as electronic health records, mobile health applications, wearable technologies, social media data, and genomic databases, plays a critical role in the early diagnosis, monitoring, modelling, and intervention processes of communicable and non-communicable diseases. Systems such as HealthMap, BioSense, GISAID, and BlueDot demonstrate the success of this technology for epidemiological applications. However, data quality, missing data, cross-system integration challenges, algorithmic bias, and ethical issues are all important factors limiting progress in this field.

Conclusion: Consequently, in the future, the development of artificial intelligence and machine learning-supported epidemiological modelling, strengthening international data sharing mechanisms, and increasing the big data literacy of health professionals will make epidemiological monitoring systems more effective and inclusive. Big data-based monitoring applications contribute to the design of timely, proactive, and predictive

interventions against public health threats and thus stand out as a strategic tool in the digital transformation of public health policies.

Keywords: Big data, digital health systems, epidemiologic surveillance, public health, health informatics.

BÜYÜK VERİ TEMELLİ EPİDEMİYOLOJİK İZLEME UYGULAMALARI

ÖZET

Amaç: Bu derleme çalışmasının amacı, sağlık alanında giderek yaygınlaşan büyük veri (big data) kullanımının, özellikle epidemiyolojik izleme süreçlerindeki rolünü ortaya koymak ve bu alandaki güncel uygulamaları, katkıları ve karşılaşılan zorlukları bütüncül bir bakış açısıyla incelemektir.

Yöntem: Bu derleme çalışmasında, literatür taraması gerçekleştirilmiştir. Tarama sürecinde Web of Science, PubMed, Scopus veri tabanları kullanılarak, "big data", "epidemiological surveillance", "public health", "health informatics" ve "real-time data analysis" gibi anahtar kelimeler ve bunların kombinasyonları kullanılmıştır. Çalışmaların seçiminde tarih sınırlaması yapılmamış, epidemiyolojik izlemeyle doğrudan ilişkili güncel ve temel kaynaklar dikkate alınmıştır. Derleme kapsamına sistematik derlemeler, özgün araştırmalar ve vaka raporları dahil edilmiştir.

Bulgular: Büyük veriye dayalı sistemlerin halk sağlığına katkı potansiyeli, teknolojik gelişmeler ve dijital dönüşüm bağlamında değerlendirilmektedir. Büyük veri, hacim, çeşitlilik, hız, doğruluk ve değer boyutlarıyla, sağlık verilerinin işlenmesini ve anlamlandırılmasını yeniden şekillendirmektedir. Elektronik sağlık kayıtları, mobil sağlık uygulamaları, giyilebilir teknolojiler, sosyal medya verileri ve genomik veri tabanları gibi çok çeşitli kaynaklardan elde edilen veriler, bulaşıcı ve bulaşıcı olmayan hastalıkların erken tanı, izleme, modelleme ve müdahale süreçlerinde kritik rol oynamaktadır. HealthMap, BioSense, GISAID ve BlueDot gibi sistemler, bu teknolojinin epidemiyolojik uygulamalardaki başarısını göstermektedir. Ancak veri kalitesi, eksik veri, sistemler arası entegrasyon zorlukları, algoritmik önyargı ve etik sorunlar, bu alandaki ilerlemeyi sınırlayan önemli faktörlerdir.

Sonuç: Sonuç olarak, gelecekte yapay zekâ ve makine öğrenmesi destekli epidemiyolojik modellemelerin geliştirilmesi, uluslararası veri paylaşım mekanizmalarının güçlendirilmesi ve sağlık profesyonellerinin büyük veri okuryazarlığının artırılması, epidemiyolojik izleme sistemlerinin daha etkili ve kapsayıcı hale gelmesini sağlayacaktır. Büyük veri temelli izleme uygulamaları, halk sağlığı tehditlerine karşı zamanında, proaktif ve öngörücü müdahalelerin tasarlanmasına katkı sunmakta ve böylece kamu sağlığı politikalarının dijital dönüşümünde stratejik bir araç olarak öne çıkmaktadır.

Anahtar Kelimeler: Büyük veri, dijital sağlık sistemleri, epidemiyolojik izleme, halk sağlığı, sağlık bilişimi.

1. Giriş

Hızlı teknolojik gelişmelerin ve artan küresel sağlık tehditlerin damgasını vurduğu çağda, büyük verinin dijital sağlık sistemlerine entegrasyonu halk sağlığında dönüştürücü bir güç olarak ortaya çıkmıştır. Son yirmi yılda üretilen veri miktarı artmaya devam ettikçe, onu işleme ve analiz etme ihtiyacı giderek daha önemli hale geldi. Bu durum, büyük veriyi işlemeye yönelik yeni araç ve tekniklerin (Hadoop ve Apache Spark gibi dağıtık hesaplama çerçeveleri, makine öğrenimi algoritmaları gibi) geliştirilmesine yol açmıştır [1]. Çeşitli alanlardaki araştırmacılar ve uygulayıcılar büyük veriyi çalışmalarına entegre etmeye başladıkça, büyük verinin uygulanması, özellikleri, potansiyel faydaları ve sınırlamalarını tartışan bir literatür ortaya çıkmıştır. Büyük Veri kavramı ve özellikleri literatürde kapsamlı bir şekilde tartışılmış ve çok sayıda araştırmacı Büyük Veri tanımlarını ve onunla yakından ilişkili özellikleri özetlemiştir

Hacmi, hızı ve çeşitliliği ile karakterize edilen büyük veri, gerçek zamanlı veri analizi için önemli fırsatlar sunmaktadır. Dijital olarak toplanan ve depolanan veri miktarı çok büyüktür ve hızla artmaktadır. Büyük veri, astronomide (örneğin, teleskopik bilgilerin Sloan Dijital Gökyüzü Araştırması), perakende satışlarda (örneğin, Walmart'ın geniş işlem sayısı), arama motorlarında (örneğin, Google'ın önceki web verilerine dayalı bireysel aramaları özelleştirmesi) ve siyasette (örneğin, bir kampanyanın web aramalarına göre adaylarını destekleme olasılığı en yüksek olan kişilere yönelik siyasi reklamlara odaklanması) başarıyla kullanılmıştır [2]. Bununla birlikte, halen halk sağlığı uygulamalarına ilişkin önemli bir bilgi boşluğu bulunmaktadır.

Epidemiyolojideki araştırmalar, hastalıkların nedenlerinin anlaşılmasını iyileştirmek ve yayılmalarını önlemek için insan hastalıklarının dağılımını, görülme sıklığını ve etiyolojisini belirlemeyi amaçlar [3]. Geleneksel olarak, epidemiyoloji hastanelerdeki sağlık personeli, muayenehanelerdeki doktorlar ve halk sağlığı kurumları tarafından toplanan verilere dayanmaktadır. Ancak son yıllarda, modern iletişimin ve elektronik cihazların kullanımının artmasının bir sonucu olarak bıraktıkları dijital izler aracılığıyla verilerin sıklıkla doğrudan bireylerden toplandığı yeni veri kaynakları ortaya çıkmıştır [4]. İnsanların yaptığı ve söyledikleri şeylerin büyük bir kısmı elektronik olarak, genellikle erişilebilir biçimde ve dolayısıyla analize uygun şekilde saklanıyor. Bu veri selinden anlamlı bilgi çıkarmak zorludur, ancak bu bilgiler epidemiyoloji için önemli bir potansiyele sahiptir.

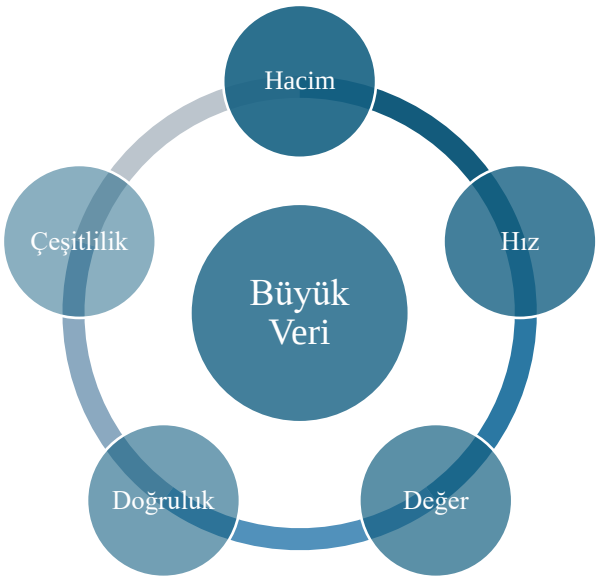
Sosyal medya trendlerini, elektronik sağlık kayıtlarını ve mobil sağlık uygulamalarını entegre eden sistemler de dahil olmak üzere, bulaşıcı hastalık gözetiminde gerçek zamanlı veri analizinin faydasını gösteren çeşitli çalışmalar bulunmaktadır [5]. Ancak, bu çalışmaların çoğu keşif amaçlı veya bölgeye özgü kalmaktadır. Dahası, büyük verinin platformlar arasında standartlaştırılması ve veri gizliliği ile güvenliğinin sağlanmasında önemli zorluklar bulunmaktadır; bu sorunlar mevcut literatürde genellikle yeterince ele alınmamaktadır. Bu sistematik olmayan derleme çalışması, sağlık alanında giderek yaygınlaşan büyük veri (big data) kullanımının, özellikle epidemiyolojik izleme süreçlerindeki rolünü ve bu alandaki güncel uygulamaları, katkıları ve karşılaşılan zorlukları bütüncül bir bakış açısıyla inceleyerek bu boşluğu gidermeyi amaçlamaktadır. Mevcut çalışma halk sağlığında dijital dönüşüm üzerine büyüyen literatüre katkıda bulunmakta ve gelecekteki araştırma ve uygulamalar için kanıta dayalı öneriler sunmaktadır.

2. Yöntem

Bu derleme çalışmasında, sağlık alanında büyük veri kullanımının epidemiyolojik izleme süreçlerindeki etkisini değerlendirmek amacıyla literatür taraması yapılmıştır. Literatür taramasında Web of Science, PubMed, Scopus ve Google Scholar uluslararası akademik veri tabanları kullanılmıştır. Taramada "big data", "epidemiological surveillance", "public health", "health informatics", "real-time data analysis" ve "digital health systems" gibi İngilizce anahtar kelimeler ve bunların kombinasyonları kullanılmıştır. Çalışmaların seçiminde tarih sınırlaması yapılmamış, konuyla doğrudan ilişkili olan güncel ve temel yayınlar dikkate alınmıştır. Derleme kapsamına, sistematik derlemeler, özgün araştırmalar, vaka analizleri ve politika raporları dahil edilmiştir. Tarama sonucunda elde edilen literatür, büyük veri kavramı ve önemi, sağlık alanında büyük veri kaynakları, epidemiyolojik izleme yöntemleri ve başarılı uygulama örnekleri başlıkları altında incelenmiştir. Çalışmaların seçimi ve inceleme sırasında içerik uygunluğu, bilimsel geçerlilik ve çalışmanın epidemiyolojik izlemeye katkı düzeyi temel kriterler olarak dikkate alınmıştır.

3. Büyük Veri Kavramı ve Önemi

Büyük Veri'nin resmi bir tanımı konusunda fikir birliğinin olmamasına rağmen, yıllar boyunca araştırmalar ve çalışmalar ilerlemeye devam etti. Birçok araştırmacı, özünü daha iyi yakalamayı amaçlayarak Büyük Veri'nin kapsamlı tanımlarını sağlamaya çalışıyor. Ancak, evrensel olarak kabul görmüş bir tanım henüz ortaya çıkmadı. Bunun yerine, genel olarak kabul görmüş bir açıklama, Büyük Veri'yi hacim, çeşitlilik, hız gibi beş "V" özellikleri (5V: Volume, Variety, Velocity, Veracity, Value) aracılığıyla tasvir etmektedir [6]. Büyük Veri genellikle yüksek hacim (veri miktarı açısından), yüksek hız (veri giriş ve çıkış hızı açısından), yüksek çeşitlilik (veri türleri ve kaynakları aralığı açısından) ve yüksek doğruluk (doğruluk ve doğruluk açısından) özelliklerini gösterir. Büyük Veri'nin etimolojisi, ilk olarak John Mashey tarafından büyük veri kümelerinin işlenmesi ve analizi için kullanılan 1990'ların ortalarına kadar uzanmaktadır [7]. Başlangıçta Büyük Veri üç özellik ile karakterize edilirken daha sonra bu beş özelliğe genişletilmiştir. Büyük Veri'nin beş temel özelliği aşağıda şekil 1'de sunulmuştur.



Şekil 1. Büyük temel bileşenleri

Volume (hacim): Muazzam miktarda veriden oluşmaktadır [8].

Variety (çeşitlilik): Yapılandırılmış, yarı yapılandırılmış ve yapılandırılmamış [8].

Variety (hız): Gerçek zamanlı olarak oluşturulur [8].

Veracity (doğruluk): Veriler dağınık olabilir, belirsizlik ve hata içerebilir [9].

Value (değer): Birçok içgörü çıkarılabilir ve veriler yeniden kullanılabilir [9].

4. Sağlık Alanında Büyük Veri Kaynakları

Bu bölümde sağlık alanında büyük veri kaynaklarından olan, elektronik sağlık kayıtları, mobil sağlık ve giyilebilir teknolojiler, sosyal medya ve çevrim içi veri akışları ile genomik ve biyomedikal veri tabanları ele alınmış, veri üretimi ve kullanımı açısından örneklerle aşağıda açıklanmıştır.

4.1.Elektronik Sağlık Kayıtları (EHR)

Tıbbi kayıtlar sağlık hizmetlerinin ortaya çıkışından beri mevcuttur. İlk zamanlarda, tıbbi kayıtlar hastalığı ve hastalığın muhtemel nedenini kaydetmek için kullanılırdı. Elektronik Sağlık Kayıtları (EHR), tıbbi testlerin sonuçları, doktor açıklamaları, reçeteler, görüntüler vb. gibi bireysel hasta belgelerinin dijital bir temsilidir [10]. Elektronik sağlık kayıtlarının kullanımı doktorlar ve sağlık hizmeti sağlayıcıları arasında yavaş bir şekilde yaygınlaştı. EHR'lerin yavaş benimsenmesinin nedenleri arasında, maliyet, ulusal standartların eksikliği ve sağlık hizmeti sağlayıcılarının hükümet düzenlemelerine ve hasta gizliliği gerekliliklerine uymak için büyük miktarda zaman ve para harcaması gösterilebilir [11]. 2009'da hastanelerin %8'inden azının elektronik sağlık kaydına sahip olduğu tahmin ediliyordu [12]. 2012'de, dünya çapındaki dijital sağlık hizmeti verilerinin hacminin 500 petabayta eşit olduğu tahmin edilmekle birlikte, 2020 yılında 25.000 petabayta ulaşması bekleniyordu. Bu büyük miktardaki veriler, dağıtılmış işleme mimarisi gibi belirli hesaplama yöntemleri gerektirir [13]. Dolayısıyla EHR'lerin karmaşıklığı, heterojenliği, hızlı büyümesi ve boyutu göz önüne alındığında, sağlık hizmeti verileri aynı zamanda büyük veri sorunu olarak sınıflandırılabilir ve 5V'yi etkin bir şekilde ele almak için onu analiz etmek üzere özel araçlara ihtiyaç duyulmaktadır [14].

4.2.Mobil Sağlık ve Giyilebilir Teknolojileri

Mobil sağlık (m-sağlık), mobil telefonlar ve hasta izleme cihazları vb. kullanılarak sağlığın izlenmesidir [15]. Şu anda, m-sağlık için 500'den fazla proje ve dünya çapında yaklaşık 40.000 tıbbi tabanlı mobil uygulama da mevcuttur. Özellikle kalp atış hızını, glikoz seviyesini, kan basıncını, uyku düzenlerini ve beyin aktivitesini izlemek için tasarlanmış mobil tabanlı tıbbi cihazlar yaygın olarak kullanılmaktadır [16–19]. Mobil sağlık uygulamalarının küresel kullanımı hızla artmakta ve bu ve diğer akıllı bağlantılı cihazlardan üretilen hacimli veri setleri, patlayıcı seviyelerde küresel olarak toplanan ve depolanan karmaşık, hacimli ve çok boyutlu mobil sağlık verilerine yol açmaktadır. Bu veri hacminin nasıl daha iyi yönetileceği, optimize edileceği ve analiz edileceği konusunda büyük bir baskılar bulunmaktadır. Daha da önemlisi, yüksek hacimli bu verilerin hastalara, klinisyenlere ve diğer paydaşlara fayda sağlayabilecek anlamlı bilgilere nasıl dönüştürüleceği konusundaki belirsizliktir. Apple (HealthKit), Google (DeepMind), Microsoft gibi büyük şirketlerin daha akıllı mobil sağlık sistemleri geliştirmeye yönelik son gelişmeleri bu eğilimlerin kanıtıdır [20].

4.3. Sosyal Medya ve Çevrim İçi Veri Akışları

İnternetin popülerliği ve Web 2.0 teknolojilerinin ortaya çıkışı, web içeriğini kullanıcı tarafından yaratılan içeriğe dönüştürmüştür [21]. Bu, programlamaya ihtiyaç duymadan içeriklerin yayınlanmasına yardımcı olmuştur. Günümüzde Web 2.0 ve sosyal medyadaki ilginç konulara, yorumlara ve görüşlere gerçek zamanlı olarak İnternet üzerinden küresel olarak kolayca erişilebilmektedir. Dahası sosyal medyanın yaygınlaşması ve benimsenmesi, araştırmacılar ve uygulayıcılar için kapsamlı fırsatlar ve zorluklar sağlamıştır. Dünya çapında bir milyardan fazla insan, nispeten kısa zaman dilimlerinde çok büyük miktarda yapılandırılmamış veri üreten sosyal medya platformlarını kullanmaktadır. Kullanıcılar tarafından üretilen devasa miktardaki veri, kullanıcıların geçmiş bilgilerinin ve günlük faaliyetlerinin bu platformlara entegre edilmesinin bir sonucudur [22]. Büyük miktarda yapılandırılmamış veri üreten sosyal ağ sitelerine örnek olarak Facebook, X (Eski adı: Twitter), Instagram, LinkedIn, bloglar, vikiler ve YouTube verilebilir. Sosyal medya büyük verileri ve hesaplama araçlarındaki ilerleme, insan davranışına ilişkin önemli içgörülerin anahtarı olarak ortaya çıkmıştır ve şirketler, bireyler ve hükümetler tarafından sürekli olarak depolanmakta ve işlenmektedir [23].

4.4.Genomik ve Biyomedikal Veri Tabanları

Tıp bilimi ve bilgi teknolojileri alanındaki atılımlar, sağlık sektörü ile yaşam bilimleri sektörü arasında, hastalar, doktorları ve biyofarmasötik şirketleri arasında hızla daha samimi ve etkileşimli ilişkilere yol açacak bir yakınlaşmaya yol açtı [24]. Büyük veri analitiği, bu gelişmiş ilişkilerin teşvik edilmesinde önemli ve vazgeçilmez bir role sahiptir, çünkü parmak ucundaki genomun olağanüstü ancak izole edilmiş harikasını büyük ölçüde zenginleştirmektedir. Sağlık hizmeti sağlayıcıları ve ilaç üreticileri artık sadece bir birey için değil, aynı zamanda belirli popülasyon çalışmalarında artan sayıda hastadan elde edilen omik (omics) verileri toplu olarak keşfetme ve analiz etme yeteneğine sahiptir [25]. Yeni nesil dizileme (NGS) teknolojileri, tüm genom dizileme (WGS), tüm ekzom dizileme (WES) ve/veya hedefli dizileme gibi, hastalık ve ilaçla ilişkili genetik varyantları belirleyerek hassas tıbbı ilerletmek için biyomedikal çalışma ve tıbbi uygulamada giderek daha fazla kullanılmaktadır [26]. Genomik tıp, hastaların genomik bilgilerini kullanarak tanı veya tedavi kararları için bireyselleştirilmiş stratejiler oluşturmaya çalışır. Çeşitli genomik verilerin ve EHR'lerin bir Büyük Veri altyapısında bütünleştirilmesi ve işlenmesi beraberinde birtakım zorlukları getirirken aynı zamanda bireyselleştirilmiş tanı ve tedavi için klinik olarak eyleme geçirilebilir genetik varyantları belirlemek için etkili ve verimli bir yaklaşım geliştirmek için uygulanabilir bir fırsat da sağlar [27].

5. Epidemiyolojik İzlemede Büyük Verinin Kullanımı

Epidemiyolojik izlemede büyük veri kullanımı, halk sağlığında erken tanı, risk değerlendirmesi ve müdahale stratejilerinin geliştirilmesi açısından giderek daha da önemli hale gelmektedir. Büyük veri; sosyal medya, mobil uygulamalar, sensörler, sağlık kayıtları ve coğrafi bilgi sistemlerinden gelen çok çeşitli verilerin entegrasyonunu mümkün kılar. Bu sayede hem bulaşıcı hem de bulaşıcı olmayan hastalıkların izlenmesi, tahmini ve yönetimi daha etkili hâle gelmektedir. Bu bölümde, erken uyarı sistemlerinden mekânsal-zamansal modellemeye kadar çeşitli dijital çözümlerle desteklenen büyük veri uygulamaları ele alınmıştır.

5.1.Bulaşıcı Hastalık İzleme ve Erken Uyarı Sistemleri

Erken uyarı sistemleri (Early warning systems-EWS), bulaşıcı hastalık gözetimi ve salgın tespitinde önemli bir rol oynar. Etkili erken uyarı sistemleri (EUS) tanı öncesi verileri derler ve acil servis kayıtları, halk sağlığı veri tabanları ve web tabanlı platformlar dahil olmak üzere çeşitli veri kaynaklarını kullanır [28]. Son gelişmeler, tahmin yeteneklerini artırmak amacıyla blok zinciri teknolojisi, sosyal medya duygu analizi ve atık su takibi gibi yöntemlerin bir arada kullanılmasını öne çıkarıyor [29]. Sendromik ve olay tabanlı gözetimin entegrasyonu, özellikle kitlesel etkinlikler gibi yüksek riskli ortamlarda sistemin hızlı ve etkili yanıt verme kapasitesini artırmaktadır [30]. Ancak dijital gözetim sistemlerinin uygulanması, gizlilik, veri bütünlüğü ve bireysel haklar konusunda etik kaygılara yol açmaktadır [31]. Bu sorunların giderilebilmesi için açık ve etkili yönetişim çerçevelerinin oluşturulması ve kamuoyuna yeterli bilgilendirme yapılması büyük önem taşır. Bildirim gecikmelerini en aza indirmek ve olası salgın risklerini azaltmak için EUS'nin sürekli olarak değerlendirilmesi ve doğrulanması gereklidir [30]. Gelecekteki araştırmalar, erken uyarı ve tahmin kapasitesini güçlendirmek amacıyla yeni teknolojilerin sağlık ve sosyal veri kaynaklarıyla entegrasyonuna odaklanmalıdır [29].

5.2.Bulaşıcı Olmayan Hastalıkların Takibi ve Yönetimi

Bulaşıcı olmayan hastalıkların (BOH) yönetimi ve izlenmesi giderek daha fazla büyük veri ve dijital teknolojilerden yararlanmaktadır. BOH gözetimi, risk faktörlerini ve müdahale etkilerini izlemek için çok önemlidir ve birden fazla veri kaynağının entegrasyonu bu çabaları geliştirir (Li et al., 2022). Büyük veri, bulut bilişim ve nesnelerin interneti (IoT) kullanan uzaktan izleme sistemleri, kronik hastalar için öz yönetimi ve sağlık müdahalelerini iyileştirebilir [33]. Hassas halk sağlığı, ABD'de ESP ve RiskScape ve Avustralya'da PopHQ gibi platformlar, dijital sağlık verilerinden yararlanarak BOH önlemeye dönüştürücü çözümler sunar [34]. Sağlık kuruluşları, bakım kalitesi, hizmet kalitesi, kriz yönetimi ve veri yönetimi gibi alanlara odaklanan araştırmalar doğrultusunda karar alma süreçlerini desteklemek amacıyla giderek daha fazla büyük veri analitiğine yatırım yapmaktadır [35]. Bu gelişmeler, BOH'nın önlenmesi ve yönetimi için daha çevik, duyarlı ve veri odaklı kamu sağlığı sistemlerinin inşasına önemli katkılar sunar.

5.3.Mekânsal-Temporal Modelleme ve Öngörü Analitikleri

Mekansal-zamansal büyük veri analitiğindeki son gelişmeler, kaynak yönetimi, işleme platformları ve uygulamalardaki zorlukları ele almıştır (Liang vd., 2024). Yeni yaklaşımlar arasında, hesaplamalı uygulanabilirlik ve tahmin esnekliği sunan büyük veri kümeleri için yüzey zaman serisi modelleri yer almaktadır [36]. Dinamik Zaman Bükme (Dynamic Time Warping) ile K-means kümeleme gibi makine öğrenme teknikleri, mekansal-zamansal hava kirliliği modellerini analiz etmede, kentsel planlama ve halk sağlığı müdahalelerine yardımcı olmada etkili olduğunu kanıtlamıştır [37]. Mekansal ve mekansal-zamansal (Spatial and Spatiotemporal Data Analytics Systems) veri analitiği sistemlerinin ekosistemi, mekansal veritabanlarını, büyük mekansal veri işleme altyapılarını ve Coğrafi Bilgi Sistemleri (CBS) yazılımlarını kapsar [38]. Bu gelişmeler, farklı disiplinlerden elde edilen mekansal-zamansal verilerin toplanması, depolaması, yönetilmesi, analiz edilmesi ve görselleştirilmesi konusundaki yetenekleri önemli ölçüde geliştirmiştir. Bu alan hızla gelişmeye devam ettikçe, gelecekteki araştırmaların odak noktası; bulut tabanlı çözümlere, yapay zeka entegrasyonuna ve uzaysal-zamansal büyük verilerin üstel artışının beraberinde getirdiği zorlukların ele alınması olacaktır [39].

5.4. Gerçek Zamanlı Salgın Yönetimi ve Tahmin Sistemleri

Araştırmalar, salgınların yönetimi ve tahmiminde büyük veri ile yapay zekânın giderek artan rolüne dikkat çekmektedir. Grip, sıtma ve malaria gibi bulaşıcı hastalıkların tahmininde ML teknikleri kullanılmakta olsa da veri yetersizliği hâlâ önemli bir sınırlılık oluşturmaktadır [40]. Büyük veri ve yapay zekâ, özellikle EUS ve müdahale stratejilerinin geliştirilmesinde, COVID-19'un önlenmesi ve kontrolünde önemli potansiyel sunmuştur [41] Büyük veri akışlarının gerçek zamanlı analizi, karar alma süreçlerine ve kaynak kullanımının optimize edilmesine katkı sağlayacak değerli bilgiler sunmaktadır [42]. Son on yılda salgın tahminine yönelik ilgi önemli ölçüde artmış; Hastalık Kontrol ve Önleme Merkezi (Centers for Disease Control and Prevention-CDC) bu süreci kurumsal faaliyetlerine dahil etmiş ve Grip Tahmini için Mükemmeliyet Merkezleri oluşturmuştur. Arama motoru eğilimleri ve çevrimiçi anketler gibi dijital gözetim araçları ile yardımcı veri kaynakları, salgın izleme ve tahmin modellerinin doğruluğunu ve etkinliğini artırmada kritik bir rol oynamaktadır [43]. Bu gelişmeler, gerçek zamanlı ve veri temelli salgın yönetim sistemlerinin geleceğini şekillendirmektedir.

6. Büyük Veri Tabanlı İzleme Uygulamaları

HealthMap, BioSense, GISAID ve BlueDot gibi platformlar, hastalıkların erken tespiti, genetik izleme ve küresel salgın tahmini konularında önemli katkılara sunan uygulamalar olarak ön plana çıkmaktadır. Bu bölümde, büyük veri ve yapay zekâ temelli izleme sistemlerinin halk sağlığına katkısı ele alınmıştır.

6.1.HealthMap: Dijital Hastalık İzleme Platformu

HealthMap, Massachusetts General Hospital ve Boston Children's Hospital iş birliği ile geliştirilen, bulaşıcı hastalıkların dijital olarak izlenmesine olanak tanıyan bir platformdur. HealthMap gibi dijital hastalık gözetim araçları, salgınlar dönemlerine saha gözetimininin tamamlayıcısı niteliktedir ve ve bulaşıcı hastalıkların yayılma risklerini neredeyse gerçek zamanlı olarak haritalayarak halk sağlığı müdahalelerine hız ve doğruluk kazandırabilir [44]. Yapay zekâ ve doğal dil işleme tekniklerini kullanarak resmi raporlar, haber kaynakları, sosyal medya ve kullanıcı bildirilerini analiz ederek, hastalık yayılımı hakkında erken uyarılar sağlar. Özellikle 2009 H1N1 salgını ve COVID-19 pandemisinde, gerçek zamanlı veri sunma kapasitesi ile dikkat çekmiştir [45].

6.2.BioSense: ABD Halk Sağlığı Erken Uyarı Sistemi

BioSense, ABD CDC tarafından geliştirilmiş bir erken uyarı sistemidir. Amaç, bulaşıcı hastalıkların ve biyoterör tehditlerinin erken tespiti için acil servis verileri, laboratuvar sonuçları ve sağlık hizmeti sağlayıcılarının bildirimlerini entegre etmektir. Sistem, bölgesel ve ulusal düzeyde epidemiyolojik gözetimi güçlendirmeyi hedeflerken aynı zamanda sağlık güvenliğiyle ilgili stratejilere rehberlik eder [46].

6.3.GISAID: Genetik Veri Paylaşımı ve Viral Genomik İzleme

Global Initiative on Sharing All Influenza Data (GISAID), grip virüsleri, RSV ve SARS-CoV-2'nin genomik verilerinin serbest ve açık paylaşımını teşvik eden küresel bir platformdur [47]. Başta grip virüsleri olmak üzere, SARS-CoV-2 dahil olmak üzere çeşitli viral patojenlerin genetik dizilimlerinin paylaşılmasını ve analizini destekler. GISAID, özellikle COVID-19 pandemisinde varyantların takibi ve aşı stratejilerinin belirlenmesinde kritik rol oynamıştır [47,48]. GISAID, açık erişimli Uluslararası Nükleotid Dizisi Veritabanı İşbirliği'nin (INSDC) aksine virüs bilgilerine sınırlı erişim sunarken, ülkeler arasında fayda paylaşımını teşvik etmeyi amaçlamaktadır [49].

6.4.BlueDot: AI Destekli Küresel Salgın Tahmin Sistemi

BlueDot, yapay zekâ ve büyük veri analitiği kullanarak küresel hastalık tehditlerini tahmin eden bir sağlık teknolojisidir [50]. Bu tür sistemler, hükümetlerin ve sağlık otoritelerinin hızlı yanıt vermesini sağlayarak salgınların sağlık ve ekonomik etkilerini azaltma potansiyeline sahiptir [51]. Sistem, doğal dil işleme ile 65'ten fazla dilde haber raporlarını, hayvan hastalık verilerini ve uçuş bilgilerini tarayarak salgın riski taşıyan bölgeleri önceden belirler. COVID-19 pandemisinin küresel yayılımını, Dünya Sağlık Örgütü'nden günler önce tespit ederek dikkat çekmiştir [52].

7. Sonuç

Bu sistematik olmayan derleme çalışması büyük verinin epidemiyolojik gözetim ve halk sağlığı hazırlığındaki dönüştürücü rolünü vurgulamaktadır. Elektronik sağlık kayıtları, mobil sağlık uygulamaları, genomik veri tabanları ve gerçek zamanlı sosyal medya analitiği dahil olmak üzere çeşitli veri kaynaklarının entegrasyonu hem bulaşıcı hem de bulaşıcı olmayan hastalıklara daha hızlı, bilgilendirici ve veri odaklı sonuçlar sağlamıştır. HealthMap, BioSense, GISAID ve BlueDot gibi platformlar, yapay zekâ ve makine öğrenimi tekniklerinin erken uyarı sistemlerini ve salgın tahminini nasıl geliştirebileceğini örneklemektedir. Önemli gelişmelere rağmen, bu alanda birkaç zorluk hala devam etmektedir. Veri heterojenliği, gizlilik endişeleri, birlikte çalışabilirlik engelleri ve algoritmik önyargı, etkili uygulama önündeki önemli engeller bu zorluklar arasında gösterilebilir. Bu zorlukların üstesinden gelmek için gelecekteki araştırmalar ve politikaların; veri paylaşım kurallarının standartlaştırılmasına, siber güvenlik ve yönetişim sistemlerinin güçlendirilmesine ve sağlık çalışanlarının büyük veri okuryazarlığının artırılmasına odaklanması önerilmektedir. Ayrıca mekânsal-zamansal modelleme ve tahmine dayalı analizlerinin entegrasyonu, sağlık kaynaklarının doğru yerde ve zamanda kullanılması için önemli bir fırsat sunmaktadır. Sonuç olarak, büyük veri tabanlı gözetim sistemleri yalnızca teknolojik araçlar değil, aynı zamanda kamu sağlığının dijital dönüşümünde stratejik unsurlardır. Karar vericiler ve politika yapıcılar için eyleme geçirilebilir bilgiler sağlar ve ortaya çıkan sağlık tehditlerine karşı daha hızlı ve dayanıklı bir yanıt sağlar. Bu alan ilerlemeye devam ettikçe, daha akıllı, kapsayıcı ve geleceğe hazır sağlık sistemleri oluşturmada büyük verinin tüm potansiyelinden yararlanmak için iş birlikçi ve disiplinler arası bir yaklaşım gerekli olacaktır.

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INSERVICE TRAINING PRACTICES IN PREHOSPITAL EMERGENCY MEDICAL SERVICES: A LITERATURE-BASED EVALUATION

ABSTRACT

Aim: The aim of this review study is to identify supplementary in-service training and exercises recommended in the literature to address issues encountered in prehospital emergency medical services (PEMS) practices, in addition to the basic professional in-service training organized for PEMS personnel by the General Directorate of Emergency Health Services.

Method: In this review study, a literature search was conducted without any date restrictions. During the search process, the databases Web of Science, Scopus, and Google Scholar were used; the keywords “prehospital care emergency medical services,” “on-the-job training and learning,” “lifelong learning,” and “learning organizations,” as well as combinations of these terms, were employed. The review included original research studies, postgraduate theses, and both systematic and non-systematic reviews.

Results: In Türkiye, in addition to the four core training modules offered to PEMS personnel by the General Directorate of Emergency Health Services—namely "Basic Training," "Advanced Life Support for Adults," "Advanced Life Support for Children," and "Advanced Trauma Life Support"—various in-service training programs are also provided both face-to-face and online. This literature review has shown that, alongside these trainings, a number of complementary educational activities planned in line with adult learning principles could significantly contribute to service quality and patient satisfaction through improved job satisfaction among employees. These trainings may include teamwork and communication, physical and psychological resilience, anger management, social service-related practices, motivation and performance.

Conclusion: In conclusion, the significance of the basic professional in-service training designed to enhance the competencies of PEMS personnel—who operate on the fine line between life and death—cannot be overstated. Alongside these trainings, the implementation of supplementary in-service training and exercises aimed at improving the working conditions, quality of life, and lifelong learning culture of PEMS personnel has the potential

to enhance the quality and efficiency of PEMS, thereby enabling the provision of better services to patients and the injured.

Keywords: Prehospital emergency medical services, on-the-job training and learning, life long learning, learning organizations.

HASTANE ÖNCESİ ACİL SAĞLIK HİZMETLERİNDE HİZMET İÇİ EĞİTİM UYGULAMALARI: LİTERATÜR TEMELLİ BİR DEĞERLENDİRME

ÖZET

Amaç: Bu sistematik olmayan derleme çalışmasının amacı, hastane öncesi acil sağlık hizmetleri (HÖASH) çalışanlarına yönelik olarak yürütülen temel mesleki eğitim ve uygulamaları literatür temelli bir çerçevede incelemek ve uygulamaya yönelik öneriler geliştirmektir.

Yöntem: Çalışma kapsamında herhangi bir tarih sınırlaması olmaksızın kapsamlı bir literatür taraması gerçekleştirilmiştir. Tarama sürecinde Web of Science, Scopus ve Google Scholar veri tabanları kullanılmış; "prehospital emergency medical services", "inservice training and learning", "lifelong learning" ve "learning organizations" anahtar kelimeleri ile bu terimlerin çeşitli kombinasyonlarından yararlanılmıştır. Derleme sürecinde özgün araştırmalar, lisansüstü tez çalışmaları ile sistematik ve sistematik olmayan derlemeler dikkate alınmıştır.

Bulgular: Türkiye'de HÖASH çalışanlarına yönelik olarak Acil Sağlık Hizmetleri Genel Müdürlüğü tarafından "Temel Eğitim", "Erişkin İleri Yaşam Desteği", "Çocuk İleri Yaşam Desteği" ve "Travma İleri Yaşam Desteği" olmak üzere sunulan dört temel eğitim modülüne ek olarak; çeşitli yüz yüze ve online hizmet içi eğitimler verilmektedir. Literatür taraması sonuçları, bu eğitimlerin yanı sıra erişkin eğitimi ilkeleri doğrultusunda planlanacak bir takım tamamlayıcı eğitim faaliyetlerinin, çalışanların iş doyumu üzerinden hizmet kalitesi ve hasta memnuniyetine önemli katkılar sağlayabileceğini ortaya koymuştur. Bu eğitimler; ekip çalışması ve iletişim, fiziksel ve psikolojik sağlamlık, öfke yönetimi, sosyal hizmet ilişkili uygulamalar, motivasyon ve performans eğitimleri olarak sıralanabilir.

Sonuç: : HÖASH çalışanlarının mesleki yeterliliklerinin geliştirilmesi amacıyla sunulan temel hizmet içi eğitimlerin önemi yadsınamaz. Bununla birlikte, çalışanların hayat boyu öğrenme kültürünü destekleyen tamamlayıcı eğitim programlarının uygulanması ve bu programların sürdürülebilirliğinin sağlanması, yalnızca bireysel meslekî gelişimi değil; aynı zamanda sunulan sağlık hizmetlerinin kalitesini ve etkinliğini de artırarak hasta bakımının niteliğini iyileştirme potansiyeli taşımaktadır.

Anahtar Kelimeler: Hastane öncesi acil sağlık hizmetleri, hizmet içi eğitim, hayat boyu öğrenme, öğrenen örgütler.

1. Giriş

1.1.Hastane Öncesi Acil Sağlık Hizmetleri Tarihi

Kaza sonucu ortaya çıkan ölüm ve engel hali, modern toplumlarda yirminci yüzyılın ortalarına kadar üzerinde sistemli olarak durulan bir konu haline gelememiştir. Art arda gelen savaşların yarattığı katastrofik atmosferde askeri sahada ilk yardım ve acil tıbbi bakım hızlı bir ilerleme kaydederken, sivil yaşamda ölüm ve engel hali doğuran kazalara sistemli müdahale ikinci planda kalmıştır. [1-3]

Amerika Birleşik Devletleri (ABD) özelinde bakıldığında, savaş alanında mükemmelleşen ilk yardım uygulamaları, etkin taşıma yöntemleri ve uygun tedavi ile tıbbi tesislere ulaşan yaralılarda ölüm oranlarının I. Dünya Savaşı'nda %8 iken, Vietnam Savaşı'nda %2'ye düştüğü görülmektedir. Özellikle Vietnam Savaşı'nın ardından ABD'ye dönen uzmanların; ciddi yaralanması olan bir hastanın hayatta kalma şansının, savaş bölgesinde şehir merkezine göre daha yüksek olduğunu ve bir astronot ile iletişim kurmanın, bir ambulansın ulaşmayı planladığı hastane acil servisi ile iletişim kurabilmesinden daha olası göründüğünü ifade etmeleri geniş bir toplumsal farkındalık uyandırmış, sağlık otoritelerini harekete geçirmiştir. 1966 yılında ABD Ulusal Bilimler Akademisi tarafından yayınlanan rapor ile günümüzdeki anlamıyla modern hastane öncesi acil sağlık hizmetlerinin (HÖASH) temeli atılmıştır. [1,4]

Tüm gelişmelere paralel olarak Türkiye'de de I. Dünya Savaşı tecrübesi ile etkin tıbbi ilk yardım, taşıma ve tedavi sürecinin önemi anlaşılmıştır. Ancak bu tecrübelerin sivil düzeyde hayata geçirilmesi dönemin sosyoekonomik koşulları nedeniyle zaman almıştır. Önceleri hastanelere ait motorize ambulanslar yaygınlaşmış olup, ortak bir yönetim ve denetim mekanizması bulunmaması nedeniyle zamanla bu araçlar teknik olarak çağın gerisinde kalmış, sonunda da âtıl hale gelmiştir. Özellikle 1950'li yıllardan itibaren hızlanan karayolları inşası ile motorlu taşıt kazası sayıları artış göstermiş, ortaya çıkan ihtiyaç özel ambulans servislerinin faaliyete girmelerine sebep olmuştur. 1985 yılına gelindiğinde Türkiye genelinde faaliyet göstermesi planlanan, 077 numarası ile erişim sağlanabilen Hızır Acil Servisi adında bir ambulans servisi hayata geçirilmiştir. Ancak dönemin Sağlık ve Sosyal Yardım Bakanlığı ve belediyelerin ortak yönetiminde olan ve ayrıntıları mevzuat ile desteklenmemiş bu servisin başarıyla işlemesi mümkün olamamıştır. 1994 yılında 077 Hızır Acil Servis numarası yerini Avrupa Ekonomik Topluluğu önerisi doğrultusunda 112 numarasına bırakmıştır. [5-7]

1993 yılında Dokuz Eylül Üniversitesi bünyesinde Sağlık Hizmetleri Meslek Yüksek Okulu'nda Ambulans ve Acil Bakım Teknikeri (AABT) eğitimi başlatılmış, 2004 yılında Sağlıkta Dönüşüm Programı kapsamında 112 Acil Sağlık İstasyonlarında AABT kadroları açılmış ve istihdam hızla artırılmıştır. 2006 yılında yürürlüğe giren Ambulanslar ve Acil Sağlık Araçları ile Ambulans Hizmetleri Yönetmeliği ile Türkiye sınırları içinde kullanılan tüm ambulansların Avrupa standartlarına uygun donanımda olması sağlanmıştır. Aynı yıl 112 Komuta Kontrol Merkezlerinin dijital altyapı çalışmaları tamamlanmaya başlamış, 2008 yılında 81 ilde aktif hale getirilmişlerdir. 2014 yılına gelindiğinde ise 112 Acil Çağrı Merkezleri Kuruluş, Görev ve Çalışma Yönetmeliği yayınlanarak tüm acil çağrılar için 112 tek numara olarak kullanılmaya başlanmıştır. [8-13]

1.2.Türkiye'de HÖASH'nin Mevcut Durumuna Genel Bir Bakış

Günümüzde Türkiye'de HÖASH ambulanslar vasıtasıyla verilmekte olup, çalışanları temelde Acil Tıp Teknisyenleri (ATT) ile Ambulans ve Acil Bakım Teknikerlerinden (AABT) oluşmakta, az sayıda ekipte ise hekimler görev almaktadır. [14]

Acil yardım çağrısının 112 merkezi tarafından alınmasından ambulansın olay yerine ulaşması ve ambulanstaki sağlık ekibinin tıbbi müdahaleye başlaması arasındaki zaman, müdahale süresi olarak tanımlanmaktadır. [15] Müdahale süresinin komuta reaksiyon süresi ve ekibin hareket süresi bileşenleri Sağlık Bakanlığı tarafından belirlenmiş durumdadır. Acil yardım çağrısının cevaplandığı andan, çağrı noktasına en yakın mesafedeki ambulans ekibinin görevlendirilmesine kadar geçen süre 'komuta reaksiyon süresi'dir ve 120 saniye altında olmak durumundadır. Ekibin telsiz yoluyla görevi alması ile istasyonundan veya bulunduğu konumdan harekete geçmesi arasında geçen süre ise 'ekibin hareket süresi' olarak adlandırılır ve normal koşullarda 90 saniye altında olması gerekmektedir. [16] ABD'de yapılan bir çalışmada olay yerinde ölüm istatistikleri incelenmiş; reaksiyon süresinin 1-5 dakika arasında olması, bir dakikanın altında olmasına göre, olay yerine varış süresinin 9-18 dk arasında olması ise 9 dakikanın altında olmasına göre artmış olay yerinde ölüm sayıları ile ilişkili olduğu görülmüştür. [17]

Acil Sağlık Hizmetleri ambulansına en sık başvuru nedenlerinin incelendiği çalışmalarda; travmalar ile kardiyovasküler/solunumsal ve nörolojik şikayetler için hizmet aramanın en yoğun olduğu, geriatrik popülasyon özelinde bakıldığında kardiyovasküler/solunumsal şikayetler ile hizmet aramanın ön plana geçtiği saptanmıştır. [18-22]

Diğer yandan, saniyelerin öneminin konuşulduğu böyle bir sistemde bile bilinçli ve bilinçsiz kötüye kullanım engellenememektedir. HÖASH'nin kötüye kullanımını inceleyen bir çalışmada kötüye kullanımı artıran faktörler; hizmetin ücretsiz olması, 24 saat sunulması ve yararlanıcıların hizmetin doğru kullanımı hakkında yeterli bilgiye sahip olmamaları şeklinde sıralanmıştır. [23]112 acil sağlık hizmetleri ambulansı ile hastaneye ulaştırılan hastaların hastane acil servisinden yüksek taburculuk oranları uygunsuz kullanımı destekler niteliktedir. [24,25]

Hastane öncesi acil sağlık hizmetlerinde görev alan personel ile yapılan niteliksel metafor analizi çalışmasında, acil sağlık metaforları olarak en sık sarfedilen üç kelime; kapı, umut ve taksi olarak saptanmıştır. [26] Burada kapı ve umut metaforu HÖASH ruhunu yansıtırken, taksi metaforu kötüye kullanımı çağrıştırmaktadır.

Sağlık işgücü HÖASH sisteminin etkinliğinde kilit bir role sahiptir. [27,28] Bu açıdan literatürde HÖASH personelinin çalışma şartları üzerine pek çok çalışmaya rastlanmaktadır. Personelin iş doyumunu inceleyen bir çalışmada, iş doyumunu etkileyen faktörler bireysel ve örgütsel olarak ikiye ayrılmış, bireysel faktöreler, cinsiyet, yaş, medeni durum, eğitim düzeyi, kişilik ve tecrübe; örgütsel faktörler ise ücret, çalışma arkadaşı, iletişim, statü, işin niteliği, ödüllendirme ve çalışma ortamı olarak sıralanmıştır. [29] Bir diğer çalışmada çalışan güvenliğini etkileyen faktörler şu şekilde sıralanmaktadır; çalışma ortamında iletişim eksikliği, kullanılan araç ve malzemenin yeterli kalitede olmaması, çalışma ortamındaki güvenlik sorunları ve uygunsuzluklar, iş yükü fazlalığı, motivasyon eksikliği ve yetersiz personelin varlığı. [30] Dolayısıyla çalışan güvenliği faktörleri ile bağlantılı olarak HÖASH personelinin başlıca mesleki risk faktörleri; çok stresli çalışma ortamı, ağır kaldırma, hasta ve hasta yakını tacizi, enfeksiyon etkenlerine maruz kalma; başlıca sağlık sorunları bel ağrısı, uyku bozuklukları, şiddete uğrama ve araç içi yaralanmalar olarak saptanmıştır. [30]

Her geçen gün ilerleyen teknoloji ve imkânlar doğrultusunda gelişen Türk HÖASH'nin etkinlik, etkililik ve kalitesinin artılması yoluyla hasta ve yaralıların faydasını maksimize ederken, kamu maliyetlerinin de minimize edilmesi yolunda öneriler içeren pek çok yayın literaürde yer bulmaktadır. Bu çalışmada, çeşitli önerilere yer veren bu yayınların ekseriyetinde temas edilen personelin eğitimi kavramı ele alınacaktır.

2. Hayat Boyu Öğrenme Bakış Açısı ile Hizmet İçi Eğitimler

Acil sağlık hizmetleri çalışanları yoğun stres altında, sıklıkla hayati tehlikesi olan hastalara hizmet sunar. Bu durum çalışanların standardize edilmiş acil sağlık eğitimleri yolu ile kişisel ve kültürel özelliklerinin ötesinde profesyonel faaliyet göstermelerini gerekli kılmaktadır. [31,32]

Özellikle düşük ve orta gelirli ülkelerin sağlık sistemlerinin etkin işleyebilmesinde temel bir rol oynayan acil sağlık hizmetlerinde sağlık işgücü kritik bir role sahiptir ve bu açıdan sağlık profesyonellerinin eğitimi yoluyla acil sağlık hizmetlerinin etkili sunumu önem arz etmektedir. [27,33,34] Ülkelerin, bin yıllık gelişim hedefleri doğrultusunda anne-bebek ölüm oranı ve beş yaş altı ölüm oranlarını düşürebilmelerinin insan kaynağı yoğunluğu ve yönetimi ile ilişkili olduğu ortaya koyulmuştur. İşgücünün eğitimi, kariyer planlaması ve performansının izlenmesi ise insan kaynakları yönetiminin önemli bileşenlerindendir.[35]

Temeli 'öğrenmeyi öğrenmek' olan hayat boyu öğrenme kavramı, klasik örgün eğitimin bir alternatifi değil, onun eksiklerini tamamlayıp kişilerin keşfedilmemiş yeteneklerini ortaya çıkaran bir olgu olarak tanımlanabilir. [36]

Avrupa'da gerçekleştirilen bir çalışmada hastane öncesi sağlık bakımının on araştırma önceliği belirlenmiş olup bunlardan biri sürekli eğitim ve öğretimdir. Bu eğitim ve öğretim programlarının interaktif, pratik tabanlı ve disiplinler arası özellikte olması, ayrıca katılımcıların birbirlerinin pratiğini izleyip geri bildirim sağlamaları önerilmektedir.[37,38]

Türkiye özeline bakıldığında, HÖASH çalışanlarının hayat boyu öğrenme yatkınlıklarının yüksek seviyede olduğu saptanmış, hayat boyu öğrenme uygulamaları kapsamında düzenlenen hizmet içi sertifikalı eğitim programlarına katılan HÖASH çalışanlarının, katılmayanlara göre daha yüksek örgütsel ve duygusal bağlılık gösterdiği sonucuna ulaşılmıştır.[39,40]

Mevcut durumda Türk HÖASH çalışanlarına sunulan hizmet içi eğitimler aşağıda sıralanmıştır: [41]

- Temel Eğitim Modülü
- Çocuk İleri Yaşam Desteği Eğitimi
- Erişkin İleri Yaşam Desteği Eğitimi
- Travma İleri Yaşam Desteği Eğitim
- Ambulans Sürüş Güvenliği Eğitimi
- Hastane Öncesi Obstretrik Aciller Eğitimi
- Madde Kullanım Bozukluğuna Acil Yaklaşım Eğitimi

- Oksijen Tüpü ve Sistemlerinin Güvenli Kullanımı Eğitimi
- Tıbbi Acil Çağrı Yönetimi Sağlık Komuta Kontrol Merkezi Eğitimi
- Tıbbi Acil Tahliye Eğitimi (Denize kıyısı olan illerde uygulanmaktadır.)
- Tıbbi Kimyasal Biyolojik Radyolojik Nükleer Tehditler Farkındalık Eğitimi
- Adli Vakalarda Maddi Delillere Yaklaşım Eğitimi
- Online Kurslar
    - Atık Yönetimi
    - Enfeksiyonların Önlenmesi Eğitimi
    - Dezenfektan Kullanımı ile Ambulans Temizliği ve Dezenfeksiyon Eğitimi
    - El Hijyeni Eğitimi
    - Kişisel Koruyucu Ekipman Kullanımı Eğitimi
    - Hasta Mahremiyeti, Hasta Memnuniyeti, Hasta Hakları, Sorumlulukları ve Uymaları Gereken Kurallar ile İletişim Becerileri Eğitimi
    - Hasta Kimliğinin Tanımlanması ile hasta Triajı Eğitimi
    - Hastanın Güvenli nakline Yönelik Eğitim
    - SKS Doküman Eğitimi
    - İstenmeyen Olay Bildirimi ve Beyaz Kod Eğitimi
    - Telsiz ve Haberleşme Eğitimi
    - Tehlikeli Madde Sınıfını Gösteren Simgeler Hakkında Eğitim
    - Çalışma Hayatında Kadın Erkek Fırsat Eşitliği
    - Çocuk İhmal ve İstismarı Eğitimi
    - Davranışsal Bağımlılıklar ile Mücadele Eğitimi
    - İntiharın Önlenmesi Eğitimi
    - İş Sağlığı ve Güvenliği Eğitimi
    - Kadına Yönelik Aile İçi Şiddet ile Mücadele Eğitimi
    - Bilgi Güvenliği Eğitimi

Yukarıda sayılan hizmet içi eğitim faaliyetlerine ek olarak ilgili literatür doğrultusunda önerilen ilave hizmet içi eğitim ve öğretim faaliyetleri aşağıda sıralanmıştır:

- Ekip Çalışması ve İletişim

- Fiziksel ve Psikolojik Sağlamlık
- Öfke Yönetimi
- Sosyal Hizmet İlişkili Uygulamalar
- Motivasyon ve Performans

2.1.Ekip Çalışması ve İletişim

Bir ekip, görev tanımları belirlenmiş iki veya daha fazla kişinin ortak amaçlara ulaşmak amacıyla bir araya gelmesiyle oluşur. Hasta bakımı özelinde bakıldığında, verimli bir ekip çalışması hastaların uygun bakımı alarak mümkün olan en iyi sağlık çıktılarına ulaşması için önem arz etmektedir. [42,43]

Ekip üyelerinin kişilik ve sosyokültürel özellikleri ile ekip liderinin bakış açısı ve motivasyon yeteneği temelde başarılı veya başarısız bir ekip çalışmasının belirleyicileri olarak sayılabilir. Sağlık sektöründeki ekiplerin farklı statülerdeki çalışanlardan oluşması, geleneksel görüşte ekip içerisinde dengesizliklere sebep olan bir faktör olarak gösterilmekle beraber, günümüzde gücün kaynağı giderek yerini statü farklarından öte ikna gücü, hizmette özveri, alçak gönüllülük ve hayat boyu öğrenme gibi faktörlere bırakmaktadır. [44]

Kişilik özelliklerini dışadönüklük, uyumluluk, duygusal dengesizlik, deneyime açıklık ve sorumluluk olarak beş faktör altında toplayan “beş faktör kişilik kuramı”nı kullanarak HÖASH çalışanlarının yaptıkları işe uygunluğunu inceleyen bir çalışmada; dışadönüklük, uyumluluk ve sorumluluk kişilik özelliklerine sahip personelin duygularını düzenleyebilme, çatışma çözme ve gelişmiş iletişim becerilerine sahip olmaları nedeniyle iş birliği içinde çalışmaya daha yatkın oldukları sonucuna ulaşılmıştır. [45,46]

Sonuç olarak sağlık sektöründe ekip çalışması ve ekip içi iletişimi etkileyen pek çok faktörün mevcut olduğu görülmektedir. HÖASH özelinde bakıldığında da hizmetin verilmesi ambulans ekibinin faaliyeti temeline dayandığından, konunun uzmanlarınca sunulan hizmet içi eğitimler yoluyla ekip becerilerinin geliştirilmesi konusunun yöneticilerin ve politika yapıcılarının gündemine alınması, bireylere daha nitelikli hizmet sunulmasını sağlayabilir. [44,46]

2.2.Fiziksel ve Psikolojik Sağlamlık

Türkiye’de HÖASH çalışanları ile yapılan bir çalışmada, çalışanların yaşam kalitesini ve kas iskelet sistemi ağrılarını etkileyen faktörler beraber değerlendirilmiş. Her ikisinin de cinsiyet, görev yaptığı unvan, fiziksel tedavi görme veya operasyon geçirme, düzenli spor yapma, kronik hastalık sahibi olma ve gelir durumu ile ilişkili olduğu bulunmuştur. Çalışmaya katılan personelin fiziksel sağlamlık ve düzenli spor yapma durumları incelendiğinde; yaklaşık üçte birinin fiziksel rahatsızlıktan dolayı tedavi gördüğü veya operasyon geçirdiği, en sık yaşanan rahatsızlığın kas iskelet sistemi rahatsızlıkları olup; bel, sırt ve boyun bölgelerinin etkilendiği saptanmıştır. Katılımcıların düzenli spor yapma durumları sorgulandığında, olumlu cevap verenlerin oranı beşte bir olarak bulunulmuştur. [47]

Literatürde, personelin spora teşviki amacıyla, özel spor kuruluşları için maddi destek sağlanması veya T.C. Sağlık Bakanlığı ve T.C. Gençlik ve Spor Bakanlığı arasında bir protokol ile İl Gençlik ve Spor Müdürlükleri bünyesinde bulunan spor hocaları tarafından HÖASH personeline eğitim ve danışmanlık verilmesi, ayrıca iskelet sistemini etkileyen

hastalıkların erken tespiti ve tedavisi için HÖASH personelinin ilgili periyodik tıbbi muayenelerinin sıklaştırılması önerilmektedir. [47]

Schutte ve arkadaşlarının (1998) geliştirdiği Duygusal Zekâ Ölçeği; ruh halinin düzenlenmesi (iyimserlik), duyguların değerlendirilmesi ve duyguların kullanımı alt boyutları aracılığıyla kişilerin duygusal zekâ düzeylerini saptamak amacıyla kullanılmaktadır. [48] Duygusal zekanın psikolojik sağlamlık üzerinde pozitif yönde anlamlı etkisi olduğu belirtilen bir çalışmada Türk HÖASH personelinin duygusal zekalarının yüksek, psikolojik sağlamlıklarının ise orta düzeyde olduğu sonucuna ulaşılmıştır. Demografik farklılıklara inildiğinde; mesleki deneyimi daha az ve yaşı daha genç olan sağlık personelinin duygusal zekâ düzeyleri daha düşük, erkek sağlık personelinin psikolojik sağlamlık düzeyinin daha yüksek olduğu saptanmıştır. [49]

HÖASH çalışanları, travmaya doğrudan maruz kalmadıkları optimal çalışma koşulları sağlandığında bile, travmaya maruz kalan bireylerle yakın temasta olmaları sebebiyle ikincil travmatik stres yaşamaktadırlar. [50] İkincil stres ile baş etme yolları arasında duyguları düzenlemeye çalışmak, travmayı kabul etmek, psikolojik sağlamlığı artırmak, örgütsel ve sosyal destek sistemlerini kullanmak sayılmaktadır. [51-53] Türk HÖASH personelinin ikincil travmatik stres düzeylerinin incelendiği bir çalışmada; psikolojik sağlamlık azaldıkça ikincil travmatik stres düzeylerinin arttığı saptanmıştır. Ayrıca katılımcıların yarısına yakınının stres yaşadıklarında ailelerinden destek aldıklarını, yaklaşık yüzde sekseninin acil sağlık hizmetlerinde yaşanabilecek psikososyal güçlüklere karşı herhangi bir hizmet içi eğitim almadıklarını ve yüzde yetmiş beşinin böyle bir psikolojik desteğe ihtiyaç duyduklarını ifade ettiği görülmüştür. [53]

2.3.Öfke Yönetimi

Hastane öncesi acil sağlık hizmeti verilirken; yalnızca hizmete ihtiyacı olan birey değil, bireyin yakınları, ev dışı vakalarda çevredeki izleyici kalabalık, bunlara ek olarak kolluk kuvvetleri, itfaiye, arama kurtarma ekipleri ve benzeri gruplar, acil sağlık ekibinden beklenti içindedir. Bu sayılanlardan biri veya birkaçının acil vakanın etkisi ile olay yerinde gerginlik yaratması sıklıkla rastlanan bir durumdur.

Üstte tasvir edilen ortamda, HÖASH çalışanlarının öfke ve gerginlik duyguları ile uygun bir şekilde baş ederek, öfke duygusunu karşı tarafa yansıtmadan sürekli olumlayıcı bir davranış içinde olmaları beklenmektedir. Olay yerinde öfkenin uygunsuz bir şekilde ifade edilmesi, öncelikle acil sağlık ekibi içindeki iş birliğini sekteye uğratmakta, dahası kişiler ve ekipler arası iletişim ve kooperasyonu yıkmaktadır. Bunun aksine uygun bir öfke yönetimi sağlanabilirse fiziksel ve psikolojik denge hali kurulmakta, hastalara kaliteli ve güvenli tıbbi bakım verilebilmekte ve sonuç olarak ölümlerin artması engellenebilmektedir. [54,55]

Sağlık çalışanlarının karakter özellikleri ile öfke durumlarını ele alan bir çalışmada katılımcıların öfkelerini sağlıklı bir biçimde ifade etmede yetersiz oldukları ve sürekli öfke düzeylerinin yüksek olduğu ortaya konulmuştur. [56] İlk ve acil yardım programı öğrencileri ile yapılan çeşitli çalışmalarda sınıf düzeyi arttıkça öfke düzeyinin anlamlı olarak yükseldiği, kadın öğrencilerin sürekli öfke ve öfkeyi ifade etme düzeylerinin erkek öğrencilerden yüksek olduğu görülmüş, bu sonuçlar mesleki sorumluluk alma zamanı yaklaştıkça öğrencilerde oluşan kaygı ve toplumdaki cinsiyet rolleri ile ilişkilendirilmiştir. [57,58]

Sonuç olarak, acil sağlık hizmeti talebi bulunan yoğun stres ve kaygı altındaki hasta ve hasta yakınları ile primer iletişim kuran HÖASH personelinin gerek acil çağrı merkezinde gerekse

sahada sağlıklı bir öfkeyi ifade etme pratiğine sahip olması adına ilgili hizmet içi eğitim çalışmalarının planlanması önem taşımaktadır. [58]

2.4.Sosyal Hizmet İlişkili Uygulamalar

Ölüm düşüncesi, yalnızlık hissi, alkol ve madde bağımlılığı gibi nedenlerle acil servis başvurusu olan hastaların bir kısmına tıbbi sosyal hizmet müdahalesi yapıldığında, müdahale yapılan grupta acil servis başvurularının yüzde seksen oranında azaldığı görülmüştür. Bu bakımdan acil servislerdeki etkin faaliyet gösteren sosyal hizmet kadrolarının; tıbbi nedenlerle hastane yatışı gerektirmeyen ancak sosyal bakım ihtiyacı olan bireylerin değerlendirilmesi ve yönetimi yoluyla, özellikle büyük şehirlerde acil servis maliyetlerini düşüreceği öngörülmektedir. [59-61]

Dünya Sağlık Örgütü (DSÖ) sağlık acillerini otuz iki başlık altında listelemektedir. Bunun dışında kalan durumlar acil sağlık hizmetlerinin uygunsuz kullanımı olarak nitelendirilmektedir. Literatürde hastane öncesi acil sağlık hizmetlerini uygunsuz kullanımı ile ilgili pek çok çalışma yer almakta olup, bu durumun hem Türkiye hem de dünyada yaygın olduğu izlenmektedir. [62-64]

Sağlık hizmeti sunucularının geleneksel tıbbi aciller modeline ek olarak, sağlık hizmeti planlamasında hasta ve hasta yakını katılımını destekleyen bir yaklaşım benimsemeleri durumunda, psikososyal güçlendirme müdahalelerini içeren sosyal hizmet çalışmaları yoluyla daha fazla hasta memnuniyeti ve iyileşme sağladıkları saptanmıştır. [65]

Hastane öncesinde acil sağlık hizmeti sunan personelin çalışma ortamı çoğunlukla çağrıyı yapan bireylerin yaşam alanlarıdır. Bu gerçekten yola çıkılarak HÖASH personelinin, etkin bir hizmet içi eğitimin de desteğiyle, tıbbi hizmet ihtiyacı ile sosyal hizmet ihtiyacı ayrımını ilk elden yaparak gerektiğinde çağrı yapan bireyin psiko-sosyoekonomik yardım ihtiyacı açısından ilgili birimlere bildirim yapabilme potansiyelinin değerlendirilmesi gerekliliği belirtilmiş, HÖASH bünyesine adapte edilebilecek ‘tıbbi-sosyal hizmet koordine edici’ bir yapı önerilmiştir. [66,67]

2.5.Motivasyon ve Performans

Sağlık hizmetleri temelinde yüksek stres içeren bir meslek grubudur. Bu yoğun stres koşulları altında sağlık çalışanlarının iş doyumunun ve verimliliğinin; kaliteli hizmet sunumu ve hasta memnuniyeti sağlanması ile ilişkili olup, çalışanların iş motivasyonu ve performansı tarafından etkilendiği belirtilmektedir. HÖASH çalışanlarında iş doyumu ile ilişkili faktörler ise; yönetim tarafından yapılacak düzenlemelere karar verilirken personelin aktif katılımının sağlanması, iş sağlığı ve güvenliği tedbirlerinin olay yeri, ambulans ve ekipmanlar da dahil olmak üzere güçlendirilmesi, çalışanların yetki, sorumluluk ve mesleki becerilerine dair farkındalık oluşturmaya yönelik hizmet içi eğitimlerin düzenli aralıklarla sağlanması olarak sayılabilir. [68-70]

İş stresi daha yüksek olan HÖASH çalışanlarının kurumlarına karşı aidiyet seviyelerinin düşük olduğu, algılanan stres düzeyi daha yüksek olan bireylerin bilişsel yeteneklerinde kötüleşme ve kendilerine güvende azalma nedenleriyle karşılaşılan problemleri çözme becerilerinin daha düşük seyrettiği gösterilmiştir. [71,72]

Genellikle uzun çalışma saatleri olan sağlık çalışanlarının yorgunluk, bir önce müdahale ettikleri vakanın duygusal etkisi ve benzeri nedenlerle gün içinde karar ve müdahale performanslarının mümkün olduğunca stabil tutulması temeline önemlidir. [73]

HÖASH çalışanlarında iş stresini azaltma yolunda; iş ortamındaki fiziki şartların iyileştirilmesi önerileri yanında, stres ile başa çıkma ve stres altında etkin acil sağlık hizmeti verebilme becerilerine dair nitelikli hizmet içi eğitimler önerilmektedir. [71,73]

3. Sonuç

On dokuzuncu ve yirminci yüzyılda tüm dünyada yaygın görülen savaş atmosferi, özellikle travma acil sağlık bakımında ilerlemeler doğurmuştur. Bu süreçte şehirlerin kalabalıklaşması ile artan sivil hasta ve yaralı acil bakım hizmetlerinin, askeri acil sağlık bakımına göre geride kaldığı izlenmektedir. Bu durum sivil hayatta hastane öncesi acil sağlık hizmetlerine verilen önemin artmaya başlamasını getirmiştir.

Günümüzde hastane öncesi acil sağlık hizmetleri acil afet, hastalık ve yaralanma durumlarında saniyeler içerisinde reaksiyon vererek acil sağlık bakımı sunar. Özellikle düşük ve orta gelirli ülkelerin sağlık sistemleri için, kritik hasta bakımında sağlık işgücünün nitelikli olmasının önemli olduğu bilinmektedir. İşgücünün eğitimi, kariyer planlaması ve performansının izlenmesi nitelikli sağlık işgücü oluşturulması ve yönetiminde rol oynamaktadır.

Türk HÖASH özelinde bakıldığında, mevcut hizmet içi eğitimlere ek olarak, literatürde düzenli aralıklarla gerçekleştirilmesi gereken çeşitli tamamlayıcı hizmet içi eğitimler için öneriler sunulduğu saptanmıştır. Bu çalışmada ilgili eğitimler; ekip çalışması ve iletişim, fiziksel ve psikolojik sağlamlık, öfke yönetimi, sosyal hizmet ilişkili uygulamalar, motivasyon ve performans başlıkları altında toplanarak sunulmaktadır.

Literatürde ayrıca, üstte geçen tamamlayıcı hizmet içi eğitim ve öğretim programlarının interaktif bir şekilde, iş ortamında pratik uygulamaya katkı sağlayacak özellikte ve disiplinler arası platformda yapılmasının önemli vurgulanmakta, katılımcıların birbirinin pratiğini izleyerek etkin geri bildirim sağlamaları önerilmektedir. Belirli aralıklarla, verilen hizmet içi eğitimlerin etkinliğinin, HÖASH çalışanlarının sahadaki iş performansının uzman eğitimciler tarafından izlenerek değerlendirilmesi gerekliliği de üzerinde önemle durulan bir diğer konu olarak literatürde yer bulmaktadır.

4. Kaynakça

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ANKLE-FOOT ORTHOSES IN PATIENTS WITH MULTIPLE SCLEROSIS: AN INVESTIGATION OF PHYSIOTHERAPISTS' CLINICAL PERSPECTIVES, EXPERIENCES, AND EXPECTATIONS

ABSTRACT

Purpose: The aim of this study was to investigate physiotherapists' clinical experiences, attitudes, opinions, and credibility/expectations regarding ankle-foot orthoses (gait-AFOs) used to improve ambulatory performance in patients with Multiple Sclerosis (pwMS). **Participants and Methods:** Physiotherapists who had been involved in the treatment or evaluation of at least one MS patient using a gait-AFO during their professional careers were included in the study. Data were collected via a structured questionnaire covering participants' demographic characteristics, credibility/expectations regarding the gait-AFOs (Confidence/Expectation Questionnaire), and their clinical experiences and opinions. The questionnaire included yes/no questions, open-ended items, and Numeric Rating Scale (NRS)–based responses. **Results:** A total of 50 physiotherapists (30 clinical physiotherapists (60%) and 20 academicians (40%)) participated in the study, with a median (25^{th} and 75^{th} percentiles) professional experience of 9 (3–12) years and a median of 5 (3–15) pwMS treated with gait-AFOs. The mean credibility score regarding the gait-AFOs in pwMS was 20 (18–24) [70.8% (62.5%–87.5%)], while the mean expectation score was 16 (14–18) [54.2% (45.8%–62.5%)]. The relationships between the physiotherapists' experience period and their credibility and expectation scores were found to be Spearman's rho=0.357 (p=0.011) and Spearman's rho=0.198 (p=0.169), respectively. When evaluating the effectiveness of the gait-AFOs in pwMS, 86% of participants reported using observational gait analysis most frequently, while only 16% utilized performance tests (e.g., Timed Up and Go, 10-Meter Walk Test). Additionally, 42% of the participants reported no complications related to gait-AFO use in pwMS, and 76% indicated that patients had not experienced any adverse event due to the orthosis. The median score for the question 'How easy do you find the clinical decision-making process regarding the gait-AFO use in pwMS?' (rated on the NRS from 0 [not easy at all] to 10 [very easy]) was 5 (3-7). A statistically significant positive correlation was found between years of experience and ease of clinical decision-making (Spearman's rho = 0.381, p = 0.006). **Conclusions:** This study is the first

to provide data on physiotherapists' clinical experiences, attitudes, opinions, credibility, and expectations regarding gait-AFOs in the rehabilitation of pwMS. Our results are expected to contribute to the development of future studies and clinical guidelines concerning the use of gait-AFOs in pwMS.

Keywords: Multiple Sclerosis, ankle-foot orthosis, physiotherapist, clinical approach, expectation

MULTİPL SKLEROZ HASTALARINDA AYAK-AYAK BİLEĞİ ORTEZİ: FİZYOTERAPİSTLERİN KLİNİK GÖRÜŞ, DENEYİM VE BEKLENTİLERİNİN İNCELENMESİ

ÖZET

Amaç: Multipl Skleroz (MS) hastalarının ambulatuvar aktivitelerindeki performansını geliştirmek için kullanılan ayak-ayak bileği ortezleri (yürüyüş-AFO) hakkında fizyoterapistlerin klinik deneyimlerini, tutumlarını, görüşlerini, güvenlerini ve beklentilerini incelemekti. **Bireyler ve Yöntem:** Meslek hayatı boyunca; yürüyüş-AFO'su kullanan en az bir MS hastasının tedavisinde veya değerlendirilmesinde rol almış olan fizyoterapistler çalışmaya dahil edildi. Bireylerin tanımlayıcı özellikleri, yürüyüş-AFO'suna olan güven/beklentileri (Güven/Beklenti Ölçeği) ve klinikte deneyimledikleri durum/görüşleri hakkındaki bilgiler anket formu kullanılarak elde edildi. Bireyler, anket formundaki maddeleri; evet/hayır şeklinde, açık uçlu olarak veya Sayısal Oranlama Ölçeği (SAÖ) göre cevapladı. **Bulgular:** Çalışmaya, deneyim süresi 9 (3-12) [ortanca (25. ve 75. yüzdelik)] yıl; yürüyüş AFO'su kullanan MS hastası ile karşılama sayısı 5 (3-15) olan 50 fizyoterapist [30 klinik fizyoterapist (%60) ve 20 akademisyen (%40)] dahil edildi. Fizyoterapistlerin MS hastalarında yürüyüş-AFO'suna duydukları güven puanları 20 (18-24) [%70,8 (%62,5 - %87,5)]; beklenti puanları ise 16 (14-18) [%54,2 (%45,8 - %62,5)] olarak belirlendi. Bireylerin deneyim süresi ile güven ve beklenti puanları arasındaki ilişki sonuçları sırasıyla Spearman's rho=0,357 (p=0,011) ve Spearman's rho=0,198 (p=0,169) olarak bulundu. Bireyler MS hastalarında yürüyüş-AFO'sunun etkinliğini değerlendirmek için %86 oran ile en çok gözlemsel yürüyüş analizini; %16 oran ile ise en az; performans testlerini (süreli kalk yürü 10m yürüme vb.) tercih ettiklerini belirttiler. Bireylerin %42'si MS hastalarında yürüyüş-AFO'su ile ilgili herhangi bir komplikasyonla karşılaşmadığını; %76'sı ise hastaların yürüyüş-AFO'su nedeniyle herhangi bir zarar görmediğini bildirdiler. SAÖ ile puanlanan 'MS hastalarında yürüyüş-AFO'su ile ilgili klinik karar verme süreçleri size göre ne kadar kolaydır?' (0-hiç kolay değil, 10-çok kolay) sorusunun puanı 5 (3-7) olarak bulundu. Bireylerin deneyim süresi ile klinik karar verme sürecinin kolaylığı arasındaki ilişki katsayısı ise Spearman's rho=0,381 (p=0,006) olarak bulundu. **Sonuç:** Çalışma sonucunda MS rehabilitasyonunda anahtar role sahip olan fizyoterapistlerin yürüyüş-AFO'su hakkındaki klinik deneyimleri, tutumları, görüşleri, güvenleri ve beklentileri ile ilgili bilgi ilk defa literatüre kazandırılmıştır. Çalışma sonuçlarımızın MS hastalarında yürüyüş-AFO'su ile ilgili gerekli çalışmalara ve oluşturulacak tedavi kılavuzlarına yön gösterici olacağını düşünmekteyiz.

Anahtar Kelimeler: Multipl Skleroz, ayak-ayak bileği ortezi, fizyoterapist, klinik yaklaşım, beklenti

1. GİRİŞ

Multipl skleroz (MS), tam olarak nedeni bilinmeyen bir etyolojiye bağlı olarak merkezi sinir sisteminde (MSS) hasara ve disfonksiyona neden olan; kronik, inflamatuvar ve demiyelinizan bir hastalıktır (Compston ve Coles, 2008). Hastalık; MSS'de oluşan yaygın lezyonlara bağlı olarak gelişen görsel, bulber, duyusal, motor ve bilişsel bozukluklarla karakterize edilen geniş bir nörolojik bulgu ve belirti yelpazesi ile tanımlanmaktadır (Reich, Lucchinetti ve ark., 2018).

MS hastalarının lokomotor yeteneklerinde oluşan bozukluklar en bariz özürlülük nedenidir ve bireylerin %80'inde hastalığın ilk 10-15 yılında ortaya çıkmaktadır. Yorgunluk, kas kuvvetsizliği, spastisite, inkoordinasyon ve denge kaybı gibi nedenler bu bozukluklara yol açmaktadır (Souza, Kelleher ve ark., 2010).

Düşük ayak, MS hastalarının ambulatuvar aktivitelerinde bozulmaya neden olan yaygın bir problemdir ve özellikle yürüyüşün sallanma fazında ayak bileği dorsifleksiyonunun yetersizliği ile karakterizedir (Mount ve Dacko, 2006). Mobilite aktiviteleri esnasında, ayağın zemine takılmasını önlemek ve ayağın yerden yeterli yükseklikte geçişini sağlamak amacıyla, bireyler sıklıkla pelvik elevasyon ve kalça abdüksiyonu gibi kompansatuvar stratejiler kullanmaktadır (Kottink, Oostendorp ve ark., 2004). Düşük ayak ve bu problemi ortadan kaldırmak için hastanın geliştirdiği kompansasyonlar; artmış enerji tüketimi, fonksiyonel performansta azalma, takılma ve düşme ile ilişkilidir (Olgiati, Jacquet ve ark., 1986). Bu durum da MS hastalarında daha düşük fiziksel aktiviteye ve katılım kısıtlılıklarına yol açabilmektedir. Sonuç olarak, düşük ayak nedeniyle ortaya çıkan bağımsızlık ve katılım kısıtlılıkları tedavinin/müdahalenin gerekliliğini desteklemektedir (Souza, Kelleher ve ark., 2010).

MS veya diğer nörolojik hastalıklarda dorsifleksörler ve ayak bileği evertörlerindeki kuvvetsizlik nedeniyle oluşan düşük ayağa yönelik müdahaleler içerisinde; ayak-ayak bileği ortezleri (yürüyüş-AFO), standart tedavi yaklaşımı olarak öne çıkmaktadır (Sheffler, Hennessey ve ark., 2008; Bulley, Mercer ve ark., 2015). Ayak-ayak bileği ortezleri; yürüme yeteneğini geliştirmek, ayak ve ayak bileği deformitelerini önlemek veya düzeltmek, alt ekstremite eklemlerinin stabilitesini korumak ve alt ekstremitelerin yük taşıma kapasitesini artırmak amaçlarıyla kullanılmaktadır. Ayrıca ayak ve ayak bileği fonksiyonlarındaki bozukluğu telafi edebilir ve elastik malzemeler veya dış kuvvetler aracılığıyla alt ekstremitelerin fonksiyonel iyileşmesini destekleyebilir (Zhou, Yang ve ark., 2022). MS rehabilitasyonunda anahtar role sahip olan fizyoterapistlerin hastaları yürüyüş-AFO'suna yönlendirme, tavsiye etme veya tedavi aracı olarak kullanma konusunda isteksiz veya güvensiz davranması; hastaların potansiyel faydalara sahip bir müdahaleden mahrum kalmasına neden olabilmektedir (Raine, Meadows ve ark., 2013, White, 2016).

Çalışmanın amacı: MS hastalarının ambulatuvar aktivitelerindeki performansını geliştirmek için kullanılan yürüyüş-AFO'su hakkında fizyoterapistlerin klinik deneyimlerini, tutumlarını, görüşlerini, güvenlerini ve beklentilerini incelemekti. Bu sayede; MS rehabilitasyonunda yürüyüş AFO'sunun tercih edilmesine ve bu tedavi yönteminden yararlanılmasında fizyoterapistlerden kaynaklanabilecek bazı nedenlerin aydınlatılması hedeflendi.

2. YÖNTEM

Gözlemsel türde olan bu çalışma kesitsel araştırma dizaynıyla gerçekleştirildi. Meslek hayatları boyunca, en az 1 MS hastasında yürüyüş-AFO'su ile ilgili herhangi bir süreçte (AFO ile ilgili konsültasyon, değerlendirme, ortez eğitimi veya tedavi) yer almış olan Türkiye'deki fizyoterapist bireyler çalışmaya dahil edildi. Çalışmaya dahil edilme kriterleri: çalışmaya katılmak için gönüllü olmak, Türkçe okur-yazar olmak, fizyoterapist olmak, yürüyüş-AFO'su kullanan veya yürüyüş-AFO'su endikasyonu olabileceği düşünülen MS hastasını değerlendirmiş veya tedaviye almış olmaktı. Dahil edilme kriterlerini sağlamayan bireyler çalışmaya dahil edilmedi.

Bireylerin tanımlayıcı özellikleri, yürüyüş-AFO'suna olan güven/beklentileri (Güven/Beklenti Ölçeği-GBÖ) klinikte deneyimledikleri durum/görüşleri hakkındaki bilgiler anket formu kullanılarak tek oturumda elde edildi. Bireyler, anket formundaki maddeleri (GBÖ haricindeki maddeleri); evet/hayır şeklinde, açık uçlu olarak veya Sayısal Oranlama Ölçeği'ne (SOÖ; 0-hiç kolay değil, 10-çok kolay) göre cevapladı.

Tanımlayıcı özellikler bağlamında; mezuniyet yılı, çalışma deneyimi (yıl), çalışma şekli (klinik fizyoterapist/akademisyen), sahip olunan unvan (lisans/yüksek lisans/doktora), çalışılan kurum (kamu kuruluşları/özel kuruluşlar) karşılaştıkları yürüyüş-AFO'su kullanan/endikasyonu olan MS hastası sayısı değişkenleri değerlendirildi.

GBÖ, toplamda 6 maddeden oluşan tedaviye yönelik beklentiyi ve güveni değerlendirmeye yönelik öz-bildirim türünde bir ölçek olup 'güven' (ilk 3 madde) ve beklenti (son 3 madde)" olmak üzere iki alt bölümden oluşmaktadır (Devilly ve Borkovec, 2000). Her bölümün toplam puanı en düşük 3, en yüksek ise 27 puan olarak belirlenir. Maddeler; 9 (1-hiç ile 9-çok) ya da 11 dereceli (0% ile 100%) sistem ile puanlanır. Yüksek puanlar, daha yüksek güveni ve beklentiyi ifade eder. Anketin ve Türkçe versiyonunun yeterli psikometrik özelliklere sahip olduğu farklı çalışmalarla gösterilmiştir (Cronbach alfa = 0,79-0,90; test-tekrar test güvenilirliği, r = 0,75-0,82) (Devilly ve Borkovec, 2000; Smeets, Beelen ve ark., 2008; Sezer Katar, Zengin Ispir ve ark., 2024). Bu ölçek, fizyoterapistlerin MS hastalarında düşük ayağa yönelik tedavi seçenekleri arasında yer alan yürüyüş-AFO'suna(dan) güvenlerini ve beklentilerini ölçmek amacıyla kullanıldı (Swinnen, Lefeber ve ark., 2017).

Anket formunda son olarak; fizyoterapistlerin tutumlarını, deneyimledikleri durumları ve görüşlerini incelemek amacıyla bireylere 4 soru soruldu. Bu sorular: (1) 'MS hastanızda; AFO'nun gerekli/etkili olup olmadığına yönelik değerlendirme yaparken hangi yöntemleri kullanırsınız?'; (2) Deneyimlediğiniz durumlara göre; MS hastalarında yürüyüş-AFO'su ile ilgili en sık karşılaştığınız/en önemli olarak gördüğünüz; komplikasyon hakkındaki görüşünüz/deneyiminiz nedir?'; (3) 'MS hastalarında yürüyüş AFO'su nedeniyle hastanızın herhangi bir olumsuz olay yaşadığını (zarar gördüğünü) deneyimlediniz mi?'; (4) 'MS hastalarında yürüyüş AFO'su ile ilgili klinik karar verme süreçleri size göre ne kadar kolaydır?' şeklindeydi.

Çalışma sonucunda elde edilen verilerinin normal dağılıma uygunluğu; görsel (histogram ve olasılık grafikleri) ve analitik yöntemler (Kolmogorov-Smirnov testi; $p < 0,05$) ile değerlendirildi. Veriler normal dağılmadığı için sayısal değişkenlerin tanımlayıcı istatistikleri ise ortanca ve çeyrekler arası aralık (%25-%75) ile raporlandı. Kategorik değişkenlerin tanımlayıcı istatistikleri ise sayı (n) ve oran (%) ile gösterildi.

Çalışma verilerinin analitik istatistiklerinde; bireylerin deneyim süresi ile güven, beklenti ve klinik karar verme sürecinin kolaylığına ait puanlar normal dağılmadığı için aralarındaki ilişkiler için korelasyon katsayıları (r) ve p değerleri Spearman testi ile hesaplandı. Korelasyon katsayılarının düzeyi önemsiz (<0,20), düşük (0,20-0,40), orta (0,40-0,70), yüksek (0,70-0,90) ve çok yüksek seviyede (>0,90) ilişki olarak yorumlandı (Williams ve Monge, 2001). Tüm verilerin analizi Statistical Package for Social Sciences (SPSS) Version 26.0 (SPSS Inc., Chicago, Illinois, ABD) yazılımıyla gerçekleştirildi. Analitik istatistiklerin tümünde anlamlılık düzeyi p<0,05 olarak ele alındı. Tüm bireyler anketi eksiksiz doldurdu ve çalışmaya dahil edilen tüm bireylerin verileri ile istatistiksel analizler gerçekleştirildi.

3. BULGULAR

Çalışmaya 50 fizyoterapist dahil edildi. Bireylerin tanımlayıcı özellikleri Tablo 3.1'de gösterildi.

Tablo 3.1. Bireylerin tanımlayıcı özellikleri

Özellik	**Değer**
Klinik Fizyoterapist (n, %)	30 (% 60)
Akademisyen (n, %)	20 (% 40)
Deneyim Süresi (yıl), ortanca (%25-%75)	9 (3–12)
MS hastası sayısı, ortanca (%25-%75)	5 (3–15)

Fizyoterapistlerin MS hastalarında yürüyüş-AFO'suna duydukları güven/beklenti ve klinik karar verme sürecinin kolaylığı hakkındaki bulgular Tablo 3.2'de gösterildi. Bireylerin deneyim süresi ile güven puanları ve klinik karar verme sürecinin kolaylığı arasında istatistiksel anlamlı, pozitif yönde düşük seviyede ilişkiler bulurken; deneyim süresi ile beklenti puanları arasında ise istatistiksel anlamlı bir ilişki bulunmadı (Tablo 3.2).

Tablo 3.2. Güven, beklenti ve klinik karar verme sürecine ait puanlar ve deneyim süresi ile ilişkileri

	Ortanca (%25-%75)	Yüzde (%) (%25-%75)	Deneyim süresi ile ilişki (r)	p
Güven puanı	20 (18–24)	70,8 (62,5–87,5)	0,357	0,011*
Beklenti puanı	16 (14–18)	54,2 (45,8–62,5)	0,198	0,169
Klinik karar verme kolaylığı	5 (3–7)	50 (30-70)	0,381	0,006*

(r: Spearman ilişki katsayısı, *:p<0,05)

Fizyoterapistlerin tutumlarını, deneyimledikleri durumları ve görüşlerini incelemek amacıyla oluşturulan sorulara ait bulgular ise Tablo 3.3'te gösterildi.

Tablo 3.3. Fizyoterapistlerin yürüyüş-AFO'su ile ilgili klinik görüş ve deneyimleri

Soru	**Yanıt**	**Oran (%)**
Soru 1-AFO'nun etkililiğine yönelik değerlendirme	Gözlemsel yürüyüş analizi	% 86,3
	Kas kuvveti değerlendirmesi	% 76,5
	Eklem hareket açıklığı	% 76,5
	Kas tonusu değerlendirmesi	% 72,5
	Hastaya AFO ile ilgili görüşünü sorma	% 72,5
	Duyu değerlendirmesi	% 45,1
	Performans testleri	% 15,7
Soru 2- Komplikasyon ile karşılaşma (En çok bildirilen komplikasyonlar: AFO'nun uygun ayakkabıyla kullanılamaması ve AFO'nun ağır hissedilmesi)	**Evet**	% 57
	Hayır	% 43
Soru 3- Olumsuz olay/zarar görme (En çok bildirilen olumsuz olay: bası yarası oluşması ve ambulatuvar performansın olumsuz etkilenmesi)	**Evet**	% 33,5
	Hayır	% 76,5

4. TARTIŞMA VE SONUÇ

Çalışma sonucunda MS rehabilitasyonunda anahtar role sahip olan fizyoterapistlerin yürüyüş-AFO'su hakkındaki klinik deneyimleri, tutumları, görüşleri, güvenleri ve beklentileri ile ilgili bilgi ilk defa literatüre kazandırılmıştır. Çalışmamız, ele alınan araştırma soruları açısından literatürden farklıdır.

Bu çalışmada fizyoterapistlerin MS rehabilitasyonunda yürüyüş-AFO'suna(dan) güvenleri ve beklentileri GBÖ ile değerlendirildi (Devilly and Borkovec 2000). Bu ölçek ile değerlendirilen güven; fizyoterapistler için MS hastalarının tedavisinde yürüyüş-AFO'sunun ne kadar inandırıcı, ikna edici ve mantıklı göründüğünü ifade ederken, beklenti ise yürüyüş-AFO'su sayesinde hastada elde edilecek gelişmeye olan inancı ifade etmektedir (Smeets, Beelen ve ark., 2008; Swinnen, Lefeber ve ark., 2017). Çalışma sonucunda fizyoterapistlerin yürüyüş-AFO'suna güvenlerinin yüksek seviyelerde beklentilerinin ise orta seviyelerde olduğu gösterildi. Bu bağlamda; yürüyüş-AFO'sunun fizyoterapistler tarafından mantıklı, bilimsel ve uygulanabilir bir araç olarak görüldüğünü, ancak; yürüyüş-AFO'sunun iyileştirici etkisi konusunda tam bir ikna durumunun sağlanamadığını göstermektedir. Bu durum; konuyla ilgili teorik desteklerin olduğunu, ancak pratikte daha fazla kanıta ve güven artırıcı sonuçlara ihtiyaç duyulduğunu düşündürmektedir. Fizyoterapistlerin deneyim süreleri ile duydukları güven arasında düşük seviyede bir ilişki olması; beklentileri arasında ilişki bulunmaması ise yürüyüş-AFO'sunun teorik geçerliliği konusunda deneyimle birlikte artan bir kabul olabileceği; ancak klinik sonuçlara yönelik beklentinin deneyimden bağımsız olarak şekillenebileceğini düşündürmüştür.

Çalışmamızda fizyoterapistlerin yürüyüş-AFO'sunun etkinliğinin değerlendirilmesinde en çok gözlemsel yürüyüş analizini; en az ise performans testlerini (süreli kalk yürü testi, 10m yürüme testi vb.) tercih ettikleri gösterildi. Bu durum; her zaman olmasa da yürüyüş-

AFO'sunun etkinliğinin belirlenebilmesinde gözlemsel yürüyüş analizine göre daha objektif ve sayısal veri elde edilmesini sağlayabilecek performans testlerine fizyoterapistlerin daha fazla önem vermeleri gerektiğini göstermiştir.

Çalışma sonucunda, fizyoterapistlerin yürüyüş-AFO'su ile ilgili klinik karar verme süreçlerini orta seviyelerde kolay buldukları ve deneyim süreleri ile klinik karar verme sürecinin kolaylığı arasında düşük seviye bir ilişki olduğu gösterildi. Her ne kadar deneyim süresi ile klinik karar verme süreci bir miktar kolaylaşsa da bu sonuç; MS hastalarında yürüyüş-AFO'su hakkında klinik uygulama rehberlerine ve daha fazla mesleki eğitime ihtiyaç olduğunu göstermektedir. Ayrıca; çalışmamızda, yürüyüş-AFO'su ile ilgili komplikasyon yaşama oranlarının orta seviyelerde ve olumsuz olay yaşama oranlarının ise düşük/orta seviyelerde bulunmuş olması da bu ihtiyaçları destekler niteliktedir. Bununla birlikte; komplikasyon ve olumsuz olay oranları diğer fizyoterapi yaklaşımlarında olduğu gibi uygun hasta seçimi ve hastaya özel yaklaşımların önemini de göstermiştir.

Literatürde, yürüyüş-AFO'sunun MS hastalarının fonksiyonel ambulasyon üzerindeki etkilerini kapsamlı biçimde ortaya koyacak ileri düzey araştırmalara ve yürüyüş-AFO'su ile ilgili kanıta dayalı klinik uygulama kılavuzuna gereksinim duyulduğu belirtilmektedir (Bulley, Mercer ve ark., 2015; Swinnen, Deliens ve ark., 2018; Byrnes-Blanco, Reed ve ark., 2023). Konu ile ilgili güncel sistematik bir derlemede; MS hastalarında yürüyüş-AFO'su kullanımının gerekli olup olmadığının tam olarak belirlenemediği, bazı çalışmaların tabanlık ve yürüyüş-AFO'sunun MS hastalarında dengeyi iyileştirebileceğini gösterirken, bazı çalışmaların ise sadece tabanlık ve yürüyüş-AFO'sunun dengeyi iyileştirmediğini, hatta kötüleştirdiğini gösterdiği bildirilmektedir (Ashkar, Razeghinezhad ve ark., 2022).

AFO'nun motor bozuklukları telafi edebileceği ve ambulasyonu iyileştirebileceği klinik olarak kabul görmektedir ve özellikle inme hastalarında kanıt düzeyi yüksek çalışmalar ile gösterilmiştir (Gök, Küçükdeveci ve ark., 2003; Sheffler, Hennessey ve ark., 2008; Tyson ve Kent 2013). Ancak, inme rehabilitasyonunda dahi AFO'nun tedavi yöntemi olarak yeterince tercih edilmediği literatürde bildirilmektedir (Raine, Meadows ve ark., 2013; White, 2016). Bu duruma yol açan nedenler ise; hastaya (estetik kaygı, toplumsal damgalanma, orteze alışamama vb.), rehabilitasyon ekibi üyelerine (bilgi eksikliği, etkili olmadığını düşünme vb.) veya orteze (maliyet, giyip çıkarma zorluğu vb.) bağlı olarak meydana gelebilmektedir (Golding-Day, Walker ve ark., 2022). Bu nedenlerle bireyler etkili bir tedavi yönteminden mahrum kalabilmektedir (White, 2016).

Fizyoterapistlerin MS ve inme gibi nörolojik hastalıklarda yürüyüş-AFO'su önerme veya müdahale aracı olarak tercih etme konusunda isteksiz olduklarını gösteren kanıtlar bulunmaktadır (Raine, Meadows ve ark., 2013). Bazı fizyoterapistlerin AFO'nun işlevini tam olarak anlayamaması; AFO sayesinde fonksiyonel yürüyüşün ve kas kontrolünün kolaylaşabileceğini görememesi ve son olarak; yürüyüş-AFO'su nedeniyle hastanın kullanması gereken kaslarını tembelleştirerek kas kuvvetinin azalmasına ve hatta atrofi oluşumuna neden olabileceğine dair endişeler bu isteksizliğe yol açan nedenlerden bazılarıdır (Sackley ve Lincoln 1996; Davidson ve Waters, 2000; Downing, Van Ryn ve ark., 2014; Mayer, Warring ve ark., 2015).

Bu çalışma ile MS rehabilitasyonunda yürüyüş AFO'sunun tercih edilmesine ve bu tedavi yönteminden yararlanılmasında fizyoterapistlerden kaynaklanan bazı nedenler aydınlatılmıştır. Bu doğrultuda, çalışma sonuçlarımızın MS hastalarında yürüyüş AFO'su ile ilgili ileri çalışmalara ve geliştirilecek kanıta dayalı klinik uygulama kılavuzlarına yön gösterici olacağını düşünmekteyiz.

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ANALYSIS OF FEATURES OF IATROGENIC DAMAGE OF EXTRARENAL BILE DUCTS DURING CHOLECYSTECTOMY

Keywords: iatrogenic injuries, cholecystectomy, bile ducts, choledoch

Damage to extrarenal bile ducts (VЖП) continues to be one of the most dangerous complications in hepatobiliary surgery. As a rule, ductal trauma occurs during operations on the biliary tract, most often during cholecystectomy, less often during operations on the stomach, duodenum, pancreas.

Interest in this problem has increased in recent decades due to the widespread introduction of minimally invasive technologies into surgical practice: video laparoscopy and minilaparotomy with elements of open laparoscopy. The frequency of damage to the extrahepatic bile ducts during open cholecystectomy (OX) is 0.1-0.3%, but with the introduction of laparoscopic cholecystectomy, it has increased to 0.4-3.5% (5,6,7).

The specific weight of this complication in minilaparotomy cholecystectomy is 0.2-2.5% (2.3).

In this regard, many researchers note that the nature of iatrogenic damage to the extrarenal bile ducts has changed somewhat. Thus, if in open cholecystectomy (OX) the main mechanisms of trauma are crossing, excision and ligation, then in laparoscopic (ЛХЭ) clipping and diametrical necrosis of the wall of the bile duct are added to them (4,6,8).

Considering the relevance of this problem, our topic of work is dedicated to solving this problem.

The purpose of our work: to specify a more objective examination program for patients with iatrogenic damage to the extrarenal bile ducts at different times of their detection and the validity of rational options for surgical restorative-reconstructive interventions.

Task of this work:

1) Conduct a comparative evaluation of the informativeness of modern studies in the diagnosis of damage to the extrahepatic bile ducts during cholecystectomy.

2) Develop and implement. In clinical practice, the algorithm of surgical tactics for iatrogenic injuries of the extrarenal bile ducts and to choose a more rational biliodigestive anastomosis tactic for the treatment of iatrogenic injuries of the extrarenal bile ducts B depending on the nature of the clinical manifestations and timing of the trauma.

3) To evaluate the immediate and remote results of the choice of modification of one or another method of surgical treatment for iatrogenic damage of the extrarenal bile ducts and to study the quality of life of patients in the immediate and remote postoperative period.

Materials and methods of research:

Included in the study were 56 patients with damage to the main bile ducts during cholecystectomy, who were treated at the National Center for Disease Control and Prevention. Acad. M.A. Topchibasheva, city of Baku, Azerbaijan state for the period 2018-2024. All patients were divided into two groups.

- the main group is patients who received iatrogenic damage to extrarenal bile ducts in our clinic: 24 (42.8%) patients with traditional cholecystectomy, 32 (57.14%) with laparoscopic cholecystectomy.

- the control group consisted of 48 patients who were transferred to our clinic from other medical institutions and private clinics and who came on their own.

The long-term results of treatment were evaluated on the basis of outpatient and inpatient examinations, questionnaires and patient surveys.

According to evaluation criteria, remote results were defined as excellent, good, satisfactory and unsatisfactory

Statistical processing used non-parametric statistical methods: У-criterion Mann-Whitney criterion x2 Pearson.

For the purpose of diagnosis and treatment of patients with iatrogenic damage to the extrarenal bile ducts, observation of the flow dynamics and assessment of the results of the objective status of these persons, we performed biochemical blood tests, performed general clinical and instrumental non-invasive and invasive methods of research.

The physical examination was based on the study of the victims' complaints, anamnestic data and their objective examinations.

Ultrasound - performed with the purpose of detecting free fluid in the abdominal cavity, assessing the condition of the extrahepatic bile ducts.

To determine the state of the upper parts of the gastrointestinal tract, to assess the patency of the bile ducts and to rule out the pathology of the large papilla of the duodenum (VSDC), fibrogastroduodenoscopy was performed for diagnosis.

Patients admitted with an external biliary fistula (drainage) underwent percutaneous fistulography under X-ray examination. As a radio-contrast substance, the preparation "Ultravist" 37% was used.

Results of own studies and discussions. When choosing treatment tactics and surgical interventions, we analyzed the results of our own studies of patients of our clinic with iatrogenic injuries of the extrarenal bile ducts - this is the main group of 8 (14.2%), and patients transferred and independently admitted to us from district and private clinics - this is the control group of 48 (85.7%). The analyzed results of treatment with ЯПВЬПП and stricture of the extrarenal bile ducts for the period 2018-2024 in both groups comprised a total of 56 (100%) patients. Discussion of the obtained results took into account: character, localization, severity, condition of patients, types of performed operations of iatrogenic damage of extrarenal bile ducts and their primary surgical intervention tactics with subsequent restorative-reconstructive operations.

Analyzing the results according to the nature of the primary pathology, it can be concluded that the number (number) of complications - damage to the extrarenal bile ducts is higher in patients with acute calculous cholecystitis (ACC) in both groups. This is connected with the development against the background of inflammatory changes not only of the gallbladder, hepatoduodenal ligament, adhesion processes, but also inflammatory conditions of the adjacent organs, such as stricture of the choledochal compartment and their combination with the symptoms of Myrizia, which aggravated the infiltrative changes of the hepatoduodenal ligament. Precisely in such conditions, hemostasis was difficult in LXЭ with acute calculous cholecystitis, where trauma occurs in non-standard situations, as a result of which surgeons made tactical and technical errors, leading to iatrogenic damage to the extrarenal bile ducts.

Examination of the patients of our clinic in the main group of 8 patients with LHA - complete transection was found in 1 patient (12.5%), partial clipping of the OHP in 1 patient (12.5%), parietal wound of the lower level of the gallbladder in 1 patient (12.5%), damage to the vessels of the gallbladder in 2 patients (15.0%).

With traditional cholecystectomy, the marginal excision of the choledochus was found in 1 (12.5%) patient, and damage to the gallbladder vessels in 1 (12.5%) patient out of 8 patients, the main group.

In the control group, according to the data from the medical history of patients admitted to our clinic with LXЭ out of 48 patients, complete transection of the common bile duct without damage to the confluent was found in 2 patients (4.1%), with damage to the right part of the confluent in 2 patients (4.1%), clipping of the common bile duct in 6 patients (12.5%), parietal wound of the common bile duct in 1 patient (2.0%) of them the lower level of 1 patient (50.0%) and the middle level of the gallbladder in the 1st patient (50.5%), coagulation trauma: marginal punctate damage to the gallbladder in the region of the entry of the duct of the gallbladder into the gallbladder in the 1st patient (12.5%), damage to the vessels of the gallbladder in the 6th patient (12.5%).

With traditional cholecystectomy in the control group, 28 (58.3%) of 48 patients with iatrogenic lesions of the extrarenal bile ducts underwent from 2 to 3 or more different surgical interventions in different clinics after the primary operation of iatrogenic lesions of the extrarenal bile ducts with complications in the hepatobiliary zone.

According to the medical record, the main type of surgical intervention that became the primary cause in 28 patients who underwent 2 to 3 repeated surgical interventions in different clinics was LHE - this is complete transection of the cholangiocarcinoma in 3 patients out of 28 patients (10.7%), excision in 2 (7.1%), clipping in 9 (32.1%), wall injuries in 4 (14.2%), 11 (39.2%) patients have coagulation thermal injuries.

In the majority of patients admitted to our clinic from other hospitals, where repeated operations were performed after primary iatrogenic damage to the extrarenal bile ducts, there was no complete information about the nature and level of damage to the extrarenal bile ducts. In our clinic, in addition to instrumental studies, the causes of iatrogenic damage to the extrarenal bile ducts were revealed during repeated laparotomy, since some medical documentation did not contain the necessary information,

Despite the temporary effectiveness of the results of operations performed for iatrogenic damage to the extrarenal bile ducts, after the application of all types of operations, the blood pressure level in the remote period is not fully restored. Temporarily obtained satisfactory results in the distant period, each proposed method of surgical treatment has its own shortcomings. Therefore, every proposed new method of surgical treatment will make a big contribution to improving the quality of life of patients.

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ETIOLOGICAL STRUCTURE OF GENITOURINARY TRACT INFECTIONS CAUSED BY CONDITIONALLY PATHOGENIC MICROORGANISMS IN WOMEN

Keywords: genitourınary tract, infections, bacterial vaginosis

The vaginal microbiocenosis is a collection of microorganisms living in a specific biotope, usually consisting of lactobacilli. The state of the vaginal microbiocenosis is of great importance for reproductive health. Bacterial vaginosis (BV) and aerobic vaginitis (AV) are infectious, non-inflammatory diseases of the vaginal tract, which are caused by an imbalance between the physiological microflora of the vagina and conditionally pathogenic microflora [1].

Diseases of the genitourinary system are among the most common diseases in urological practice. Besides, the increase in the level of pathology occurs with a decrease in the quality of life and unfavorable environmental conditions [2].

In recent years, the management of urinary tract infections has become increasingly difficult due to the emergence of multidrug-resistant pathogens. The use of narrow- and broad-spectrum antibiotics in treatment remains a topic of wide discussion in clinical trials [3].

BV is more common in females aged 15-24 (42%) than in older age groups (48-60%), but no significant association with age has been identified. The prevalence of BV is influenced by educational level, marital status, or hygienic aspects of behavior, such as daily changing of underwear and regular water procedures [4].

BV occurs in 51% of African-American women, 32% of Hispanic women, and 23% of Caucasians. However, these differences are largely due to the dietary and sexual behaviors of representatives of different races. In a study conducted among indigenous peoples living in the North, Khanty and Mansi, BV was found in only 7% of those surveyed. In recent years, an increase in urinary tract infections has been observed [5,6].

The human microbiome is very diverse and includes bacteria, fungi, protozoa, and viruses, having species that intensively colonize different tissue areas.

The nature of the symbiotic relationship between macroorganisms and mycoplasmas depends on the state of the body's immunobiological defense mechanisms and the pathogenic properties of the bacteria[7].

At the same time, mycoplasmas are carriers of a number of unique properties. In particular, in addition to participating in the formation of the inflammatory response, they can have an immunosuppressive effect, cause the synthesis of autoantibodies and autoimmune reactions, have pro- and/or antiapoptotic activity, provide genome instability, and cause chromosomal aberrations and transformations in the genetic apparatus of infected cells[8].

According to many authors, the main causative agents of UTIs are Escherichia coli (64.6%), Klebsiella spp. (9.5%), Enterococcus spp. (6.46%), and Staphylococcus spp. (5.1%). Depending on the nature of the infection, UTIs are divided into complicated and uncomplicated forms. Uncomplicated infections are observed in patients without obstructive uropathy and structural changes in the kidneys, as well as in patients without serious diseases. The high resistance of pathogens to antimicrobial drugs in the treatment of patients with recurrent UTIs causes certain difficulties[9].

Taking all this into account, it becomes clear that the study of bacterial vaginosis and infection of the urogenital tract with opportunistic pathogens in women is a relevant issue. In this regard, we considered it appropriate to conduct research to analyze the etiological structure of infection of the urogenital tract with opportunistic pathogens.

Purpose of the research: Microbiological evaluation of urogenital tract infections associated with opportunistic microorganisms.

Materıals and methods of the research. The study included 110 patients and 22 healthy women who applied for routine examinations at the Ganja City Women's Clinic. Out of 110 patients, 20 were diagnosed with chronic recurrent genital candidiasis, 29 with recurrent bacterial vaginosis, and 39 with both chronic recurrent genital candidiasis and bacterial vaginosis. In the first stage of the study, the number of annual recurrences of the corresponding diseases in the patients registered in 2017 (defined as 10-12 times, 6-9 times, and less than 6 times per year) was calculated in number and % for each group of patients. In the second stage of the study, the incidence and percentage of normomenorrhea, oligomenorrhea, hypomenorrhea, hypermenorrhea, algodysmenorrhea, and premenstrual syndrome were studied in each group of patients (groups composed of 20 patients with chronic recurrent genital candidiasis, 29 patients with recurrent bacterial vaginosis, and 39 patients with both chronic recurrent genital candidiasis and recurrent bacterial vaginosis) and a group of healthy individuals (22 persons).

The occurrence and colony-forming ability of S. epidermidis, S. aureus, E. coli, Enterococci, S. Saprophyticus, and C. albicans microorganisms in vaginal smears and vaginal fluid samples of the affected groups (39 patients – Group III, 29 patients - Group II, 20 patients – Group I), and 22 healthy women (Control group) who applied to the Ganja City Women's Counseling Center were determined and expressed in number and %, CFU. Both the patient and control groups included women in the age range of 30-35. The reason we chose such a narrow age range is to minimize the effects of age on the results of the study.

The study of quantitative indicators of various microorganism types in vaginal smears of patients with mixed etiology of bacterial urogenital infections revealed the occurrence of S. epidermidis species in 10 biological samples taken from a group of 29 women suffering from bacterial vaginosis, which covered 34.5% of the group. In these patients, the S.aureus species was observed in 5 of the biological samples, the E.coli species in 8 samples, Enterococci in 2 samples, S.saprophyticus in 2 samples, and Candida strains in only 1 sample, which is accounted for

17.5%, 27.59%, 6.9%, 6.9%, and 3.45% of the women in the respective groups, suffering from this nosological unit.

Quantitative indicators of various microorganism types were studied in vaginal smears of patients with mixed etiology of bacterial urogenital infections during associations with various microorganisms. In biological material samples taken from a group of 20 women diagnosed with chronic recurrent genital candidiasis, S. epidermidis was found in 6 smear samples (30% of the total group), S. aureus in 5 samples (25%), E. coli in 10 samples (50%), and Enterococcus species, S. saprophyticus species, and C. albicans fungi were found in only 1 sample each (5% of the total samples in the group).

During the microbiological examination of vaginal smear samples taken from 22 women who were accepted as a control group and who were not diagnosed with any genital infection and simply applied to the antenatal clinic for routine prophylactic examinations, S. epidermidis was found in 4 samples or 18.2% of the corresponding group, and Enterococci and S. saprophyticus were found in 1 sample each, accounting for 4.55% of each group. However, Candida albicans, E. coli, and S. aureus were not found in the biological samples of these women. The qualitative indicators of various microorganism types in vaginal smears of patients with mixed etiology of bacterial urogenital infections were studied in association with various opportunistic microorganisms. In a group of 39 women suffering from both chronic recurrent genital candidiasis and bacterial vaginosis, the colony-forming units of S. epidermidis, S. aureus, E. coli, Enterococci, S. saprophyticus, and C. albicans were 7.88±0.07 CFU, 2.22±0.16 CFU, 4.11±0.12 CFU, 0.68±0.04 CFU, 2.02±0.34 CFU, and 4.34±0.23 CFU, respectively.

In a group of 22 healthy women without any genital problems, when studying the colonization abilities of the above-mentioned microorganisms, the colony-forming units of S. epidermidis, Enterococci, and S. saprophyticus were 1.04±0.044, 0.026±0.006 and 0.012, respectively, while the corresponding indicators of S. aureus, E. coli and C. albicans were 0. The qualitative characteristics of lactobacilli and bifidobacteria (with CFU) and the nature of vaginal discharge were studied in vaginal fluid samples from patients with mixed-etiology of bacterial urogenital infections during associations with various opportunistic microorganisms. While the colonization capacity of lactobacteria in a group of 39 women suffering from both chronic recurrent genital candidiasis and bacterial vaginosis was 3.78±0.19 CFU, in a group of 29 women suffering from recurrent bacterial vaginosis it was 1.17±0.16 CFU, and in a group of 20 women suffering from chronic recurrent genital candidiasis, the average value of this indicator was estimated to be 3.08±0.27 CFU. In the group of 22 women who visited the women's clinic for a routine preventive examination, which we accepted as a control group, this indicator was found to be 6.07±0.21 CFU on average. As a result of the study of the colonization ability of lactobacilli, the highest indicator was recorded in the healthy women who made up the control group, and the lowest in the group of patients with vaginosis. The average colony-forming ability of bifidobacteria in the group of women suffering from both bacterial vaginosis and chronic recurrent genital candidiasis was found to be 1.87±0.08 CFU, in the group of 29 women suffering from recurrent bacterial vaginosis, it was 0.31±0.03 CFU, and in the group of women suffering from chronic recurrent genital candidiasis, it was 1.24±0.05 CFU.

In the second phase, the nature of the vaginal discharge of patients with mixed etiology of bacterial urogenital infections was studied in association with various opportunistic microorganisms. In a group of 39 women suffering from both chronic recurrent genital

candidiasis and bacterial vaginosis, white vaginal discharge was recorded in 18 women, which accounts for 46.2% of the corresponding group. In this group, mucous vaginal secretion was observed in 20 patients, accounting for 51.3% of the group. Purulent vaginal discharge was detected in 4 patients, accounting for 10.3% of the group (Table 3.9). Yellow secretion was observed in 6 patients, accounting for 15.4% of the group. No cases of absence of vaginal discharge were recorded in this patient group.

In a group of 29 women with recurrent bacterial vaginosis, 12 women complained of white vaginal secretion, which accounted for 41.4% of the group. In this group, mucous vaginal secretion was observed in 11 women, which accounted for 37.9% of the group. In 2 patients in the group, that is, 6.9% of the group, purulent vaginal discharge was recorded. Yellow vaginal fluid was recorded in 5 patients in this group, covering 17.2% of the corresponding group. Vaginal discharge was recorded in all patients in this group.

In a group of 20 patients suffering from chronic recurrent genital candidiasis, cases of white vaginal discharge were observed in 4 women, which covered 20% of the corresponding group. Mucous vaginal discharge was observed in 12 women in this group, which covered 60% of the group. Purulent vaginal discharge was observed in 5 people in the group, which accounted for 25% of the group. In this group, yellow vaginal discharge was also recorded in 5 people (25%). In this group, no vaginal discharge was observed. Of the 22 healthy women we accepted as the control group, only 1 (4.5%) had vaginal discharge, which was white. In the remaining 21 women (95.5%), no vaginal discharge was observed.

Although the average group CFU for Streptococcus species in the group of healthy women was calculated to be 1.13±0.082, in the biological samples taken before treatment in the group of 39 women suffering from both bacterial vaginosis and recurrent genital candidiasis, this indicator was found to be 4.17±0.090 CFU.

During the study, the average colonization capacity of streptococcal species in the group of healthy women was calculated to be 1.13±0.082 CFU. However, in the biological samples taken before treatment in a group of 39 women suffering from both bacterial vaginosis and recurrent genital candidiasis, this indicator was found to be 4.17±0.090 CFU. The treatment of these patients was accepted as a “basis”, and after the measures detailed above were implemented, the average CFU of streptococci in vaginal smear samples was calculated to be 3.92±0.103 for the group. After the patients were treated with “basis” treatment + bactistatin (probiotic), the CFU of streptococci was slightly lower, 3.66±0.107, in vaginal smear samples. After the next relapse of the patients included in this group, for the patients treated according to the “basis” treatment + bactistatin (probiotic) + sambovin (immunomodulator) scheme, the qualitative indicator of the mentioned opportunistic microorganism in the biological samples was calculated to be 2.86±0.093 CFU, which is closer to the corresponding indicators of healthy individuals compared to the indicators resulting from other treatment measures. While the average quality index of staphylococcal species in vaginal smear samples obtained from a group of 22 healthy women involved in the study was calculated to be 2.38±0.109 CFU, the average quality index of the microorganism species in vaginal smear samples taken from a group of 39 women suffering from both recurrent chronic genital candidiasis and bacterial vaginosis was calculated to be 5.36±0.138 CFU.

After the basis treatment was applied in patients, this indicator was slightly higher, 6.42±0.229 CFU, than the indicator before treatment. When the next relapse occurred

after the disease was cured, the treatment according to the “basis” + bactistatin (probiotic) scheme was applied and this indicator was slightly lower than the indicator before treatment, 5.15±0.295 CFU.

During relapses after patients recovered from treatment with a combination of “basis” treatment and parabiotics, treatment was performed according to the “basis” treatment + bactistatin + sambovin scheme. Then after the patients were recovered, vaginal swab samples were taken again and analyzed for the mentioned opportunistic pathogen, and as a result, the CFU of that microorganism was found to be lower, 4.17±0.234, than that of after other treatment measures.

In vaginal smear samples taken from the group of 29 women with recurrent bacterial vaginosis, the average CFU of microorganisms such as S. epidermidis, S. aureus, E. coli, Enterococci, and S. saprophyticus were 3.08±0.11, 2.09±0.12, 3.14±0.2, 1.03±0.17, and 2.20±0.45, respectively, while Candida fungi were not found in vaginal smears. In a group of 20 women suffering from chronic recurrent genital candidiasis, the average group CFU of S. epidermidis, S. aureus, E. coli, Enterococci, S. saprophyticus, and C. albicans species was 6.06±0.20, 7.86±0.31, 5.46±0.35, 0.74±0.08, 2.27±0.17, and 1.00±0.12, respectively.

The recorded CFU for Candida albicans in vaginal smear samples taken from 22 women who visited the women's clinic for periodic preventive examinations was 0.30±0.08. In a study of 39 patients suffering from both bacterial vaginosis and recurrent genital candidiasis, this indicator was found to be ten times higher, 5.38±0.119 CFU, than that of healthy women, before any treatment was performed. After the “basis” treatment was applied, the average CFU for the fungal species in the biological samples was found to be 4.25±0.214 per group, which is significantly lower than the indicator before treatment. In the patients who recovered with the help of “basis” treatment, but later relapsed, the colony-forming ability of C. albicans in biological samples obtained after treatment with the “basis” treatment + bactistatin scheme was almost at the same level as the corresponding indicator in women who recovered with only “basis” treatment, 4.26±0.270 CFU. However, the corresponding indicator was calculated to be significantly lower, 2.28±0.235 CFU, as a result of treatment of patients with the “basis” treatment + bactistatin + sambovin regimen during their next relapse. According to the results, those with bacterial vaginosis and recurrent vaginal candidiasis would benefit more from using probiotics and immunological preparations in addition to generally accepted treatment measures.

The average scores of the indices were compared with those of other illnesses, such as asthma and chronic obstructive pulmonary disease, in order to examine the quality of life of women who had chronic infections. The study revealed that these women have a worsening psycho-emotional state, low self-esteem, social and physical activity. Deterioration of the vaginal microflora, the presence of discharge and bad odor cause discomfort, and a feeling of shame in front of their sexual partner. Thus, when studying the diagnostic markers of bacterial vaginitis using traditional and modern examination methods, it becomes clear that for the correct diagnosis, it is necessary to start with the determination of clinical and anamnestic indicators. Although microscopic and microbiological examinations are considered the gold standard for the examination of BV, new molecular examinations also attract attention as they are more effective and convenient. It became evident from the literature review that identifying the main clinical symptoms is also crucial for BV evaluation.

To study the sensitivity of microorganisms to various antibiotics in biological samples taken from patients suffering from both bacterial vaginosis and chronic recurrent genital candidiasis, smear samples were sent to the microbiology laboratory of the same medical institution. In these samples, the sensitivity of E. coli, Staphylococcus spp., Enterococcus faecalis, Ureaplasma urealyticum, and Mycoplasma hominis species to antibacterial drugs such as Azithromycin, Macropen, Amoxicillin, Cefataxime, Ceftriaxone, Ampicillin, Oxacillin, Doxycycline, Amikacin, and Gentamicin was determined by applying antibiotic "disks" in terms of number of incidences and percentage.

As a result of the study, sensitivity to Azithromycin was recorded in 77 out of 88 samples, which is 87.5±3.53% of the total samples. The sensitivity of E. coli to Amoxicillin was recorded in 42 samples, to Cefotaxime in 21 samples, to Oxacillin in 5 samples, to Doxocillin in 20 samples, to Amikacin in 9 samples, and to Gentamicin in 45 samples, which accounted for 47.7±5.32%, 23.9±4.54%, 5.7±2.47%, 22.7±4.47%, 10.2±3.23%, and 51.1±5.33% of the total samples, respectively. However, no significant susceptibility of E. coli to Macropen, Ceftriaxone, and Ampicillin was observed in any sample (Table 5).

As a result of the study, 55 out of 88 samples (62.5±5.16% of the total samples) showed sensitivity of Staphylococci to Azithromycin, 75 samples (85.2±3.78%) to Amoxicillin, 3 samples (3.4±1.93%) to Cefotaxime, 25 samples (28.4±4.81%) to Doxycycline, and 19 samples (21.6±4.39%) to Gentamicin. Staphylococci were not sensitive to Macropen, Ceftriaxone, Ampicillin, Oxacillin, and Amikacin in the samples.

As a result of the study, Streptococci were found to be susceptible to Azithromycin in 70 samples, which accounts for 79.5±4.30% of the total samples. The susceptibility of this microorganism to Amoxicillin was found in 83 samples, to Cefotaxime and Ceftriaxone in 5 samples each, and to Gentamicin in 10 samples, which accounted for 94.3±2.47%, 5.7±2.47%, 5.7±2.47% and 11.4±3.38% of the total samples, respectively. Streptococci were not found to be susceptible to Macropen, Ampicillin, Oxacillin, Doxycycline, and Amikacin in any of the samples.

Enterococcus faecalis was found to be susceptible to Azithromycin in 8 samples, to Amoxicillin in 7 samples, to Doxocillin in 4 samples, and to Gentamicin in 8 samples, which accounted for 9.1±3.06%, 8.0±2.88%, 4.5±2.22%, and 9.1±3.06% of the total samples, respectively. None of the total samples showed significant susceptibility of Enterococcus faecalis to Macropen, Cefotaxime, Ceftriaxone, Ampicillin, Oxacillin, and Amikacin.

As a result of the study, the sensitivity of Ureaplasma urealyticum to Azithromycin was recorded in 51 samples, sensitivity to Macropen in 14 samples, and sensitivity to Doxocillin in 63 samples, which is 58.0±5.26%, 15.9±3.90%, and 71.6±4.81% of the total samples, respectively. The sensitivity of Ureaplasma urealyticum to Amoxicillin, Cefotaxime, Ceftriaxone, Ampicillin, Oxacillin, Amikacin, and Gentamicin was not recorded.

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FEATURES OF THE ETIOPATHOGENESIS OF UPPER RESPIRATORY TRACT INFECTIONS CAUSED BY CONDITIONALLY PATHOGENIC MICROORGANISMS

Keywords: upper respıratory tract, pathogenıc mıcroorganısms, infections

Currently, respiratory infections with various etiopathogenesis constitute the most widespread group of diseases, affecting a certain contingent of the population. İN many cases, patients purposefully avoid prompt, thorough treatment of the life-threatening complications that such illnesses might induce. Despite affecting the upper respiratory tract, respiratory infectious processes can progress to more serious and recurring disorders such as tonsillitis, pharyngitis, laryngitis, bronchitis, and bronchial asthma. These conditions can have a substantial impact on the patient's quality of life [1]. The role of the body's own immune system in tolerance to the causative agents of the infectious process is indisputable in cases, such as the transition of infectious processes of the upper respiratory tract to the chronic diseases listed above, the formation of antibodies against it, the hapten nature of these antibodies, and the spread of the inflammatory process to various parts of the upper respiratory tract [2]. In addition to the pathogenetic mechanisms mentioned above, it is also important to study the characteristic features of microorganisms that constitute the etiological factors of the mentioned diseases. The prompt and targeted investigation of the fight against microorganisms and the administration of effective antimicrobial treatment against them are of crucial importance [3].

Several recent studies have demonstrated that microorganisms play a role in the development of infectious processes in various mucous membrane areas of the body, including the mucous membrane of the upper respiratory tract, not separately, but together, interacting with each other [4]

Therefore, research on how pathogenic, opportunistic, and non-pathogenic microorganisms interact with mucosal membranes and which species are important for infectious processes is currently a relevant topic. In addition to providing a topic for further research, these studies could potentially increase the utilization of probiotics and antibiotic therapy intended for the subsequent elimination of respiratory infectious processes [5].

Direct identification of the main causative agents and organization of the optimal prophylactic measures are the most effective methods against microorganisms. Infectious processes of the upper respiratory tract can be of bacterial origin, for which specific treatment tactics should be selected. To eliminate infectious processes caused by bacteria,

probiotics are successfully used along with antibiotic therapy, and in most cases, positive results are achieved.

The positive effects of probiotic microorganisms on human health are mediated through three main mechanisms of action. First, certain probiotics can directly displace or inhibit the growth of pathogens, either by acting directly or by affecting commensal microorganisms of the human microbiota. Second, some probiotics can enhance epithelial barrier function by modulating signaling mechanisms. Third, most probiotic strains can also modulate the immune responses of the human body, exert specific local and systemic effects and regulate the balance of pro- and anti-inflammatory cytokines [6].

Studies have shown that the use of probiotics and synbiotics reduces infectious complications in patients in intensive care units, and meta-analyses have demonstrated that the use of probiotics is safe and effective for preventing infectious processes in postoperative and mechanically ventilated patients in intensive care. Bacteria of the genera Lactobacillus, Bifidobacterium, Streptococcus, and Bacillus, some E. coli species, and fungi of the genus Saccharomyces are most commonly used as probiotics.

Human health is also affected by prebiotics in addition to probiotics. Prebiotics are substances that are not digested by human digestive enzymes but can be fermented by the intestinal microbiota, causing specific changes in the composition or activity of the gastrointestinal microbiota, thereby benefiting the health of the host.

Purpose of the research: Determination of the role of various microorganisms in the etiopathogenesis of upper respiratory tract infections and optimization of treatment and preventive measures.

The research was conducted in the laboratory of the Bacteriological and Clinical Department of the Republican Clinical Hospital. The material of the work was patients who applied to the Republican Clinical Hospital. The objects of the study were patients who applied to the departments of Allergology, Pulmonology, ENT, and Pathological Pregnancy with acute respiratory infections. Patients with acute respiratory infections (ARI) were taken materials (smears) from the nose, pharynx, and larynx during the early stages of the disease, complications, and recovery. For comparison, materials (smears) were taken from the upper respiratory tract of 45 healthy individuals.

Our study, conducted to comparatively evaluate the occurrence of various bacteria in the palatine tonsils during acute respiratory infection, found Enterococcus spp. in the samples of only 1 patient from a group of 15 patients with acute respiratory infection, which accounted for 6.67±6.44% of the group. However, in biological samples obtained from a group of healthy individuals consisting of the same number of healthy persons, no species of the corresponding genus of microorganisms were found. It should be noted that although viruses are the main causative agents of acute respiratory infections of viral origin, due to the pathological condition they cause and the failure of local immune factors, various opportunistic bacterial genera and species also increase, crowding out microorganisms characteristic of other normal microflora.

During the research examinations on the occurrence of species belonging to the Micrococcus genus, the corresponding microorganism species were found in 2 biological samples in the group of patients with acute respiratory infections, which accounted for 13.33±8.78% of the group. However, in the group of healthy persons, this indicator was 6.67±6.44%, with 1 person.

Klebsiella spp. species were found in only 1 sample in biological samples taken from patients, which was 6.67±6.44% in the group. In biological samples taken from the palatine tonsils of healthy individuals, this indicator was almost equal to 0.

Species of the Neisseria spp. genus was detected in one of the biological samples taken from the palatine tonsils of 15 individuals with acute respiratory infections, which was 6.67±6.44% in the group.

Staphylococcus spp. species were detected in 9 of the 15 biological samples taken from the tonsils of individuals with acute respiratory infections, which accounted for 60.0±12.65% of the patient group, while in the group of healthy individuals, these species were found in 6 individuals, which accounted for 40.00±12.65% of the control group.

Streptococcus spp. was found in 5 of the biological samples taken from the tonsils of patients in the group of 15 patients with acute respiratory infection, which represented 33.33±12.17% of the total samples. However, unlike other types of microorganisms, streptococcal species were found in 7 samples taken from healthy individuals, which constituted 46.67±12.88% of the group of healthy persons. The main reason for the higher prevalence of streptococcal species in healthy persons compared to sick individuals is that many representatives of the normal microflora of the upper respiratory tract of humans belong to this group. As a result of our study conducted to comparatively evaluate the occurrence of various bacterial associations in the tonsils during acute respiratory infection, in biological materials taken from the tonsils of 15 patients with acute respiratory infection, associations of Staphylococcus aureus and Streptococcus pyogenes microorganisms were found in 8 samples, which accounted for 53.33% of the total number of patients suffering from acute respiratory infection.

As a result of the study, in biological samples obtained from the tonsils of 15 patients with clinical signs of acute respiratory infection, the association of Staphylococcus aureus microorganisms was observed in 5 samples, which represented 33.33% of the total patients. Association of Staphylococcus epidermicus and Streptococcus pyogenes was observed in 4 of the patients with acute respiratory infections (n=15) included in the examinations, which is 26.67% of the total patients.

Enterococcus faecalis species were identified in 4 out of 16 biological samples taken from patients with tonsillitis, which accounted for 25% of the group. The occurrence of Staphylococcus aureus species in patients with pharyngitis and tonsillitis was almost identical. The occurrence of Streptococcus pyogenes species was higher in patients with tonsillitis. This is further evidence of the special place of streptococci among the main causative agents of tonsillitis. The same situation was recorded in the occurrence indicators of Enterococcus faecalis species. Klebsiella pneumoniae was found in 3 of the biological samples obtained from patients with pharyngitis, which constituted 20% of the group with 15 persons that we conventionally considered as the pharyngitis patient group. However, this species was found in 2 of the biological samples obtained from the tonsillitis patient group, which comprised 12.5% of the group with 16 persons that we conventionally considered as the tonsillitis patient group. During our studies on the occurrence of Candida albicans, it was detected in only 1 of the biological samples we obtained from the pharyngitis group, which constituted 6.7% of the group. In the group of patients with tonsillitis, the occurrence of this microorganism was in 2 samples, covering 12.5% of the group. The occurrence of the Klebsiella pneumoniae microorganism was higher in the group of patients with pharyngitis than in patients with tonsillitis, and the occurrence of the Candida albicans species was higher in the group of patients with tonsillitis. As a result of our study on the occurrence of various microflora in smears taken from the

nasopharynx of patients with pharyngitis and tonsillitis, the occurrence of S. aureus species was recorded in 8 samples in the relevant biological materials obtained from a group of 15 patients with pharyngitis, which accounted for 53.3% of the group. In the respective biological materials obtained from a group of 16 patients with tonsillitis, S. aureus was found in 10 nasopharyngeal smear samples, which is 62.5% of the group. Of the nasopharyngeal samples obtained from 15 patients with pharyngitis, representatives of the S. pyogenes species were found in 5, which included 33.3% of patients in the group. S. pyogenes was isolated from 6 of the 16 patients with tonsillitis who underwent an anatomic biopsy, which represented 37.5% of the group. The occurrence of E. faecalis in nasopharyngeal smear samples obtained from the group of patients with pharyngitis was recorded in 4 samples, accounting for 26.7% of the samples in this group. The presence of the corresponding species in the biological materials obtained from the group of patients with tonsillitis was observed in 3 biological materials, which represented 18.8% of the group of patients with tonsillitis (n=16).

The K. pneumoniae species were isolated from only 2 of the nasopharyngeal smears taken from a group of 16 patients with tonsillitis, and it accounted for 12.5% of the total samples taken from patients with tonsillitis. The number of K. pneumoniae species found in the biological materials we collected from the group of patients with pharyngitis was similar to that found in patients with pharyngitis, but these samples accounted for 13.3% of patients with pharyngitis. Candida albicans was isolated from only 1 of the nasopharyngeal samples obtained from a group of 15 patients with pharyngitis, and this was 6.7% of the group. Candida albicans was isolated from 2 of the nasopharyngeal smear samples obtained from a group of 16 patients with tonsillitis, which represented 12.5% of the corresponding group.

The occurrence of various microflora in smears taken from the nasal cavity of patients with pharyngitis and tonsillitis was determined. S.auresi species was isolated from 5 analogical smears out of 16 taken in the group of patients with tonsilitis, which represented 31.3% of the group. S. aureus was isolated in 4 of the nasal mucosa smears obtained from the group of patients with pharyngitis (n=15), accounting for 26.7% of these patients.

In 3 samples taken from a group of 15 patients with pharyngitis, representatives of the S. pyogenes species were isolated, which was 20% of the analogous samples taken from the corresponding group. This species was found in 4 of the analogous biological samples obtained from 16 patients with tonsillitis, accounting for 25% of the total samples taken from the corresponding group.

E. faecalis was isolated from 2 nasal smears taken from a group of 15 patients with pharyngitis, which represented 13.3% of the corresponding group. E. faecalis was also observed in 2 nasal smears taken from a group of tonsillitis patients (n=16), which represented 12.5% of the corresponding group. Representatives of the E. faecalis species were also observed in 2 of the nasal smears obtained from the group of patients with tonsillitis (n=16), which accounted for 12.5% of the corresponding group.

The occurrence of K. pneumoniae in nasal smears obtained from the group of patients with pharyngitis was 6.7%, observed in only 1 sample. The occurrence of the corresponding species in analogous biological material samples obtained from patients with tonsillitis was 6.3%, which corresponded to 1 smear sample in this group.

The occurrence of the C. albicans species was 0. It was not found in any sample in both the tonsillitis and pharyngitis groups.

We determined the occurrence of various representatives of the microflora in nasopharyngeal smears obtained from pregnant women. S. aureus was isolated in 9 of the nasopharyngeal smear cultures obtained from 50 pregnant women, which accounted for 18% of the total cases. Of the studied smear cultures, S. haemolyticus was recorded in only 1, or 2% of them. S. epidermidis was isolated in 4, or 8% of the nasopharyngeal smears obtained from pregnant women. Among the streptococci, the S. mitis species was found in 5 of the mentioned biological materials, which was 10% of the total materials. In the mentioned biological materials, Candida was found in only 3 samples, which represented 6% of the total nasopharyngeal smears. A similar result was recorded when studying the occurrence of E. coli in cultures of smears taken from the nasopharyngeal areas of pregnant women. The primary reason why studying the microflora of pregnant women is important is that, even though the female body is in a healthy state, changes in hormonal status and, as a result, the local immune system of anatomical and physiological areas can lead to the development of conditionally pathogenic microorganisms. During the study of biological material obtained from a group of 12 women in the last trimester of pregnancy, this indicator was detected in 3 cases, which is 25% in the corresponding group. According to the corresponding biological materials obtained from this group, S. pneumoniae dominated the inflammatory process in the pharynx in 1 sample, which represented 8.3% of the corresponding group. However, in a group of 20 pregnant women in the first trimester, no study object showed dominance of the relevant microorganism in the process. The same results were recorded for the E. auruginosa species. In immunological examinations, 5 patients had high IgE, which accounted for 10% of the total cases.

We determined the sensitivity of K. pneumoniae isolates from patients with acute tonsillitis to various new-generation antibiotic drugs. Seven out of ten pure K. pneumoniae isolates from patients with acute tonsillitis were observed to be highly sensitive to penicillin, which was 43.8% of the total isolates. Resistance to the relevant antibacterial drug was observed in only 1 isolate, which represented 6.3% of the total isolates.

To study the sensitivity of the isolates to various antibacterial drugs, we took smears from the oropharynx of patients aged 30-50 years. K.pneumoniae was detected in 35 patients among them. 16 colonies were selected in which the K. pneumoniae microorganism was detected, and pure isolates of the mentioned species were obtained.

High sensitivity to Cefotaxime was recorded in the isolate of K. pneumoniae. During the study of the sensitivity of K. pneumoniae colonies isolated from the respective patients to Cefotaxime, high sensitivity to the mentioned drug was recorded in 15 cases, which constituted 93.8% of the total cases. No resistance to Cefotaxime was recorded in any of the isolate samples.

The susceptibility of pure K. pneumoniae isolates to amoxicillin was recorded in 12 isolates, which was 75% of the total isolates, and resistance to amoxicillin was recorded in only 1 case, which represented 6.3% of the total samples.

Microbiological examinations are also considered mandatory during clinical and laboratory examinations of patients suspected of having an upper respiratory tract infection. Microbiological examination of biological material taken from the nasopharynx is of great importance in the timely detection of bacteria, fungi or viruses that cause the disease and in the implementation of targeted treatment measures.

To conduct a comparative microbiological assessment of the effectiveness of treatment for various acute infectious diseases of the respiratory tract, we recruited 12 patients with acute

pharyngitis, 11 with acute tonsillitis, 13 with acute bronchitis, 12 with typical pneumonia, 11 with rhinitis, and 10 with acute sinusitis, from all patients aged 30-50. Microbiological examinations were performed on the patients twice, before and after treatment.

In biological materials obtained from a group of 11 patients with acute tonsillitis, the colonization ability of Streptococcus spp. representatives, which is a qualitative indicator, was 6.73±0.26 CFU/mg before treatment procedures, but after treatment this indicator increased slightly and was found to be 6.95±0.14 CFU/mg. Nevertheless, the occurrence of representatives of the corresponding genus in biological materials was 81.8% in the group, being found in 9 samples before and after treatment.

As a result of the study, the colonization ability of Neisseria spp. in biological materials obtained from a group of 12 patients with acute pharyngitis was found to be 6.13±0.22 CFU/mg before treatment, while after treatment this indicator increased to 6.98±0.19 CFU/mg. The occurrence of the relevant microorganism group was 50%, in 6 out of 12 oropharyngeal smears before treatment, and 91.7% of the group, which was in 11 samples after treatment. In biological materials obtained from a group of 11 patients with acute tonsillitis, the colonization ability of Neisseria spp. was 6.39±0.21 CFU/mg before treatment, but after treatment and the disappearance of clinical symptoms, this indicator decreased slightly and was calculated to be 6.22±0.13 CFU/mg. The occurrence of the corresponding species in this group remained unchanged before and after treatment Thus, it occurred in 6 of the samples, which was 54.5% of the group.

Before treatment, lactobacilli were found in only 1 of the biological materials taken from 12 patients with acute pharyngitis, or 8.3% of the total group. The colonization ability of representatives of the corresponding genus in this sample was 4.03 CFU/mg.

After treatment, the occurrence of the Lactobacillus species among the relevant materials was recorded in 2 samples, which amounted to 16.7% of the group. The average colonization ability of the lactobacilli observed in the 2 samples was found to be 3.10±0.26 CFU/mg.

In the biological materials obtained from a group of 11 patients with acute tonsillitis before treatment, the presence of lactobacilli was observed in 2 samples, which was 18.2% of this group. In these 2 samples, the colonization potential of the corresponding microorganisms was calculated to be 4.14±0.18 CFU/mg on average. In the biological materials obtained after treatment, the mentioned species were found in only 1, which was 9.1% of this group. In the mentioned sample, the colonization potential of the corresponding species was found to be 3.34 CFU/mg. Microbiological examination of oropharyngeal smears taken from a group of 12 patients with acute pharyngitis before treatment, revealed Staphylococci in 7 samples, which was 58.3% of the group. After treatment, this indicator was recorded in 5 samples, representing 41.7% of the group. Although the colonization ability of total staphylococci was calculated to be 4.17±0.23 CFU/mg in the group of patients with acute pharyngitis before treatment, this indicator decreased significantly after treatment and was found to be 3.62±0.15 CFU/mg.

In the biological materials taken from 11 patients in the group of patients with acute tonsillitis, the occurrence of total staphylococci was recorded in 6 samples before treatment, which was 54.5% for the respective group. After treatment, the occurrence of total staphylococci was recorded in 7 samples, which was 63.6% for the group. The colonization index of total staphylococci in the mentioned biological material samples was calculated to be 4.12±0.25 CFU/mg before treatment but increased to an average of 4.23±0.31 CFU/mg after treatment.

The S. aureus species was found in 6 out of 12 oropharyngeal smear samples obtained before treatment from a group of patients with acute pharyngitis, or 50% of the samples in the total group. The colonization ability of the corresponding microorganism in the mentioned samples was calculated as 4.08±0.26 CFU/mg. After treatment, the occurrence of S.aureus in the group of patients with acute pharyngitis was recorded in 4 samples, accounting for 33.3% of the group. The average colonization ability of S.aureus samples observed in the mentioned 4 samples was found to be 3.56±0.18 CFU/mg.

Thus, in recent years, the study of some important aspects of the immune system and microflora disorders, as one of the main problems of infectious diseases and pediatric practice, is of particular importance in the diagnosis, treatment and prevention of acute respiratory diseases. In this regard, the basis of most clinical laboratory examinations is the study of the ratio of immune cell populations, qualitative and quantitative indicators of normal and conditionally pathogenic microflora. Thus, the basis of most clinical laboratory examinations is the study of the ratio of immune cell populations, and the qualitative and quantitative indicators of normal and conditionally pathogenic microflora. Classical bacteriological methods require extensive study of diagnostics, which allows us to judge the functional activity and clinical significance of the number of certain bacteria and the violation of the ratio of their various populations. Practitioners recommend the use of oral penicillin or erythromycin to treat streptococcal pharyngitis.

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COMPARATIVE ANALYSIS OF THE PROGNOSTIC SIGNIFICANCE OF TUMOR MARKERS HE-4 AND CA-125 IN BENIGN AND MALIGNANT OVARIAN TUMORS

Keywords: benign and malignant ovarian tumors, HE-4, CA-125, prognosis

Differential diagnosis and adequate treatment of newly formed ovaries are one of the most important problems of modern oncogynecology, taking the 7th place in frequency of occurrence. The prevalence of the disease is estimated at approximately 1.3% [1]. The risk of developing this disease increases with age, especially after 45 years. Primary ovarian cancer accounts for approximately 4–5% of all ovarian tumors. Studies show that in 66–88% of cases, ovarian tumors are first detected in stages III–IV [2]. It is characterized by a severe course from the point of view of late detection, an unfavorable prognosis, and the occurrence of massive regional and distant metastases. The latent course of the disease complicates its diagnosis. In most cases, the disease can be detected in a timely manner by specific signs and symptoms of the disease and only by the manifestation of general symptoms (anxiety, weakness, loss of appetite, gastrointestinal discomfort, etc.) [3].

As the gold standard for ovarian tumors, the tumor marker CA-125 is initially determined in the blood. The specificity and sensitivity of this biomarker is higher in serous ovarian cancer. Other studies have shown that this biomarker has significantly lower sensitivity in all types of early-stage ovarian tumors, as well as in late-stage mucinous, clear-cell, and endometrioid types. Recently, biomarker HE-4 has gained relevance due to its higher specificity and sensitivity.

Given this, determining the effectiveness of HE-4 and CA-125 tumor markers in predicting the disease in malignant and benign ovarian tumors was set as an urgent task and studies were conducted [4].

Clinical, laboratory and instrumental differential diagnostics of malignant and benign ovarian cancer were carried out, correlations between HE-4, ROMA and CA125 tumor markers and diagnostic criteria were identified. Calculations were made using various mathematical and statistical methods, the diagnostic specificity and sensitivity of all three ovarian cancer tumor markers were determined, their effectiveness was revealed. The diagnostic value of using ROMA, HE4 and CA125 for differential diagnostics of benign and malignant ovarian tumors was assessed. The expediency and relevance of studying tumor markers in malignant and benign ovarian tumors is substantiated, which allows us to expand our understanding of the pathogenesis of diseases. Having identified tumor markers, we were able to accurately differentiate two types of cancer. ROMA and HE4 were proposed as markers of diagnostic value in malignant ovarian cancer, and all three tumor markers - in

benign tumors. The study of the characteristics of ovarian tumor tumor markers is recommended as an effective screening method that allows us to detect the disease at early stages and determine whether the cancer has progressed to other stages [5,6].

During the study, a detailed medical history was collected from patients, laboratory blood tests, tumor markers were prescribed, and instrumental studies were carried out. The results obtained were analyzed using modern statistical and mathematical methods.

Materials and methods of the study. The study included 100 women who were treated at the Oncology Clinic of the Azerbaijan Medical University in 2019-2021. Patients were divided into two groups depending on the type of ovarian cancer. Group I included 72 patients with malignant tumors, and Group II included 28 patients with benign tumors.

Exclusion and inclusion criteria were defined to form study groups. The inclusion criteria were as follows:

- Women diagnosed with derivative USM;

- whether the derivative is unilateral or bilateral;

- tumor 30 mm or more.

The following were defined as exclusion criteria from the study.

- pregnancy

- the presence of a defect in the fallopian tube.

We determined the body mass index of women included in the study. Women are divided into 3 groups: underweight, normal weight, and overweight. It was found that 61% of women in Group I had a normal body mass index, while 64% of women in Group II had a normal body mass index. In both groups, women with overweight/obesity were in second place. This was observed in 36% of women in Group I and 32% in Group II. The body mass deficit was 2.8% in Group I and 3.6% in Group II. There was no statistically significant difference between the groups in body mass index.

The frequency of somatic diseases in the study groups was determined. Women were diagnosed with diabetes mellitus, hypertension, varicose veins, respiratory and kidney diseases. No statistically significant differences were found between the groups.

The main symptoms of ovarian cancer were identified in the study groups. Women often report symptoms such as abdominal and back pain, bloating, frequent urination, and fatigue. Only abdominal pain and malignant ovarian cancer were statistically significantly more common in patients.

A comparative analysis of the obstetric and gynecological status in the study groups was conducted depending on the type of ovarian cancer. The study was conducted based on data on the birth of children in the study groups. 15.3% of women in Group I and 21.4% of women in Group II did not give birth. Then the women were grouped by the number of births: 1, 2, 3 or more. There was no statistically significant difference between the groups in the number of births.

The women included in the study were also analyzed for the number of abortions they had.

The average indicator of women who did not have an abortion was statistically significantly higher among women with malignant tumors than among women with benign tumors. There was no statistically significant difference between women who had 1 and 2 abortions. The number of women who had 3 or more abortions was also statistically significantly higher among women with malignant tumors than among women with benign tumors. The study groups were analyzed for the use of combined oral contraceptives, antiestrogens, and gestagens. No statistically significant differences were found between women with malignant and benign ovarian tumors in the types of contraception they used.

During a clinical blood test, ESR, hemoglobin, and leukocyte levels were determined in patients included in the study. In addition, ALT, AST, bilirubin, and blood protein levels were determined during a biochemical blood test. No statistically significant differences were found between the groups in laboratory parameters.

In Group I, serous neoplasms were detected in 81.9% of women, and in Group II - in 50%, which is a statistically significant indicator. Mucous membrane nodules were statistically significantly more common in Group II. Endometrioid carcinoma was detected only in women with malignant cancer, with a frequency of 9.7%. In women with benign ovarian cancer, in contrast to group I, 10.7% of myomas, 10.7% of ovarian cysts, and 7.1% of immature teratomas were also recorded. The average values of Doppler and ultrasound parameters, as well as intrauterine hemodynamic parameters in the study groups, were determined. The study revealed that the average septum thickness, the average size of the uterine component, and the average velocity of arterial and venous blood flow were statistically significantly higher in women with malignant tumors. The resistance index, a parameter of the vascular flow volume in ovarian tumors, was statistically significantly higher in women with benign tumors than in women with malignant ovarian cancer. The average mixed exogeneity index was statistically significantly higher in patients with malignant neoplasms than in patients with benign neoplasms. Anexogeneity, i.e., homogeneous exostructure, was statistically significantly higher in women with benign ovarian cancer.

Determination of correlations between tumor markers and ultrasound parameters between the groups revealed two indicators. As can be seen, there are a number of parameters for which negative correlations were found. A relatively strong statistically significant correlation was found between CA125 and maximum venous blood flow.

A strong positive correlation was found between CA125 and HE4 and ROMA.

A strong positive correlation was found between arterial blood flow velocity and the size of the derivative component, between IR and septal thickness ($r = 0.967$), arterial blood flow velocity ($r = 0.991$) and venous blood flow velocity ($r = 0.991$).

Certain correlations were also found between age, tumor markers and ultrasound parameters in patients with ovarian cancer. A stronger positive correlation was recorded between age and ROMA. The patients were also analyzed by age groups, regardless of whether they were premenopausal or postmenopausal. A very strong negative correlation was found between age and the US septal thickness in premenopausal women. The correlation between the CA125 tumor marker and the US parameters was not clear. A negative and strong relationship was found between HE4 and thickness. No strong correlation was found between other USM parameters. A positive and negative correlation was observed between ROMA and the fence gable.

No moderate or strong correlation was found between age, tumor markers and US parameters in the postmenopausal period.

In the first study group, i.e. 72 patients with malignant tumors, 81.9% had serous tumors, 8.3% had mucinous tumors and 9.7% had endometrioid carcinoma. We studied the diagnostic value of the tumor markers we studied in these patients depending on the tumor type.

The diagnostic value of HE-4 and CA-125 was high in serous carcinoma.

In malignant mucinous ovarian tumors, the sensitivity and specificity of the HE-4 tumor marker were relatively higher, while the sensitivity and specificity of the CA-125 tumor marker were relatively higher.

In patients with endometrioid carcinoma, HE-4 and CA-125 were equally satisfactory.

Biostatistical analysis methods were also used for binary classification when examining patients with malignant and benign ovarian cancer. We determined the diagnostic value of tumor markers (HE-4, Ca-125, ROMA) studied in the groups using ROC analysis. Based on the results of the ROC analysis, tumor markers HE4 and ROMA can be used as effective markers of malignant ovarian tumors due to their high diagnostic value.

It was also found that ROMA is a highly diagnostic tumor marker for malignant ovarian tumors and has the highest value for the Youden index. Although the CA125 marker was slightly behind the ROMA tumor marker, it was superior to NE4 in specificity and sensitivity.

Based on the ROC curve, we identified an tumor marker with a higher diagnostic value for benign ovarian tumors. In this regard, the ROMA tumor marker was identified, which has higher threshold values. This tumor marker is also highly valuable for malignant tumors. However, unlike malignant tumors, the HE-4 tumor marker, along with ROMA, also has a high diagnostic value.

We identified an tumor marker with a higher diagnostic specificity and sensitivity for benign ovarian tumors based on the Youden index. In this regard, the ROMA tumor marker was identified, which has higher threshold values. This tumor marker is also highly valuable in malignant tumors.

Thus, significant differences were revealed in patients with malignant and benign ovarian cancer both in clinical symptoms and in the diagnostic efficiency of tumor markers, which will be of great practical importance for differential diagnostics.

Thus, based on the obtained results, we have developed practical recommendations for effective differential diagnostics of patients with malignant and benign ovarian cancer. We consider it advisable to screen postmenopausal women for ovarian cancer if they experience symptoms such as abdominal pain, bloating, and frequent urination.

We recommend using Doppler ultrasound in postmenopausal and premenopausal women to assess the echostructure of the lesion, venous and arterial blood flow velocity as highly informative indicators of malignant neoplasms.

When examining for ovarian tumors, the presence of the HE-4 tumor marker above CA125 allows diagnosing the presence of a malignant tumor. NE-4 and CA125, determined at

approximately the same levels, can be used as a comparative prognostic marker in benign tumors.

Among women with malignant tumors, the number of postmenopausal women (76.4%) was significantly higher than the number of women with benign tumors (42.9%) (p=0.0014). The frequency of abdominal pain in these women (34.7%) was significantly higher than in women with benign tumors (7.1%) (p=0.0053). The frequency of abortions was significantly higher in women with malignant oncological diseases (43%) than in women with benign oncological diseases (7.1%) (p=0.0006). Serous neoplasms were more common in Group I (81.9%) than in Group II (50%). Unlike Group I, women with benign tumors also had fibroma (10.7%), ovarian cysts (10.7%), and immature teratoma (7.1%). In Doppler ultrasonography, IR (p=0.0008, p<0.005), mixed exogeneity (p=0.0001), as well as venous and arterial blood flow velocity in the derivative (p<0.0001) were statistically significantly higher in Group I. The frequency of anexogenic exostructure was significantly higher in women with benign tumors (21.4%) than in women with malignant tumors (2.8%) (p=0.0041). In women with malignant tumors, the specificity of the HE4 tumor marker (84.2%) and the sensitivity of CA125 (84.2%) were higher in serous tumors. The diagnostic value of CA125 (Se-50.0%, Sp-60.0%) was higher than HE4 (Se-33.3%, Sp-42.9%) in mucinous malignant neoplasms. In patients with endometrial carcinoma, the diagnostic value of HE4 (Se-57.1%, Sp-66.7%) was higher than that of CA125 (Se-50%, Sp-60%).

According to the ROC analysis, ROMA (19,923) and HE-4 (13,830) have a higher diagnostic value for malignant ovarian tumors. ROMA (94.12%) and HE4 (85.45%) have high sensitivity and specificity according to the Youden index.

In benign ovarian tumors, the ROC analysis has a higher diagnostic value than the ROC analysis of Rome (14,199) and NE-4 (13,395). According to the Youden index, ROMA (85.45%, 96.67%) was a more sensitive and specific tumor marker. The sensitivity of HE (Se-94.12, Sp-89.47) and CA125 (Se-94.12, Sp-89.47) was higher than that of ROMA, but the specificity was slightly lower.

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CLINICAL FEATURES OF ENDO-PERIODONTAL LESIONS OF SUPPORTING TEETH DURING PROSTHETICS

Keywords: implant, perimucositis, prophylaxis, clinic

Endo-perio lesions might be interdependent because of the vascular and anatomic connections between the pulp and the periodontium.

Endo-periodontal lesions are complex conditions that involve both the dental pulp (endodontic) and the surrounding periodontal tissues. These lesions can result from a variety of factors, including infections, trauma, or systemic conditions that affect the teeth and gums. Proper diagnosis and treatment planning are essential for managing these conditions effectively.

Endo-periodontal lesions represent a challenging clinical scenario, requiring accurate diagnosis and a well-coordinated treatment plan that addresses both the endodontic and periodontal components. Early detection and appropriate therapy can significantly improve the prognosis of affected teeth, and multidisciplinary care often yields the best results.

Clinical Features of Endo-Periodontal Lesions

Endo-periodontal lesions are complex conditions that involve both the dental pulp (endodontic) and the surrounding periodontal tissues. These lesions can have a variety of clinical manifestations, and understanding these features is critical for accurate diagnosis and effective treatment planning. Here are the main clinical features that are typically observed in endo-periodontal lesions:

Pain:

- **Type of Pain:** Pain is one of the most common complaints in patients with endo-periodontal lesions. The pain can be **sharp, dull, or throbbing** and may vary depending on the extent of involvement of the pulp and periodontal tissues.

- **Pulpal Pain:** If the pulp is involved (e.g., pulpitis or necrosis), the pain may be **spontaneous** or **provoked** by hot or cold stimuli. In severe cases, the pain may worsen at night.

- **Periodontal Pain:** Periodontal involvement typically leads to **dull, constant pain** that can be aggravated by chewing or pressure on the affected tooth, especially if there is an abscess or significant periodontal inflammation.

2. Swelling:

- **Localized Swelling:** In cases where infection has spread from the pulp to the periodontal tissues, or vice versa, **localized soft tissue swelling** around the affected tooth is often present. This swelling may involve the gingiva, and in more severe cases, it may extend into the buccal or palatal vestibule.

- **Abscess Formation:** An **abscess** can develop in both endodontic and periodontal conditions. If the lesion is primarily endodontic, it may lead to a **periapical abscess**. If it is periodontal, a **periodontal abscess** can form, which can present as swelling around the gum line.

The clinical features of endo-periodontal lesions vary depending on whether the lesion primarily involves the pulp, the periodontal tissues, or both. A comprehensive evaluation, including a detailed patient history, clinical examination, and radiographic assessment, is crucial for accurate diagnosis and appropriate treatment planning. Understanding these clinical features helps differentiate between pure endodontic lesions, pure periodontal lesions, and combined lesions, ensuring the right approach for management and prognosis.

The constant increase in the number of patients suffering from inflammatory diseases of the maxillofacial region of odontogenic and periodontal origin again and again raises the question of both the quality of endodontic interventions and effective, adequate therapy for inflammatory diseases of the periodontium [1].

Recently, there has been increasing talk about the so-called endoperiodontal syndrome, the issues of which have not been sufficiently covered in the literature [2-5].

The anatomical and functional commonality of the pulp and periodontium determines the high degree of probability of their joint involvement in the pathological process. Therefore, combined lesions of the endodontium and periodontium, when endodontic pathology develops against the background of periodontitis already present in the patient, occupy a special place in the clinical practice of both a dentist-therapist and an orthopedist. In modern dental science, such lesions are designated by various terms: periodontal syndrome [4], pulpo-periodontal lesions, periodontal-endodontic lesions [2], endo-periodontal pathology [5], combined endodontic-periodontal pathology [3].

An indisputable fact is the unity of such structures as a tooth and periodontium. The commonality of these components of the oral cavity structures is emphasized in the works of a number of researchers. An analysis of the ways of spreading infectious inflammation from periodontal tissues to the dental pulp has been conducted. However, researchers cannot give an unambiguous answer regarding medical tactics in prosthetics if these changes are significant [6-8].

Communication routes between the dental pulp and periodontal tissues. The tooth is connected to the periodontium by the unity of embryonic development: this connection is expressed in the presence of anatomical structures that serve as potential routes for the spread of infection. These include dentinal tubules, lateral and additional canals, and the apical foramen [18]. However, modern studies have shown that the permeability of intact dentin is insufficient for the exchange of inflammatory mediators and waste products of microorganisms between the pulp and periodontal tissues [19]. An important route for

infection penetration is the lateral and additional canals, as well as the apical foramen [20, 21]. Waste products of microorganisms and inflammatory mediators can enter the pulp from a deep periodontal pocket reaching the apical or lateral foramen and cause the so-called retrograde pulpitis, and vice versa, with pulp necrosis - into the periapical tissues, which can be accompanied by bone and root resorption [22].

Mutual influence of inflammatory processes in the pulp and periodontal tissues Researchers are unanimous in their opinion that inflammatory processes in the dental pulp and periodontal tissues mutually influence each other. Long-term periodontal inflammation triggers degenerative processes in the pulp, such as deposition of replacement dentin, fibrosis, a decrease in the number of cellular elements and collagen resorption, which limits the possibility of pulp regeneration in case of damage. When studying the state of the microcirculatory bed of the dental pulp in patients of different ages with generalized periodontitis, pronounced circulatory disorders and a decrease in the intensity of blood flow were noted. There is an opinion that against the background of periodontal inflammation, the physiological age of the pulp exceeds the chronological age. Data on the electrical excitability of the pulp show a deterioration in its condition with periodontitis of any severity. However, summarizing the literature data, it can be said that the inflammatory process in the periodontium does not have a clinically significant effect on the pulp until the periodontal pocket reaches the lateral canal or apical foramen. Only at this stage can pathogens penetrate the pulp and cause its inflammation with subsequent necrosis. At the same time, the negative effect of inflammatory mediators of the affected pulp is not sufficient to lead to clinically significant damage to the periapical tissues. The greatest damaging effect is caused by toxins released during the destruction of the wall of gram-negative bacteria in the root canal during pulp necrosis. Their effect causes inflammatory changes in the periapical region. Thus, clinically significant damage to the periapical tissues in most cases occurs after pulp necrosis, and not during the inflammation process.

Classification of endodontic-periodontal lesions The first classification proposed by Simon, Glik and Frank in 1972 was based on the localization of the primary focus from which the infection occurred and included:

• primary endodontic lesions with transient, clinically unexpressed effect of the inflamed pulp on the periodontal tissues;

• primary endodontic lesions with secondary involvement of the periodontium, which develops during the long-term course of endodontic pathology;

• primary periodontal lesions with transient, clinically unexpressed effect of the inflamed periodontal tissues on the pulp;

• primary periodontal lesions with secondary involvement of the pulp, when in the process of periodontitis progression the pulp becomes infected through the lateral canal or apical foramen;

• truly combined lesions, when endodontic and periodontal pathology arose simultaneously and developed in parallel. Since endodontists deal with primary endodontic lesions, and the effect of pulp inflammation on the periodontium in this case, although it exists, is not clinically expressed and does not require treatment, and the same applies to primary periodontal lesions without pulp involvement, then later only those EPs were

combined into the classification that require an interdisciplinary approach to treatment, namely [29]:

• endodontic lesions with secondary periodontal involvement;

• periodontal lesions with secondary pulp involvement;

• truly combined lesions. Endodontic lesions with secondary periodontal involvement In the absence of treatment for a long time of acute periodontitis, secondary involvement of the marginal periodontium with endodontic lesions and secondary periodontal involvement is possible. In this case, biofilm (and subsequently tartar) accumulates in the area of the fistula tract, which leads to bone resorption, epithelial ingrowth, and the formation of a periodontal pocket [30]. Most often, this type of lesion develops in the area of the palatine roots of the upper molars, which is accompanied by a bone defect such as a cleft. Periodontal lesions with secondary pulp involvement In the absence of periodontal treatment for a long time, a progressive periodontal pocket can reach the apical opening or the opening of the lateral canal, which can result in inflammation and necrosis of the pulp. Thus, a periodontal lesion with secondary pulp involvement occurs. The prognosis for single-rooted teeth with this type of lesion is worse than for multi-rooted teeth, since in the latter, the destruction of supporting tissues may be different in different roots.

Materials and methods of the study. Clinical studies were carried out individually and in the "El Esthet" clinic of the Department of Periodontology of the Azerbaijan Institute of Advanced Training of Doctors named after Aziz Aliyev. Control group (20 patients) - removal of tartar mechanically using special plastic curettes in patients; Conditional control group (20 patients) - removal of tartar by the doctor using the Vector device and the patient using an antiseptic containing 0.05% chlorhexidine bigluconate; Main group (20 patients) - removal of tartar by the Vector device and the patient using a product containing hyaluronic acid (Hy + Al Gel). Comparative clinical examination methods of the oral cavity of patients in all three groups before treatment and after treatment (1, 3 months) were studied.

Comparative clinical examination methods (OHI-S, Green-Vermilion index) of oral cavity patients of all three groups before and after treatment were studied.

The simplified hygiene index of Green and Vermilion (OHI-S) is used to detect both dental plaque and calculus. For this, the vestibular surfaces of teeth 16, 21 and 24 and the lingual surfaces of teeth 36, 41 and 44 are stained. First, dental plaque is detected, then tartar.

According to this index, 0–0.6 indicates good hygiene, 0.07–1.8 — satisfactory hygiene, and 1.9–3.0 — poor hygiene.

Inclusion criteria:

Peri-implant mucositis, diagnosed at the implantation site with pocket depth <3 mm and positive bleeding on probing

Exclusion criteria:

• Persons younger than 18 years

• Those who have systemic diseases

• Those who use tobacco products

• Pregnant and breastfeeding.

• Those who have taken any medications/supplements (probiotics, antibiotics or anti-inflammatory drugs) during the last 6 months

Statistical software (IBM SPSS Statistics 22.0, IBM SPSS) was used for data analysis. The obtained numerical data were processed using statistical methods taking into account modern requirements. For group indicators, the mean values (M), their standard error (m), minimum (min) and maximum (max) values of the series, as well as the frequency of occurrence of qualitative indicators in the groups were determined. Balancing of the groups by age and gender was checked using Student's t-test and the chi-square test, respectively. Intragroup differences were assessed using the Wilcoxon signed-rank test. Differences between groups were analyzed using the Mann-Whitney U test. Calculations of the mean and complete root surface coverage were based on a previously detailed publication. Pearson's $\chi 2$ test was used for frequency analysis. Comparison of the two groups in the completeness of root surface coverage was performed using Fisher's exact test. The main outcome variables were complete root surface coverage, esthetics of root coverage, and patient satisfaction. All other parameters were considered secondary outcome variables. The significance level was $p<0.05$.

Study results and their discussion.

The table shows that the average age of patients with oral complications during dental implantation was 35.8 ± 2.76 years in all groups; 41.1 ± 2.92; was 38.7 ± 3.43 years,

Table 1

Analysis of patients with perimucositis (n=60)

N	I N=20	II N=20	III N=20
Age	35,8 ± 2,76	41,1±2,92	38,7±3,43
Male	7 (35,0)	10 (50,0)	10 (50,0)
Female	13 (65,0)	10 (50,0)	10 (50,0)

It should be noted that although the placement of implants directly into the jawbone is clinically stable, errors such as their overloading, violation of antiseptic rules, etc. can lead to inflammatory and destructive complications such as perimucositis, periimplantitis. When analyzing the components used by doctors in the symptomatic therapy of inflammatory diseases of periimplant tissues, it was found that the vast majority of them use traditional antiseptic agents that have been widely used in basic treatment for a long time in their practice. The increase in the resistance of microorganisms to these agents over the years is a growing problem worldwide. This problem poses a challenge for researchers working in various fields of healthcare to develop alternative anti-inflammatory approaches.

According to the results of our studies, at the last stage of clinical studies, the OHI-S index increased in each group, but a more pronounced negative dynamics of changes was

determined in the control group (p>0.05) (Table 2). The hygienic index recorded during the examinations in the main group in the following 1 month was calculated to be 1.64±0.041, which was lower than the index obtained in other groups before the removal of dental plaque and tartar, and similar results were obtained in the corresponding indicators obtained during the examinations in the 3rd month after the implementation of the hygienic measures.

Table 2

Dynamics of OHI-S index indicators in patients (n=60)

Groups	Müşahidə müddəti					
	Before treatment	After a month	$P_{до}<$	After 3 months	P<	$P_{1ay}<$
1 group (n = 20)	2,46±0,055	2,05±0,038	0,0000	0,63±0,029	0,0000	0,0000
2 group (n = 20)	2,53±0,046	1,92±0,039	0,0000	0,37±0,031	0,0000	0,0000
3 group (n = 20)	2,58±0,049	1,64±0,041	0,0000	0,28±0,024	0,0000	0,0000

Subsequent observation of patients in the control group showed that at the final stage of treatment, the hygienic condition of the periodontal tissues and oral cavity decreased to a satisfactory level. From this, it can be concluded that the clinical picture in the examined group of patients corresponded to the intact state. Also, in dynamics, compared with the main group and the comparison group, a weaker resolution of the inflammatory process in the soft tissues of the periodontium was observed in the control group, especially in the implant area (the presence of soft and hard dental deposits). In addition, in all groups, the index values \u200b\u200breduced significantly compared with the initial values by the end of the study ($p < 0.001$). Thus, in the control group, the index values were 0.63 ± 0.029; In the main group, it decreased to 0.28 ± 0.024, and in the comparison group - to 0.37 ± 0.03, i.e. 2 times ($p < 0.001$). Thus, dynamic monitoring of clinical signs of inflammation in the main group of patients showed a significant improvement in the condition of the soft tissues surrounding the implant superstructure in all patients during the first months of basic therapy. This was manifested in hyperemia, decreased discomfort and improved halitosis. The results of the study allow us to consider the use of a drug containing hyaluronic acid (Hy + Al Gel) as a maintenance therapy for the correction of complications after implantation as quite acceptable and will significantly improve the effectiveness of prosthetics on implants.

Evaluation of the pathogenetic significance of some important risk factors for the development of mucositis and its transition to peri-implantitis is of practical importance. The developed set of therapeutic and preventive measures will ensure the overall effectiveness of dental implantation by minimizing postoperative complications.

Results. Three months later, when examining patients, it was revealed that the hygiene index had slightly decreased, but, unlike the indicators of the control and comparative groups, the indicators in the main group remained at a good level.

Peculiarities of Innervation of the Pulpo-Periodontal Complex Innervation of the maxillofacial segment also has its own peculiarities. The pulp is innervated by branches of the trigeminal nerve, consisting mainly of specialized polymodal nociceptors, morphologically characterized as myelinated and unmyelinated fibers (C-fibers). Of interest is the role of the so-called nerve tissue growth factor in the vital activity of the pulp - a protein regulator of the development and differentiation of neuronal and non-neuronal cells. In addition to the regulatory function, it also has a signaling function. The results of the studies show that the release of this protein regulator is closely associated with pathological and regenerative processes in human teeth. Based on this, a potential role of this neurotrophic molecule in pulp regeneration is assumed.

Nerve endings, Schwann cells (cells surrounding nerve fibers) and immune cells play a significant role in the vital activity of the pulp. They create a multicellular barrier at the dentin-pulp interface, responding to environmental changes. In addition, during the development of peripheral nerves, Schwann cells bind to blood vessels and influence the differentiation of arteries. This is accomplished by local expression of vascular endothelial growth factor, which allows the vessels to grow following the proliferation of nerve fibers. The number of nerve endings and receptors decreases during physiological root resorption. The periodontium is innervated by branches of the dental plexuses of the second and third branches of the trigeminal nerve. Deep in the alveolus, the dental nerve bundles are divided into two parts: one goes to the pulp, the other - along the surface of the periodontium parallel to the main nerve trunk of the pulp. Along with myelinated fibers, unmyelinated nerve fibers are also observed. At different levels of the periodontium, myelinated fibers branch or become thinner. In the periodontium and gums there are free nerve endings located between the cells. The main nerve fibers of the periodontium in the interroot space run parallel to the cement and in the upper part are curved parallel to the interroot septum. Immunohistochemical analysis of the bone showed the presence of neuropeptides and neurotransmitters that act on bone cells through receptors. In addition to transmitting sensory information, sensory neurons produce various neuropeptides that play an important role in maintaining homeostasis of bone tissue and dental pulp, as well as the formation of dentin. Innervation affects homeostasis and mineralization of hard tissues. The presence of a large number of nerve receptors allows us to consider the periodontium an extensive reflexogenic zone; it is possible to transmit a reflex from the periodontium to the heart, gastrointestinal tract organs and other body systems.

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THE IMPORTANCE OF MICROBIOLOGICAL PARAMETERS OF INDIVIDUALS WITH HARMFUL HABITS IN FORENSIC MEDICINE

Keywords: forensic medicine, drug addicts alcoholics, microbioloji, fungi

Forensic microbiology is a discipline that deals with the study of microbiology in the context of forensic science. Its applications mainly focus on the diagnosis of cause of death, crime scene determination, post-mortem interval (PMI) estimation, and personal identification. Numerous studies have been devoted to the use of microorganisms in forensic practice. Some specific microorganisms have been shown to contribute to the determination of various causes of death, including drowning, poisoning, and hospital-acquired infections.

Given the distinctive features of microbial communities in soil obtained from crime scenes and other objects, the soil microbiome can be used to determine geolocation. Moreover, since microorganisms contribute to post-mortem decomposition, forensic researchers have begun to explore the possibility of using the microbiome to infer post-mortem interval over the past few years. Some studies have used machine learning and other technologies to create microorganism-based PMI estimation models, which indeed improves the accuracy of PMI inference. In addition, the microbiome composition in humans varies depending on the location of the body; host characteristics such as gender, age and lifestyle; and skin care status. Individuals can therefore be identified using skin, hair and body fluid microbiomes.

This review examines the progress in forensic microbiology from classical to high-throughput methods coupled with artificial intelligence technologies and discusses future prospects.

Next-generation sequencing (NGS) technology can measure tens of thousands to millions of DNA simultaneously and can provide a high-throughput microbiome database. With the advancement of sequencing technology, third-generation sequencing technology has more advantages in studying community diversity due to ultra-long sequencing reads. Meanwhile, the 16S rRNA analysis results are collected into operational taxonomic units (OTUs). Most microbiome high-throughput sequencing data cannot be identified and classified due to the limitations of reference genomes and genetic databases. The use of targeted 16S rRNA with short amplifiers has not achieved reliable species-level resolution, and full-length 16S rRNA sequences do not necessarily reduce this limitation. Whole-genome sequencing (WGS) targets the entire gene content of microbial ecosystems and can differentiate microbial species and taxa to a greater extent than 16S rRNA amplicons. Although the increasing role of NGS and WGS combined with artificial intelligence will likely become a routine tool in forensic microbiology, the isolation, detection and confirmation of specific microbes and the use of nucleic acid sequencing remain less relevant for forensic applications. Some researchers propose using nanotechnology to develop biosensors for the identification of foreign pathogens. Recently, computer-aided microbial image analysis technology combined with machine learning and deep learning has enabled the identification of specific

microbiomes (Ma et al., 2022). In addition, some challenges remain in the study of forensic microbiology related to standardization, validation and bioinformatics procedures. Further advances in technology will help improve the application of microbiology in forensic science.

The available data suggest that forensic microbiology using machine learning can be used to some extent for geolocation determination. Human gut microbiota plays an important role in geolocation determination, as evidenced by correlations based on traditional statistical methods. In 2014, UniFrac and ANOSIM were used to analyze the human saliva microbiome. The inter-individual variance was 6.75-10.21%. In 2020, Huang et al. applied a machine learning system to determine geolocation with an accuracy of 86%.

The study involved 122 people. The participants were divided into groups as follows. Group I included those who did not use drugs and did not suffer from alcohol addiction. 31 practically healthy people who had never been exposed to these bad habits. Group II included 43 drug addicts who had used various drugs (opioids, cocaine, amphetamines and hallucinogens) for more than 5 years, and Group III included 48 people with varying degrees of alcoholism (1–5 ppm, ppm and higher). In Group I, the age category was 18–63 years, the average age was 42.3±2.33 years, in Group II, the age category was 18–45 years, the average age was 31.4±1.16 years, in Group III, the age category was 28–62 years, the average age was 44.1±1.33 years. Considering that such dangerous diseases as drug addiction and alcoholism cause great harm to human health and are of great importance for forensic medical examination, the study of fungal skin lesions in them is proposed as a relevant topic.

Biological materials taken from skin scrapings of all participants were examined for the presence of fungi of the genera Candida, Zygomycota, aspergillosis and mucormycosis.

Cryptococcus, which was found with greater frequency in skin samples of drug addicts (n=43) included in the study, was detected in 32 (74.4%) people. After that, C. albicans was detected and identified in 22 (51.2%) people. According to the authors, these strains are considered very dangerous.

A. fumygatus and Absidia were found less frequently in drug addicts included in the study, each of which was found in 15 (34.9%) patients. Absidia is a genus of zygomycetes, found mainly in wet places.

P. notatum and Rhizopus were not detected when determining fungal seeding of the skin of patients with alcoholism (n=48). Cryptococcus, which is widespread among drug addicts (74.4%), is less common among alcoholics and was recorded in 18 (37.5%) people. C. albicans and C. tropicalis were found more often in people suffering from alcohol addiction, and were detected in 22 (45.8%) and 23 (47.9%) people, respectively. Absidia, a rather dangerous type of fungus, which is widespread (34.9%) among drug addicts, was found in very few patients with alcoholism — in 6 (12.5%) people.

Among alcoholic mushrooms, C. tropucalis, which belongs to the genus Absidia, is found 35.4% less often. It is also calculated as less than 3 times. Fungi of the genera A.fumygatus (14.6%) and P.glaucum (18.8%) were also rarely found.

In group I, that is, in healthy people (group I), dangerous fungi C. krusei, Mucor, Rhizopus, Absidia, Penicillium, P. notatum were not detected. 45% of Candida, 42% of A. fumygatus and P. glaucum were found in this group. Thus, in healthy persons and persons suffering

from alcohol addiction (group II), these highly dangerous fungi were not found. However, unlike healthy people, C. krusei was detected in 21% of them, Mucor in 21% and Absidia in 38%. When calculating the statistical significance of the frequency of occurrence of fungi, it was found that C. tropicalis was statistically significantly more often detected in persons suffering from alcohol dependence than in healthy persons ($p=0.0014$, $p>0.005$, $xi2=10.26$). Although other types of navels were also more common in alcoholics than in healthy people, no statistical difference was observed between these differences.

In drug addicts (group III), the incidence of skin fungi was very high, and many dangerous fungal species were detected.

In them, the genus C.tropicalis was detected significantly more often than in healthy individuals ($p=0.0041$, $p>0.005$, $xi2=8.23$). Fungi of the genus Cryptococcus were also statistically significantly more frequent in drug addicts than in healthy individuals ($p=0.002$, $p>0.005$, $xi2=9.53$).

Fungi of the genus Cryptococcus were also statistically significantly more frequent in drug addicts than in alcoholics ($p=0.0004$, $p>0.005$, $xi2=12.49$). Although there was no statistical significance in the incidence of other fungal species found together in drug addicts and alcoholics, all fungi were more frequent. Only fungi of the genus C.tropicalis were found more often in alcohol addicts (48%) than in drug addicts (44%).

The study shows that the study of the fungal composition of the skin in people with harmful habits has been of considerable scientific and practical importance, and provides a basis for future research.

During the microbiological examination of blood in drug addicts and alcohol addicts, the frequency of occurrence of microorganisms such as Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae, Candida albicans, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae was determined. It was determined that during the examination of blood in drug addicts, among drug addicts (n=43), Staphylococcus aureus 14 (32.6%), Staphylococcus epidermidis 7 (16.3%), Klebsiella pneumonia 12 (27.9%), Candida albicans 20 (46.5%), Escherichia coli 13 (30.2%), Pseudomonas 30.3. It was recorded in 15 (34.9%) people. As can be seen, Candida albicans was recorded in patients with a high frequency. According to the authors, this invasive pathogen has a diverse species composition. The detection of Klebsiella pneumoniae in 12 (27.9%) people is also a dangerous issue. Pseudomonas aeruginosa was detected in the blood of 10 (23.3%) drug addicts.

Candida albicans was detected in 22 (45.8%) patients with alcoholism, and Candida tropicalis in 23 (47.9%). Staphylococcus aureus was not detected in any alcoholic. In this group, Klebsiella pneumoniae 11 (22.9%), Nesseria spp. It was detected in 11 (1.20%) people and was found in the same number of patients. S. pyogenes and Pseudomonas aeruginosa were detected less frequently, each of which was detected in 5 (7.88%) people. The limits of statistical reliability were very high among all groups included in the study. In this case, we should talk about statistical dishonesty. Such dishonesty was recorded only among drug addicts and alcoholics. Among them, Enterobacteriaceae spp. Statistical inaccuracy in the composition was found. The amount of these factors in the blood of drug addicts is statistically significantly higher than in individuals with alcohol dependence ($p=0.0104$, $p<0.001$, $t=2.63$). The level of M. catarrhalis was also statistically significantly higher in drug addicts than in alcoholics ($p=0.0354$, $p<0.001$, $t=2.14$). The level of S. capitis

was also statistically significantly higher in drug addicts than in alcoholics (p=0.0655, p<0.001, t=1.87). The level of Candida albicans was statistically significantly lower in healthy individuals than in alcoholics (p=0.0379, p<0.05, xi2 = 4.31). The level of Candida albicans was statistically significantly higher in drug addicts than in alcoholics (p=0.0177, xi2 = 5.62). The study included studies of the nasopharyngeal microbiome in healthy individuals, drug addicts and patients with drug addiction. S. Hominis (920345.3±11065.18 CFU/ml) and Staphylococcus spp. were detected in individuals suffering from alcohol dependence. (8090327.9±173543.08 CFU/ml) were predominant. Less S. capitis was detected (907.0±22.42 CFU/ml). S. Xylosus (3431.8±203.99 KYV/ml), Nesseria spp. (6714.0±232.67 CFU/ml), S. pyogenes (4482.6±118.61 CFU/ml) were present in low content. Micrococci spp. were found in individuals suffering from alcohol dependence included in the study. (1030716.3±185852.72 CFU/ml), S. aureus (277261.9±11626.09 CFU/ml), S. haemolyticus (7984492.1±214909.54 CFU/ml), S. hominis (920345.3±11065.18 CFU/ml) were also found in fairly large quantities.

Studies have shown that when taking narcotic substances, especially cocaine addicts, the nasopharyngeal mucosa is infected with a high number of infectious agents. It is known that in people who take narcotic substances through the nose for a long time, necrotic disorders occur in the mucous membrane, cartilage and bone structures. Often, the first manifestation of cocaine abuse is the formation of perforation of the nasal septum in the cartilaginous part. As a rule, patients complain of periodic nosebleeds, dry nose, and crusting.

Staphylococcus spp. was statistically significantly higher in alcohol addicts (884,475±13,834 CFU/ml) than in drug addicts (8,090,328±173,543 CFU/ml). Statistically significant differences were found between the groups regarding the nasal cavity microbiome, almost for all indicators. In this case, it is necessary to talk about microorganisms with statistically insignificant differences.

The amount of Enterobacteriaceae spp. was statistically significantly higher in alcoholics (71,301±3,449 CFU/ml) than in healthy individuals (4,808±88 CFU/ml) (p=0.0104, p<0.001, t=2.63). S. Capitis was statistically significantly higher in drug addicts (907±22 CFU/ml) than in alcoholics (844±25 CFU/ml) (p=0.0655, p<0.001, t=1.87).

Healthy people, as a rule, have normal functioning of all organs and systems of the body. They do not have chronic diseases or other serious diseases such as heart disease, diabetes, hypertension, liver disease or kidney disease, which are common in people suffering from addiction. The physical health of healthy people is maintained by a healthy lifestyle, balanced nutrition, regular physical activity and the absence of bad habits.

Healthy people have a stable psycho-emotional state. They are able to adequately perceive reality, solve life problems, maintain emotional stability and effectively interact with others. Mental health is supported by good social relationships, a favorable social environment and the ability to cope with difficulties without resorting to bad habits.

Microbiology plays an important role in forensic medicine, as it helps determine the cause of death, diagnose diseases, and investigate crimes related to infections, poisoning and other microbiological factors. Forensic experts use microbiology methods to analyze biological materials such as blood, urine, tissue and body fluids, as well as traces left at crime scenes, to draw conclusions about health, deaths and identify potential criminals.

Addiction to psychoactive substances such as drugs and alcohol is a global problem that affects not only the health of an individual, but also social processes as a whole. Drug and substance abuse have devastating effects on all aspects of a person's life, including their physical, mental, and social well-being. This paper presents a comparative analysis of the microbiome of healthy individuals and people with drug addiction, which will allow us to better understand their impact on the body and society.

Drug addiction leads to numerous physical diseases, such as damage to internal organs, including the heart, liver, kidneys, and lungs, as well as a weakened immune system. Long-term drug use can lead to brain damage, decreased cognitive function, and impaired memory and attention. In addition, drug use increases the risk of infectious diseases such as HIV/AIDS and hepatitis, as it is often associated with the use of unsterile needles.

Alcohol addiction also leads to serious physical diseases. Regular consumption of alcoholic beverages leads to cirrhosis of the liver, pancreatic diseases, problems with the cardiovascular system (hypertension, heart attack, stroke). Alcohol has a toxic effect on the nervous system, which can lead to psychosis, memory loss, and cognitive impairment.

Alcoholism is also associated with various mental illnesses, including depression, anxiety, panic attacks, and cognitive impairment. Alcohol-related problems can lead to chronic psychoses, such as delirium tremens, as well as nervous breakdowns and personality destruction. An important aspect is the development of addiction, when a person loses the ability to control alcohol consumption, which negatively affects his psychoemotional state.

Healthy people are able to function effectively in a social environment and build healthy relationships with loved ones, colleagues, and friends. They actively participate in public life, have stable jobs, and strive for development. The ability to cope with difficulties and stress reduces the likelihood of developing addictions.

Drug addiction often leads to a breakdown in social relationships. Dependent people may have difficulty maintaining relationships with family, friends, and colleagues. Drug addiction causes problems at work, often leading to job loss and financial problems. Drug addicts often isolate themselves from society, which increases their addiction and contributes to the development of antisocial behavior.

Alcoholism has similar social consequences, such as the destruction of family relationships, job loss, financial problems and social isolation. Alcoholics often become a source of family conflicts, their social behavior becomes problematic, which leads to a deterioration in their status in society. People with alcohol dependence are also at higher risk of committing crimes, since they can commit crimes while intoxicated.

Research has shown that drug addicts and alcoholics have skin problems. The microflora of the nasopharyngeal mucosa differs in species composition from that of healthy people. The integration and application of the results of studying the microbiome of various environments of the human body in forensic medicine lays the foundation for future prospects. Drug addicts and alcoholics are exposed to more dangerous microorganisms. Drug addicts also have a higher incidence of dangerous strains. Unlike healthy people, S. pyogenes is found in the nasopharyngeal contents of drug addicts and alcoholics. The discovery of microorganisms such as S. capitis indicates that they are susceptible to dangerous infections.

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MATHEMATICAL MODELING OF HIV/AIDS CONSIDERING THE EFFECT OF TREATMENT NON-ADHERENCE

ABSTRACT

The Human immunodeficiency Virus (HIV) is one of the deadliest epidemics in human history and remains a significant global health challenge, with millions of people worldwide living with the virus. The disease continues to spread despite advances in treatment and prevention and there is an urgent need for understanding and controlling the spread and transmission of the dynamics. This study investigates a four compartmental mathematical model considering the effect of inconsistent treatment with saturated incidence function.

The positivity of solutions and the equilibrium points of the model were analyzed qualitatively and the basic reproduction number was determined using the next generation matrix technique. The local and global stability analysis of the disease free and endemic equilibrium was carried out. This analysis provides a much needed understanding and conditions necessary for the disease to persist or die out.

Sensitivity analysis of R_0 was carried out in order to identify key parameters influencing the model's behavior. Numerical simulations are then conducted to further explore the dynamics of the system. Our results highlight the importance of targeted interventions to control the transmission and spread of the disease, informing public health policy and intervention strategies.

Keywords: *HIV/AIDS, Mathematical Modeling, Non-Adherence, treatment, Stability*

1. Introduction

HIV is seen as a chronic disease and a viral infection that attacks the body's immune system, potentially leading to Acquired immunodeficiency Syndrome (AIDS) if left untreated, highlighting the importance of awareness, prevention, and timely medical intervention [1].

Transmission of HIV/AIDS causing virus occurs most commonly through sexual intercourse. HIV can also be transmitted through transfusions of HIV-contaminated blood or by using a contaminated needle or syringe to inject drugs into the blood stream. Infection with HIV does not necessarily mean that a person has AIDS. Some people who have HIV infection may not develop any of the clinical illnesses that define the full-blown disease of AIDS for ten years or more. Physicians prefer to use the term AIDS for cases where a person has reached the final, life-threatening stage of HIV infection [20]. In a person infected with HIV, the virus steadily destroys $CD4^{+}T$ cells over a period of years, diminishing the cells protective ability and weakening the immune system. HIV infects some other cells and wrecks the largest part of the $CD4^{+}T$ cells and this causes the $CD4^{+}T$ cells destruction and decline, hence reducing the confrontation of the susceptible system [21], [22].

It is however important to put extra effort on prevention, diagnosis, screening, vaccination and treatment. This could be achieved by increasing access to antiretroviral therapy, promoting awareness and implementing targeted interventions to reduce new infections and increase quality of life for those living with HIV/AIDS in the population [3,4,5,6].

However, inconsistent treatment can lead to development of drug-resistant HIV strains, reducing the effectiveness of antiretroviral therapy and increasing the rate at which disease are been progressed and transmitted [7,8,18].

Many researchers have explored various approaches on Infectious disease modeling using different infection rates to understand how dynamics of disease spread including saturated and monotone formulations, to improve the accuracy of these models. One such approach is the saturated incidence rate, which considered the impact of inhibition effects on disease transmission. Mathematically, it is presented as a function of the infection rate, susceptible population, infected population and inhibition coefficient.

This study is organized as follows: Section 2 explains the formulation of model, including the model's positivity and boundedness. Section 3 presents an in-depth mathematical examination of the model, encompassing key aspects such as the basic reproduction (R_0), local stability analysis of the disease-free equilibrium, global asymptotic stability of disease-free equilibrium and endemic equilibrium, and a sensitivity analysis of the basic reproduction number. Section 4 focuses on numerical simulations and discussions while Section 5 summarizes the findings.

2. Model Formulation

In this study, the susceptible and infectious epidemic model (SI) is presented. A population size of $N(t)$ was partitioned into 4 subclasses of individuals which are; susceptible population, Infected population, AIDS population, and treated population with sizes denoted by $S(t), I(t), A(t), \text{and} T(t)$, respectively such that $N = S + I + A + T,$ as shown in figure 1 below:

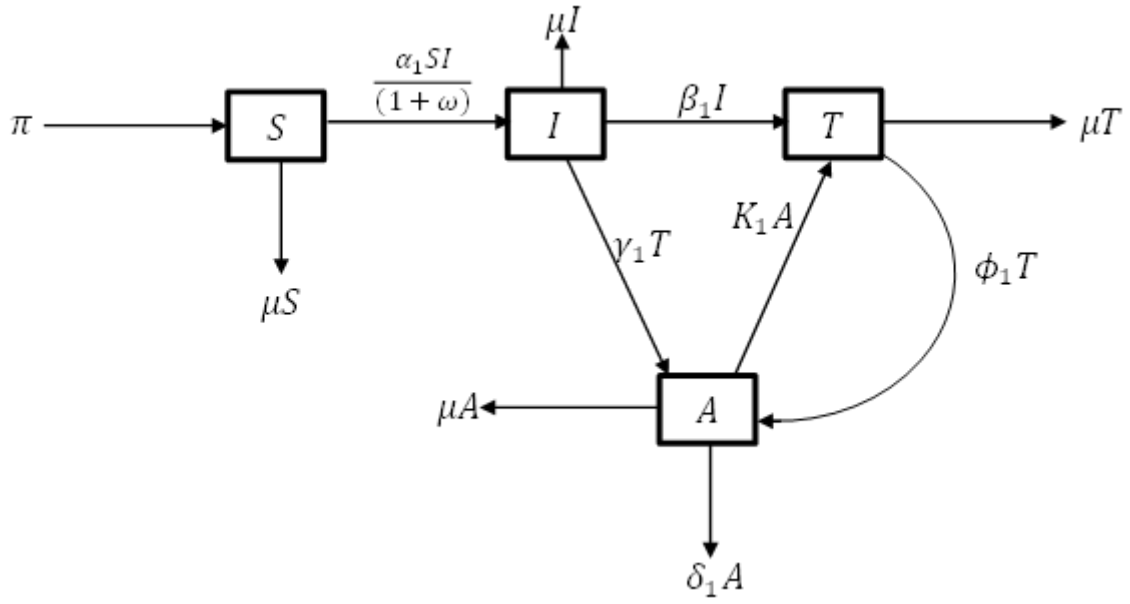


Figure 1: Schematic flow chart for HIV spread dynamics

The model explores the dynamics of HIV transmission, incorporating a saturation term. The model is governed by a system of nonlinear differential equations, which capture the complex interactions between the compartments. The model consisting of four compartments: Susceptible, Infected, AIDS, and treated, with the susceptible population entering through recruitment by immigration at a constant rate (π). Newly infected individuals become infected at a rate (α_1) and progressed to the infected compartment. Infected individuals' later progress to the AIDS compartment at a rate (ϕ_1) if left untreated. Infected individuals receive ART treatment at (β_1), while those in the AIDS compartment receive treatment at a rate of (k_1). AIDS-related mortality removes individuals from the AIDS compartment at a rate (σ_1). Natural death occurs in all compartment.

Considering all the above assumptions made, the following system of ordinary differential equations of the proposed model is therefore formulated:

$$\left.\begin{aligned}
\frac{dS}{dt} &= \pi - \frac{\alpha_1 SI}{1+\omega S} - \mu S \\
\frac{dI}{dt} &= \frac{\alpha_1 SI}{1+\omega S} - (\mu + \beta_1 + \gamma_1) I \\
\frac{dA}{dt} &= \gamma_1 I + \phi_1 T - (k_1 + \delta_1 + \mu) A \\
\frac{dT}{dt} &= \beta_1 I + k_1 A - (\mu + \phi_1) T
\end{aligned}\right\} \qquad (1)$$

$$S(0) = S_0, I(0) = I_0, A(0) = A_0, T(0) = T_0 \qquad (2)$$

where, $\frac{\beta I_1 S}{1+\omega S}$ is the incidence rate and ω is the saturation term to the susceptible.

Table 1: Model variables and parameters are defined as follows:

Parameters/ variables	**Description**
π	Recruitment rate
β_1	Rate of treatment after infection
γ_1	Progression rate from infected to AIDS
α_1	Infection rate
μ	Natural mortality rate unrelated to AIDS
δ_1	Death rate due to AIDS
ϕ_1	Progression rate from treated to AIDS
k_1	Progression rate from AIDS to treated
$S(t)$	Susceptible population at a given time (t).
$I(t)$	Infected population
$T(t)$	Treated population
$A(t)$	AIDS population

2.1 **Positivity and boundedness of the model**: In this section we shall show from model (1) that the state variables are non-negative and the solutions remain positive for all $t \geq 0$. Hence, the parameters in the model are assumed to be positive.

Theorem 1: Let the initial conditions or values of the state variables be such that $\{(S(0)\geq 0, I(0)\geq 0, A(0)\geq 0, T(0)\geq 0,)\in \Omega\}$, then the set $(S(t), I(t), A(t), T(t))$ is non-negative in Ω for all $t\geq 0$.

Proof: Considering the first equation in (1), are considered for the positivity of the state variables as follows using the approach of [3,8,9],

$$\frac{dS}{dt}\geq -\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)S$$

$$\frac{dS}{dt}\geq -\int\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)S$$

Using variable separable

$$\frac{dS}{S}\geq -\int\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)dt$$

$$\ln s\geq -\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)t+C$$

$$S(t)\geq e^{-\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)t}.e^{C_1}$$

$$S(t)=S_0 e^{-\left(\frac{\alpha I_1}{1+\omega S}+\mu\right)t}.$$

$$S(0)=S_0\Rightarrow A_1=S_0$$

Since $S(t)\geq 0,$ for all $t>0$ provided that $S_0\geq 0.$

Hence, $S(t)\geq 0$

For the second compartment of (1)

$$\frac{dI}{dt}\geq \frac{\alpha_1 SI}{1+\omega S}-(\mu+\beta_1+\gamma_1)I$$

$$\frac{dI}{dt}\geq -\int(\mu+\beta_1+\gamma_1)I$$

Using variable separable

$$\frac{dI}{I}\geq -\int(\mu+\beta_1+\gamma_1)dt$$

$$I(t)\geq e^{-(\mu+\beta_1+\gamma_1)t}.e^{C_1}$$

$$I(t)=I_0 e^{-(\mu+\beta_1+\gamma_1)t}.$$

$$I(0)=I_0\Rightarrow A_1=I_0$$

Since $I(t)\geq 0,$ for all $t>0$ provided that $I_0\geq 0.$

Hence, $I(t)\geq 0$

It is possible to show using the same procedure for other state variables that:

$I(t)\geq I_1(0)e^{-(\mu+\beta_1+\gamma_1))t}\geq 0, A(t)\geq A(0)e^{-(k_1+\sigma_1+\mu)t}\geq 0,$

$T(t)\geq T(0)e^{-(\mu+\phi_1)t}\geq 0,$

This shows that all the solutions of equation (1) are positive for all $t\geq 0$. Therefore, the HIV/AIDS transmission model stated in (1) is both epidemiologically significant and numerically well posed in an attainable given region $\Omega\geq 0$

Theorem 2

Every solution in the region $\Omega = \left\{ \left(S(t), I(t), A(t), T(t) \in \Omega_+^4 : N(t) \le \frac{\pi}{\mu} \right) \right\}$ is positively invariant with respect to the HIV/AIDS model (1) in the populations. The solutions for the system are contained and remain in the region Ω for all time $t \ge 0$.

Proof: Considering the equation of the model, and adding up all the derivatives with respect to time t, we obtained

$$\frac{dN(t)}{dt} = \pi + \mu(S + I + A + T) - \sigma_1 A$$

$$\frac{dN(t)}{dt} = \pi + \mu N$$

$$N \le \frac{\pi}{\mu} + \left(N_0 - \frac{\pi}{\mu} \right) e^{-\mu t}$$

Where N_0 is the initial size of the population

Therefore,

$$\lim_{t \to \infty} N(t) \le \frac{\pi}{\mu}$$

This result implies that HIV/AIDS model (1) has non-zero negative and bounded solution in the region Ω and all the solutions starting in Ω approach, enter or stay in Ω. Hence, it is sufficient to conclude that the model is epidemiologically well posed.

3 Mathematical Analysis of the Model

3.1 Disease free equilibrium point*:* This is a state where the disease is completely eliminated from the population, that is, there is no infected individuals, no disease transmission and population is entirely susceptible.

At the equilibrium,

$$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dI_1}{dt} = \frac{dI_2}{dt} = \frac{dT}{dt} = \frac{dA}{dt} = 0$$

$$\left.\begin{aligned} \frac{dS}{dt} &= \pi - \frac{\alpha_1 SI}{1 + \omega S} - \mu S \\ \frac{dI}{dt} &= \frac{\alpha_1 SI}{1 + \omega S} - (\mu + \beta_1 + \gamma_1) I \\ \frac{dA}{dt} &= \gamma_1 I + \phi_1 T - (k_1 + \delta_1 + \mu) A \\ \frac{dT}{dt} &= \beta_1 I + K_1 A - (\mu + \phi_1) T \end{aligned}\right\} \quad (3)$$

At the disease free equilibrium, we set $S \ne 0, I = A = T = 0$ substituting these to equation (3) and solving gives the infection – free equilibrium as

$$E^0 = (S^0, I^0, A^0, T^0) = \left(\frac{\pi}{\mu}, 0, 0, 0 \right) \quad (4)$$

3.2 Endemic equilibrium point*:* The endemic equilibrium is a steady- state solution where the disease persists in the population at a stable level. At endemic equilibrium, $S \ne 0, I \ne 0, A \ne 0, T \ne 0,$

Solving equation (3) simultaneously, we have the endemic equilibrium points of the HIV model (3) designated by $x^* = (S^*, I^*, A^*, T^*)$ is obtained as:

$$\left\{\begin{array}{l} s^* = \dfrac{\pi}{\left(\lambda^* + \mu\right)} \\ I^* = \dfrac{\lambda^* \pi}{Z_1\left(\lambda^* + \mu\right)} \\ T^* = \dfrac{\beta_1 \lambda^* \pi Z_2 + k_1 \gamma_1 \lambda^* \pi}{Z_1 Z_2 Z_3 - \phi_1 Z_2\left(\lambda^* + \mu\right)} \\ A^* = \dfrac{\gamma_1 \lambda^* \pi\left(Z_1 Z_2 - \phi_1\right) + \phi_1 \beta_1 \lambda^* \pi Z_2 + \phi_1 k_1 \gamma_1 \lambda^* \pi}{Z_1 Z_2\left(\lambda^* + \mu\right)\left(Z_1 Z_2 - \phi_1\right)} \end{array}\right\} \quad (5)$$

Where,

$$Z_1 = \left(\mu + \beta_1 + \gamma_1\right), Z_2 = \left(k_1 + \delta_1 + \mu\right), Z_3 = \left(\mu + \phi_1\right), \quad \lambda^* = \frac{\alpha_1 I}{1 + \omega S}$$

3.3 Basic Reproduction Number (R_0)

The next generation matrix is constructed by examining novel infection routes and inter-compartmental transmission dynamics. Utilizing the methodology outlined by [10].

Let M be the next generation matrix. It comprises of two parts F and V^{-1} where

$$F = \left[\frac{\partial f_1(x_0)}{\partial x_j}\right], \qquad V = \left[\frac{\partial V_1(x_0)}{\partial x_j}\right]$$

The term f_i and v_i are computed as

$$f_i = \begin{bmatrix} \dfrac{\alpha_1 SI}{1 + \omega S} \\ 0 \\ 0 \end{bmatrix}, v_i = \begin{bmatrix} -\left(\mu + \beta_1 + \gamma_1\right) I \\ \gamma_1 I + \phi_1 T - \left(k_1 + \delta_1 + \mu\right) A \\ \beta_1 I + k_1 A - \left(\mu + \phi_1\right) T \end{bmatrix}$$

, $Df(E_0) = \left[\dfrac{\partial f_1(E_0)}{\partial x_j}\right]$, $DV = \left[\dfrac{\partial V_1}{\partial x_j}\right]$

$$F_i = \begin{bmatrix} \dfrac{\alpha_1 S}{1 + \omega S} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}, V_i = \begin{bmatrix} \left(\mu + \beta_1 + \gamma_1\right) & 0 & 0 \\ -\gamma_1 & \left(k_1 + \delta_1 + \mu\right) & -\phi_1 \\ -\beta_1 & -k_1 & \left(\mu + \phi_1\right) \end{bmatrix}$$

The Jacobian matrices of F_i and V_i at the disease free equilibrium point, $x_0 = \left(\dfrac{\pi}{\mu}, 0, 0, 0\right)$ are:

$$DF(x_0)=\left[\frac{\partial F_i(x_0)}{\partial x_j}\right]=\begin{bmatrix}\frac{\alpha_1 S_0}{1+\omega S_0} & 0 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0\end{bmatrix}\Rightarrow\begin{bmatrix}\frac{\alpha_1\pi}{\mu\left(1+\frac{\omega\pi}{\mu}\right)} & 0 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0\end{bmatrix}$$

$$V^{-1}=\begin{bmatrix}\frac{1}{(\mu+\beta_1+\gamma_1)} & 0 & 0\\ \frac{\mu\gamma_1+\beta_1\phi_1}{(\mu+\beta_1+\gamma_1)(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)} & \frac{\mu}{(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)} & \frac{\phi_1}{(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)}\\ \frac{\mu\beta_1+k_1\beta_1+\beta_1\delta_1+\gamma_1 k_1}{(\mu+\beta_1+\gamma_1)(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)} & \frac{k_1}{(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)} & \frac{k_1+\delta_1+\mu}{(\mu^2+\mu k_1+\mu\delta_1-k_1\phi_1)}\end{bmatrix} \quad (5)$$

$$FV^{-1}=\begin{bmatrix}\frac{\alpha_1\pi}{\mu\left(1+\frac{\omega\pi}{\mu}\right)(\mu+\beta_1+\gamma_1)} & 0 & 0\\ 0 & 0 & 0\\ 0 & 0 & 0\end{bmatrix} \quad (6)$$

The basic reproduction number, which is the dominant Eigen-value of the product FV^{-1}, is therefore obtained as:

$$R_0=\frac{\pi\alpha_1}{\pi\mu\omega+\pi\omega\beta_1+\pi\omega\gamma_1+\mu^2+\mu\beta_1+\mu\gamma_1} \quad (7)$$

3.4 Stability analysis of the Disease free equilibrium

Theorem 4*:* The disease-free state is locally asymptotically stable if the basic reproduction number $R_0<1$ and unstable if otherwise.

Proof:

We evaluate the Jacobian matrix of the model at the disease free equilibrium

$$x_0=\left(\frac{\pi}{\mu},0,0,0\right)$$

$$J=\begin{bmatrix} -\mu & \frac{\alpha_1 S_0}{1+\omega S_0} & 0 & 0 \\ 0 & \frac{\alpha_1 S_0}{1+\omega S_0}-(\mu+\beta_1+\gamma_1) & 0 & 0 \\ 0 & \gamma_1 & -(k_1+\delta_1+\mu) & \phi_1 \\ 0 & \beta_1 & k_1 & -(\mu+\phi_1) \end{bmatrix} \quad (8)$$

The jacobian matrix at DFE,

$$J(E_0)\Rightarrow\begin{bmatrix} -\mu & \frac{\alpha_1\pi}{\mu\left(1+\frac{\omega\pi}{\mu}\right)} & 0 & 0 \\ 0 & \frac{\alpha_1\pi}{\mu\left(1+\frac{\omega\pi}{\mu}\right)}-(\mu+\beta_1+\gamma_1) & 0 & 0 \\ 0 & \gamma_1 & -(k_1+\delta_1+\mu) & \phi_1 \\ 0 & \beta_1 & k_1 & -(\mu+\phi_1) \end{bmatrix}\Rightarrow$$

$$\begin{bmatrix} -\mu & \frac{\alpha_1\pi}{\mu+\omega\pi} & 0 & 0 \\ 0 & \frac{\alpha_1\pi}{\mu+\omega\pi}-(\mu+\beta_1+\gamma_1) & 0 & 0 \\ 0 & \gamma_1 & -(k_1+\delta_1+\mu) & \phi_1 \\ 0 & \beta_1 & k_1 & -(\mu+\phi_1) \end{bmatrix} \quad (9)$$

$$|A-\lambda I|=0\Rightarrow$$

$$\begin{bmatrix} -\mu & \frac{\alpha_1\pi}{\mu+\omega\pi} & 0 & 0 \\ 0 & \frac{\alpha_1\pi}{\mu+\omega\pi}-(\mu+\beta_1+\gamma_1) & 0 & 0 \\ 0 & \gamma_1 & -(k_1+\delta_1+\mu) & \phi_1 \\ 0 & \beta_1 & k_1 & -(\mu+\phi_1) \end{bmatrix}-\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}=0$$

$$\Rightarrow\begin{vmatrix} -\mu-\lambda & \frac{\alpha_1\pi}{\mu+\omega\pi} & 0 & 0 \\ 0 & \left(\frac{\alpha_1\pi}{\mu+\omega\pi}-(\mu+\beta_1+\gamma_1)\right)-\lambda & 0 & 0 \\ 0 & \gamma_1 & -(k_1+\delta_1+\mu)-\lambda & \phi_1 \\ 0 & \beta_1 & k_1 & -(\mu+\phi_1)-\lambda \end{vmatrix}=0 \quad (10)$$

The eigenvalues are

$$\begin{vmatrix} -\mu \\ -\dfrac{\pi\mu\omega + \pi\omega\beta_1 + \pi\omega\gamma_1 - \pi\alpha_1 + \mu^2 + \mu\beta_1 + \mu\gamma_1}{\pi\omega + \mu} \\ -\mu - \dfrac{1}{2}\delta_1 - \dfrac{1}{2}k_1 - \dfrac{1}{2}\phi_1 - \dfrac{1}{2}\sqrt{4\phi_1 k_1 + \delta_1^2 + 2\delta_1 k_1 - 2\delta_1\phi_1 + k_1^2 - 2k_1\phi_1 + \phi_1^2} \\ \sqrt{k_1^2 + \left(4\phi_1^2 + 2\delta_1 - 2\phi_1\right)k_1 + \left(\phi_1 - \delta_1\right)^2} < 2\mu + \delta_1 + k_1 + \phi_1 \end{vmatrix} \quad (11)$$

All the eigenvalues in (11) are negative,
Therefore, the disease free equilibribium is locally asymptotically stable since all the $\lambda's$ are negative.

3.7 Sensitivity Analysis of the basic Reproduction number

Sensitivity analysis is crucial for evaluating the stability and accuracy of mathematical models. This process helps researchers pinpoint the most influential factors driving disease transmission and assess the potential impact of interventions. It investigates how changes in certain epidemiological features of the model affect the transmission dynamics of the HIV/AIDS model (1).
The normalized forward sensitivity index of a variable to a parameter is a ratio of the relative change in the variable to the relative change in the parameter. When a variable is differentiable function of the parameter, the sensitivity index may be alternatively defined using partial derivatives.
Adapting the methodology introduced by [12], the normalized forward sensitivity index of a variable "k" that depends differentiable on a parameter "e" is defined as:

$$X_e^k := \frac{\partial k}{\partial e} * \frac{e}{k} \quad (12)$$

Following the approach used in [13,17], the sensitivity indices of the parameters relative to the basic reproduction number (7) is established. Therefore, the normalized forward sensitivity indices of the basic reproduction number (7) associated with parameters, ρ, is calculated as

$$X_\rho^{R_0} := \frac{\partial R_0}{\partial \rho} * \frac{\rho}{R_0} \quad (13)$$

As we have an explicit formula for R_0 in equation (7), and we derive an analytical expression for the sensitivity of R_0, as $X_\rho^{R_0} := \frac{\partial R_0}{\partial \rho} * \frac{\rho}{R_0}$ with respect to each of the parameters involved in R_0 as computed in table 2 below:

Table 2: Sensitivity Result

Parameter	Value	Sensitivity Index	Source
π	0.06	+0.178082	[14]
α_1	0.0009	+1.00000	[16]
μ	0.0013	-0.17938	[15]
γ_1	0.999925	-0.99869	[7]
ω	0.1	-0.82192	[1]
β_1	0.000075	-0.000749	[15]

3.8 Interpretation of Sensitivity Indices*:* The sensitivity indices provide valuable insights into the relationships between model parameters and outcomes. A high sensitivity index for a particular parameter indicates that small changes to that parameter can significantly impact the model's behavior. Conversely, a low sensitivity index suggests that the model is relatively insensitive to changes in that parameter. Positive sensitivity indices reveal parameters that increase the outcome, while negative indices identify parameters that decrease the outcome. By analyzing the sensitivity indices, researchers can identify key parameters driving model behavior, prioritize parameters for further investigation and also targeted interventions to optimize outcomes.

The sensitivity indices of the basic reproduction number R_0, relative to its parameters are summarized in Table 2. It can be seen that there are parameters with positive and negative sensitivity indices. Parameters representing recruitment rate (π), and Infection rate (α_1), are parameters with positive indices while parameters such as $\beta_1, \gamma_1, \mu,$ and ω are parameters with negative sensitivity indices accordingly. It is worth noting that unhindered increase in the values of parameters with positive sensitivity indices will lead to a corresponding increase in the value of the associated basic reproduction number. For instance, $X_{\alpha_1}^{R_0}$ = +1.0000 means that increasing or decreasing α_1 by 10% increases or (decreases) R_0 by 10% while $X_{\mu}^{R_0}$ = - 0.17938 means that increasing or (decreasing) μ by 10% decreases (or increases) R_0 by 1.7938%. we can easily compute same for every other parameters following similar trend.

4. NUMERICAL SIMULATIONS AND DISCUSSION

A computational simulation of the model was conducted using Maple 18 Mathematical software to gain deeper insights into the dynamic transmission patterns of HIV/AIDS. This simulation facilitated an examination of how various parameters influence the basic reproduction number, providing a clearer understanding of their role in shaping the epidemic's trajectory.

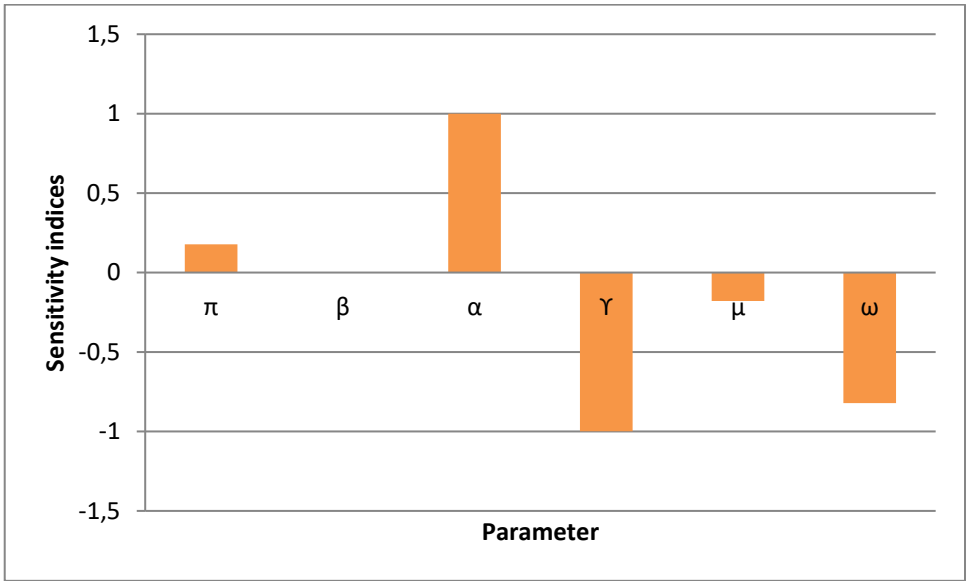


Fig 4. 1: **Graphical Representation of the Sensitivity indices of** R_0

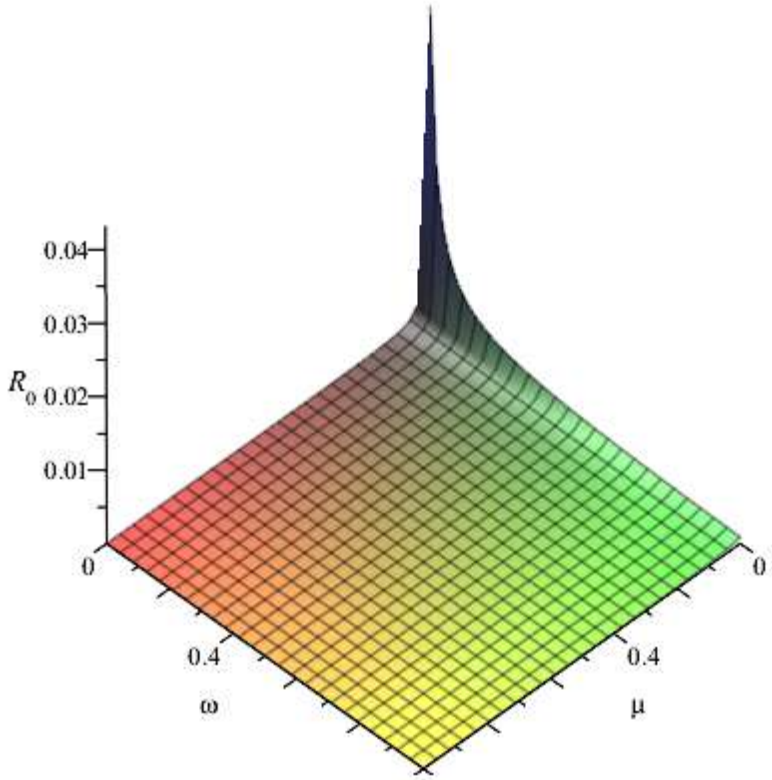


Fig. 4.2: Sensitivity of the basic reproduction number to the parameters π and ω

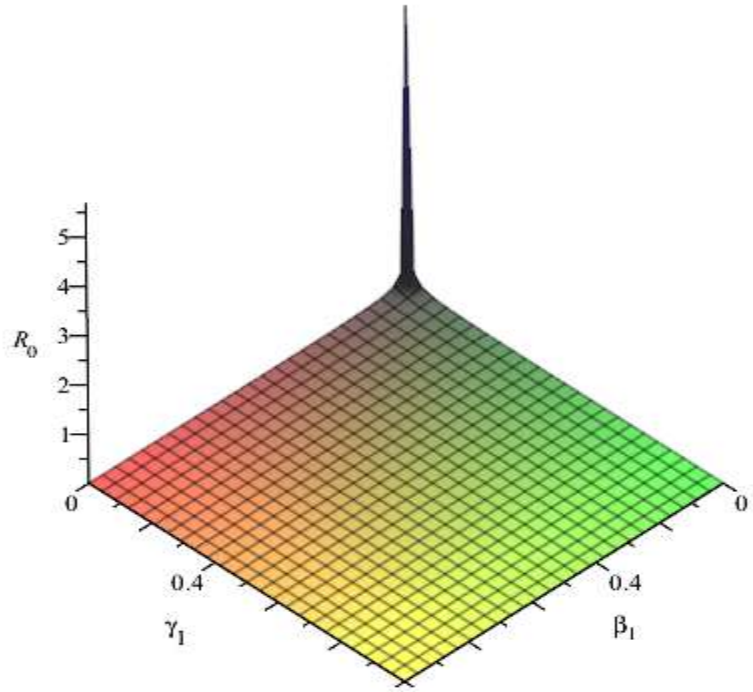


Fig. 4.3: Sensitivity of the basic reproduction number to the parameters γ_1 and β_1

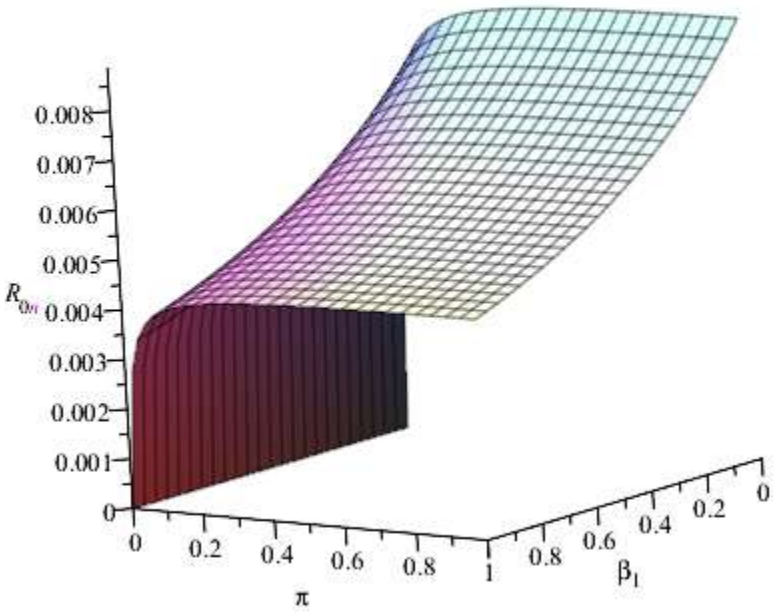


Fig. 4.4: Sensitivity of the basic reproduction number to the parameters π and θ

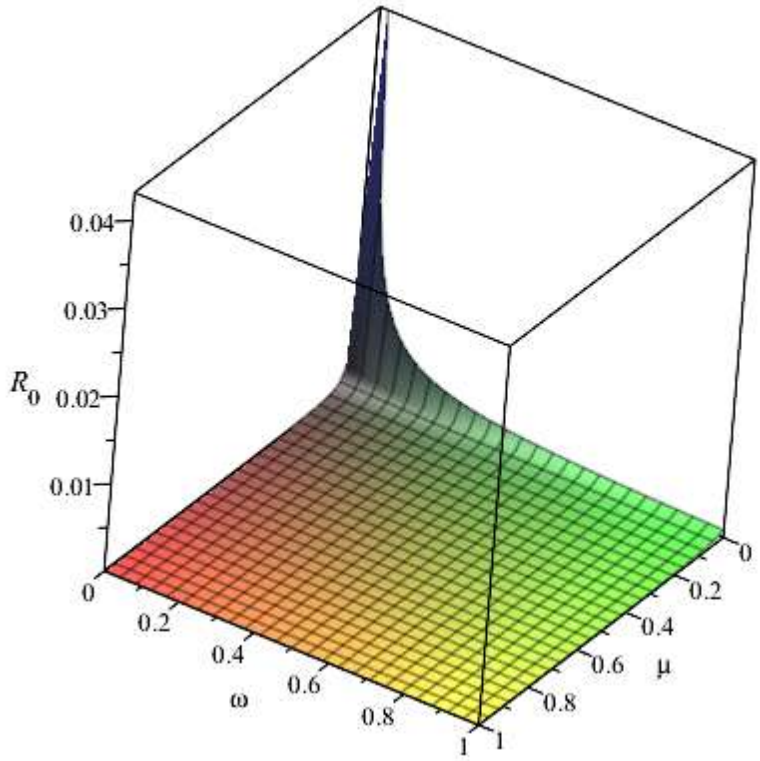


Fig. 4.5: Sensitivity of the basic reproduction number to the parameters ω and μ

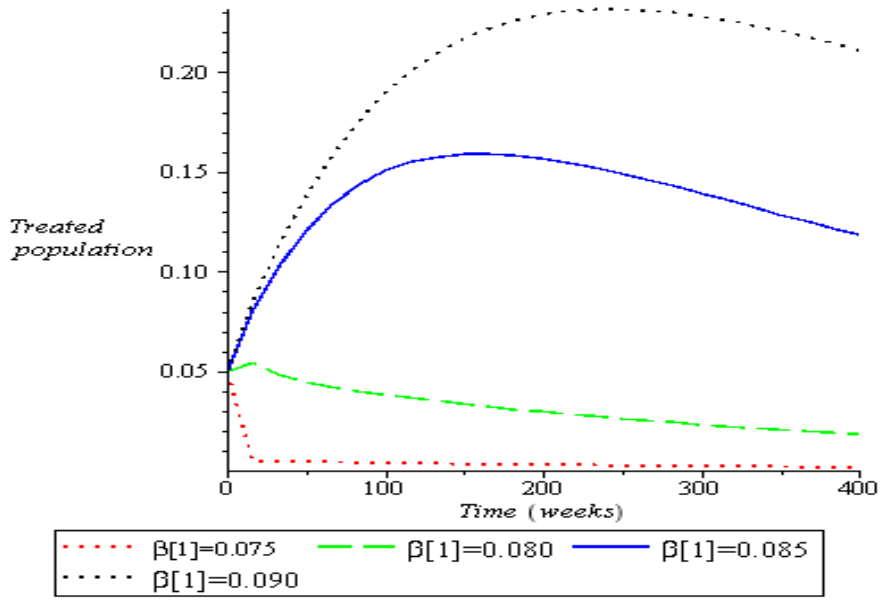


Fig 4.6: graph of treated infective population against time t, showcasing various rate of treatment after infection , (β),

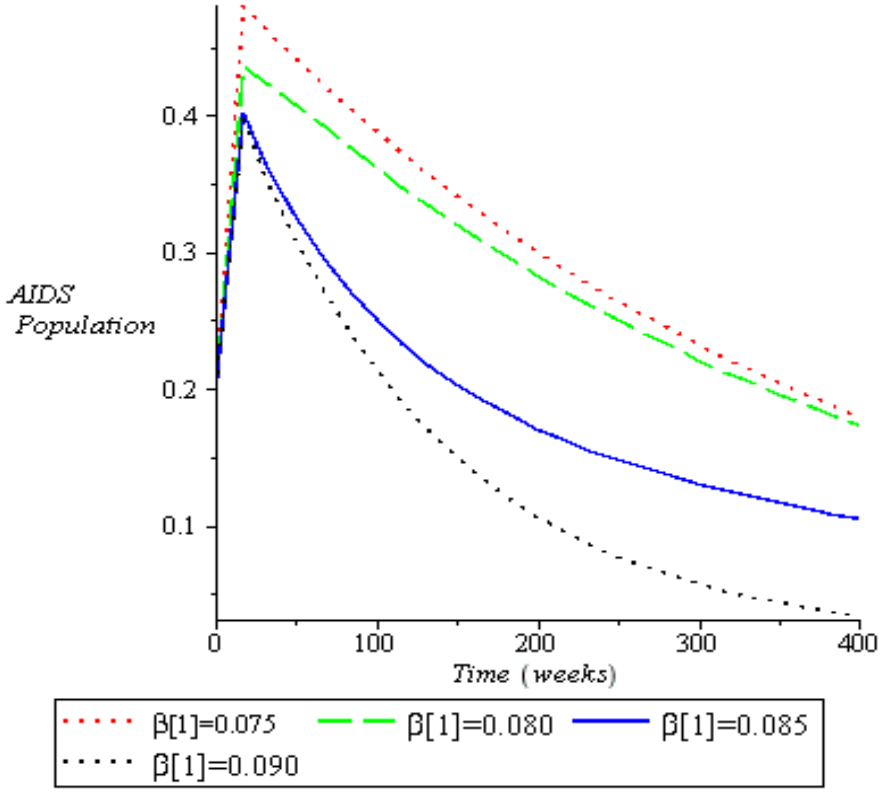


Fig 4.7: graph of treated infective population against time t, showcasing various rate of treatment after infection , (β),

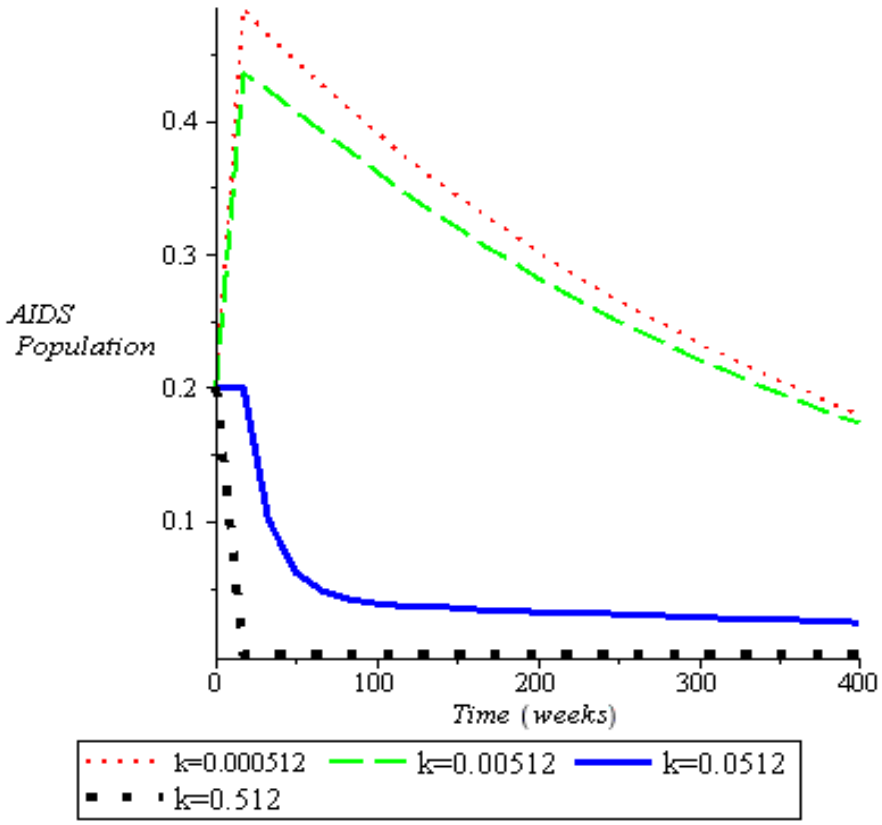


Fig 4.8: graph of treated infective population against time t, showcasing various rate of (k_1).

Discussion:

Fig 4.1 illustrates the graphical representation of the basic reproduction in form of a bar chart. The most sensitive parameter is infection rate.

Fig 4.2 illustrates the relationship between recruitment rate of susceptible (π) and saturation term (ω) on the basic reproduction number, Notably, as the recruitment rate increase, the basic reproduction number increase. Conversely, increase in saturation rate, enhances a decrease in the basic reproduction number. Fig4.3 illustrates the relationship between progression rate and the basic reproduction number. The simulation results demonstrates that as the progression rate from infected population to AIDS, (γ_1) increases, the basic reproduction decreases and also, an increase in β, leads to a decrease in the basic reproduction number. The decrease in R_0 indicates that the number of secondary infections generated by an infected individual is reduced, which can help control the outbreak. Fig 4.4 reveals the effect of recruitment rate (π) and treatment rate (β_1). As the recruitment rate increases, the basic reproduction number also increases, indicating a potential growth in the spread of the disease. In contrast, an increase in the rate of treatment after infection leads to a decrease in R_0, suggesting that treatment is effective in reducing the spread of the disease. Fig 4.5 also illustrates that as saturation term increases the basic reproduction number.

Fig 4.6 and 4.7 shows the effect of treatment rates on infected and AIDS population. The model simulations show that as the rate at which infected individuals seek treatment increases, the treatment population grows. This suggests that improving access to treatment can lead to more people receiving care. Additionally, as the rate at which AIDS population receive treatment increases, the AIDS population decreases as seen in Figure 4.7. Timely and proper HIV treatment decreases the likelihood of disease progression, aligning with existing research findings of [1],[7],[8].

Fig 4.8 shows the effect of progression rate from treatment class to AIDS compartment. This explains that when there is an increase at the rate at which AIDS population receives treatment, (k_1), increases, the population of AIDS compartment decreases. This also support findings from previous studies of [7],[8].

V. CONCLUSSION

This study presents a mathematical modeling analysis to investigate the transmission dynamics of HIV. The disease free and endemic analysis was investigated to gain a deeper understanding of the long-term dynamics of the disease. A sensitivity analysis was conducted to assess the impact of key parameters on the basic reproduction number, providing valuable information on the factors driving the spread of HIV. Computational simulation of the model was also conducted showing the dynamics of the disease. The findings suggest that increasing the rate at which infected individuals seek treatment leads to a rise in the population receiving treatment, while a higher rate of treatment among AIDS patients results in a decline in the AIDS population. The model's findings highlight the impact of non-adherence to treatment on HIV transmission dynamics and provide insights for the development of effective intervention strategies. The results show that non-adherence to treatment can significantly affect disease prevalence and its transmission dynamics.

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INNOVATIONS IN NEUROSURGERY: EXPLORING THE LATEST ADVANCEMENTS AND TECHNIQUES IN BRAIN AND NERVE SURGERY

ABSTRACT

Neurosurgery, the branch of surgery dedicated to treating conditions affecting the brain, spine, and nervous system, has seen remarkable advancements over the last few decades. These innovations have significantly improved surgical outcomes, minimized patient risks, and shortened recovery times. This paper explores the cutting-edge techniques and technologies transforming the field of neurosurgery. Notable advancements include the development of robotic-assisted surgery, which allows for enhanced precision and minimally invasive procedures, reducing the need for large incisions and improving recovery rates. Neuronavigation systems have revolutionized the ability to accurately map the brain, ensuring surgeons can navigate complex regions with minimal disruption to critical structures. Endoscopic and minimally invasive techniques, such as keyhole surgeries, have transformed spinal and brain surgeries, making them less invasive, with fewer complications and reduced hospitalization times. Additionally, the integration of artificial intelligence (AI) and machine learning in surgical planning and real-time decision-making is providing neurosurgeons with powerful tools to predict patient outcomes and improve surgical precision. The role of 3D printing in creating patient-specific models for pre-surgical planning is also being increasingly recognized for its value in complex surgeries. Furthermore, advancements in intraoperative imaging, such as intraoperative MRI and CT scanning, have allowed for better visualization of the surgical site, enhancing the surgeon's ability to make real-time adjustments during procedures. This paper discusses these innovations, their applications in clinical practice, and the potential for future developments in the field of neurosurgery. The evolving landscape of neurosurgery continues to push the boundaries of what is possible, offering hope for patients with complex neurological conditions.

Keywords: Neurosurgery, robotic-assisted surgery, neuronavigation, minimally invasive surgery, endoscopic techniques, artificial intelligence, 3D printing, intraoperative imaging, brain surgery, spinal surgery, surgical precision, patient outcomes, advanced surgical technologies.

Introduction

Neurosurgery—an intricate and highly specialized branch of surgery that deals with disorders of the brain, spine, and nervous system—has long been regarded as one of the most challenging medical fields, often associated with significant risks and prolonged recovery times. However, in recent decades, a remarkable evolution in technology and surgical methodology has revolutionized neurosurgical practices. From the development of advanced imaging and navigation systems to the integration of robotics, artificial intelligence, and minimally invasive techniques, these innovations have dramatically enhanced the precision, safety, and efficacy of neurosurgical procedures. As a result, patients now experience reduced complication rates, shorter hospital stays, and improved prognosis. This article delves into the cutting-edge advancements that are shaping the future of neurosurgery, highlighting how these transformative tools and techniques are redefining possibilities in the operating room and beyond.

1. Robotic-Assisted Surgery: Redefining Precision in the Operating Room

One of the most impactful advancements in neurosurgery is the integration of robotic-assisted systems into the operating room. Robotic systems such as the ROSA® (Robotized Stereotactic Assistant) and the da Vinci® Surgical System are being increasingly used for procedures involving the brain and spine.

These systems offer:

- Enhanced dexterity: Robotic arms can perform extremely precise movements, often beyond human capabilities.
- Stabilized control: The elimination of natural hand tremors ensures high accuracy during delicate procedures.
- Minimally invasive access: Robots assist in performing surgeries through tiny incisions, leading to faster recovery, reduced blood loss, and less postoperative pain.

In spinal surgeries, robotic systems help in accurate placement of screws and hardware, significantly lowering the risk of complications.

2. Neuronavigation Systems: The GPS of the Brain

Neuronavigation has revolutionized how neurosurgeons approach surgeries involving complex and delicate regions of the brain and spinal cord. These systems use data from MRI or CT scans to create real-time, 3D maps of a patient’s anatomy, guiding the surgeon throughout the procedure.

Key benefits include:

- Real-time tracking: Instruments and surgical tools are tracked in real time with respect to the patient’s anatomy.
- Improved safety: Critical brain structures and functional areas are identified and preserved during tumor resections or epilepsy surgeries.
- Increased accuracy: Enables precise targeting in procedures like stereotactic biopsies and deep brain stimulation.

Neuronavigation is especially critical for tumor resections, allowing for maximal tumor removal while minimizing damage to surrounding healthy tissue.

3. Endoscopic and Minimally Invasive Techniques: Less Is More

Modern neurosurgery is increasingly moving towards minimally invasive techniques, which involve smaller incisions and minimal disruption to healthy tissues.

Endoscopic neurosurgery, often referred to as "keyhole surgery," uses thin tubes equipped with cameras and surgical instruments to access deep regions of the brain and spine. These techniques are commonly used for:

- Pituitary tumors
- Ventricular tumors
- Hydrocephalus treatments
- Herniated discs and spinal decompressions

Advantages:

- Smaller incisions and scars
- Reduced blood loss and risk of infection
- Shorter hospital stays and faster recovery
- Lower postoperative pain

For patients, these techniques represent a significant leap forward in terms of quality of life and reduced physical and emotional stress.

4. Artificial Intelligence and Machine Learning: Smart Surgery

The integration of Artificial Intelligence (AI) and Machine Learning (ML) into neurosurgery is creating new possibilities for personalized, predictive, and data-driven care.

AI-powered tools can:

- Analyze patient data to predict outcomes, complications, and surgical success.
- Support decision-making during surgery by identifying anatomical landmarks or suggesting optimal surgical paths.
- Assist in radiological interpretations to detect abnormalities with higher accuracy than conventional methods.

For example, AI is being used in glioma grading, seizure prediction in epilepsy, and optimizing surgical plans for spinal deformities. As AI continues to evolve, its role in enhancing surgical precision and improving patient safety will only grow stronger.

5. 3D Printing: Customized Surgical Planning

3D printing has emerged as a powerful tool in neurosurgery, especially for preoperative planning and education. By using patient-specific imaging data, 3D-printed anatomical models can be created to simulate surgeries before they happen.

These models:

- Allow surgeons to visualize complex anatomies in three dimensions
- Help in planning approaches for challenging tumors or deformities
- Enable patient-specific implants and prosthetics tailored to individual anatomy

This technology not only improves surgical accuracy but also enhances patient understanding and consent by offering a visual representation of the procedure.

6. Intraoperative Imaging: Seeing the Unseen During Surgery

Modern neurosurgical suites are increasingly equipped with intraoperative imaging technologies, such as intraoperative MRI (iMRI) and CT scanners, which provide real-time images during surgery.

Applications and advantages:

- Allow surgeons to assess the extent of tumor resection during the operation
- Help in adjusting surgical plans dynamically based on real-time feedback
- Improve safety by reducing the need for reoperations

In procedures like brain tumor excisions, iMRI ensures that the maximum amount of tumor is removed while preserving healthy brain tissue.

7. The Future of Neurosurgery: What Lies Ahead?

As we look to the future, neurosurgery is expected to become even more precise, personalized, and data-driven. Emerging technologies such as:

- Brain-computer interfaces (BCIs)
- Augmented reality (AR) in surgery
- Neuroprosthetics and bioelectronics

…are pushing the boundaries of what's possible. The convergence of engineering, data science, and biology is set to redefine how neurosurgical care is delivered—making it more targeted, less invasive, and more effective.

Conclusion

The evolution of neurosurgery from traditional open procedures to cutting-edge, minimally invasive, and AI-enhanced interventions marks a monumental transformation in modern medicine. Historically, neurosurgical operations were characterized by large incisions, extensive manipulation of delicate tissues, and a high risk of complications. Today, however, the field stands at the forefront of technological innovation, driven by tools and techniques that are redefining what is surgically possible.

Robotic-assisted systems have introduced a new era of precision and control, allowing surgeons to perform complex procedures through millimeter-scale incisions with unparalleled accuracy. Neuronavigation technologies, often compared to GPS systems for the brain, enable real-time tracking and mapping of critical neurological structures, significantly reducing the risk of damage to vital areas. Artificial intelligence and machine learning algorithms are now being harnessed to support surgical decision-making, analyze preoperative imaging, and predict patient-specific outcomes with increasing accuracy—ushering in the era of personalized neurosurgery.

Meanwhile, advancements in intraoperative imaging, such as MRI and CT scans conducted during surgery, allow for real-time visualization of tumor boundaries and neural tissue, facilitating more complete resections while preserving function. The advent of 3D printing has further expanded the capabilities of pre-surgical planning by producing patient-specific anatomical models, which enhance the understanding of complex cases and improve surgical preparation.

Collectively, these innovations are not merely improving outcomes—they are transforming the patient experience. Procedures that once required weeks of hospitalization and carried significant morbidity can now be completed with less pain, fewer complications, and faster recovery. Most importantly, patients with conditions once deemed inoperable—such as deep-seated brain tumors, severe spinal deformities, or intricate vascular malformations—now have access to treatment options that were unimaginable a generation ago.

As these technologies continue to evolve, neurosurgery is poised to become even safer, smarter, and more efficient. The integration of emerging fields like virtual reality, augmented reality, and tele-neurosurgery holds further promise, especially for education, global collaboration, and expanding access to expert care. Ultimately, the future of neurosurgery is not only about technological sophistication but also about redefining hope and healing for patients worldwide. The ongoing innovation in this field stands as a testament to the power of science and medicine to overcome the most formidable challenges of the human body and mind.

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DETERMINATION OF HUMAN RESOURCES RECRUITMENT CRITERIA IN HEALTH SECTOR: AN APPROACH BASED ON MULTI-CRITERIA DECISION MAKING METHODS AND ARTIFICIAL INTELLIGENCE

ABSTRACT

Objective: Human resources management in the health sector is considered as a strategic element that directly affects service quality. Healthcare services are highly dependent on employee quality due to its human-oriented structure. In this context, recruitment processes in healthcare services are critical for service effectiveness, patient safety and organizational efficiency. The aim of this study is to make an evaluation based on artificial intelligence and fuzzy logic with multi-criteria decision-making methods in order to make recruitment strategies more efficient in healthcare services. At the same time, the secondary objective is to provide a decision support mechanism for human resources specialists in recruitment processes.

Material and Method: In this study, five main criteria (pre-assessment, professional qualification, personal characteristics, management skills and cognitive-social skills) and sub-criteria of these criteria were determined. These criteria were transformed into a questionnaire form within the framework of the Analytic Hierarchy Process (AHP) method and applied to three different stakeholder groups in the field of health management (academicians of the faculty of health sciences, active employees in the sector, health management graduate students). The data obtained will be analysed with Fuzzy AHP (Analytic Hierarchy Process), which is one of the fuzzy multi-criteria decision-making methods used in the solution of real-life problems, and the priorities of the criteria will be calculated.

Findings: As a result of the analysis, the main criteria of management skills, professional equipment and cognitive and social skills have the highest weight. When all sub-criteria were evaluated together with the main criteria, the top three were the sub-criteria of compliance

with working hours belonging to the main criterion of pre-assessment, the sub-criterion of experience belonging to the main criterion of professional equipment and the sub-criterion of crisis management belonging to the main criterion of management skills.

Conclusion: Considering the most important criteria in the recruitment processes of human resources in the health sector, the sector expects its employees to be experienced, to comply with working hours meticulously, and to manage crises well.

Keywords: Health services, Human Resources Management, Recruitment Strategies, Fuzzy Multi-Criteria Decision Making, Fuzzy AHP.

SAĞLIK SEKTÖRÜNDE İNSAN KAYNAKLARI İŞE ALIM KRİTERLERİNİN BELİRLENMESİ: ÇOK KRİTERLİ KARAR VERME YÖNTEMLERİ VE YAPAY ZEKA TABANLI BİR YAKLAŞIM

ÖZET

Amaç: Sağlık sektöründe insan kaynakları yönetimi, hizmet kalitesini doğrudan etkileyen stratejik bir unsur olarak değerlendirilmektedir. Sağlık hizmetleri, insan odaklı yapısı nedeniyle çalışan niteliğine son derece bağımlıdır. Bu bağlamda, sağlık hizmetlerinde işe alım süreçleri hizmetin etkinliği, hasta güvenliği ve kurum verimliliği açısından kritik öneme sahiptir. Bu çalışmanın amacı, sağlık hizmetlerinde işe alım stratejilerini daha verimli hale getirmek amacıyla çok kriterli karar verme yöntemleri ile yapay zekâ ve bulanık mantık temelli bir değerlendirme yapılmasıdır. Aynı zamanda insan kaynakları uzmanlarına işe alım süreçlerinde karar destek mekanizması sunmakta ikincil amaçtır.

Materyal ve Yöntem: Bu çalışmada beş ana kriter (ön değerlendirme, mesleki donanım, kişisel özellik, yönetim becerisi ve bilişsel-sosyal beceri) ve bu kriterlere ait alt kriterler belirlenmiştir. Belirlenen bu kriterler Analitik Hiyerarşi Prosesi (AHP) yöntemi çerçevesinde bir anket formuna dönüştürülerek sağlık yönetimi alanındaki üç farklı paydaş grubuna (sağlık bilimleri fakültesi akademisyenleri, sektörde aktif çalışanlar, sağlık yönetimi yüksek lisans öğrencileri) uygulanmıştır. Elde edilen veriler gerçek hayat problemlerinin çözümünde kullanılan bulanık çok kriterli karar verme yöntemlerinden olan Bulanık AHP (Analitik Hiyerarşi Prosesi) ile analiz edilerek kriterlerin öncelikleri hesaplanacaktır.

Bulgular: Analiz sonucunda yönetim becerisi, mesleki donanım ile bilişsel ve sosyal beceri ana kriterleri en yüksek ağırlığa sahiptir. Ana kriterlerle birlikte tüm alt kriterler değerlendirildiğinde ilk üç ön değerlendirme ana kriterine ait çalışma saatlerine uyum alt kriteri, mesleki donanım ana kriterine ait deneyim alt kriterli ile yönetim becerisi ana kriterine ait kriz yönetimi alt kriteri bulunmuştur.

Sonuç: Sağlık sektöründe insan kaynaklarını işe alım süreçlerinde en önemli kriterler dikkate alındığında sektör çalışanlarının deneyimli, çalışma saatlerine titizlikle uymasını, krizleri iyi yönetebilmesini beklemektedir.

Anahtar Kelimeler: Sağlık hizmetleri, İnsan Kaynakları Yönetimi, İşe Alım Stratejileri, Bulanık Çok Kriterli Karar Verme, Bulanık AHP.

1. GİRİŞ

Teknolojik ilerlemelerle beraber oluşan değişim süreci çalışma hayatının işleyişi de etkisi altına almıştır. Bu dönüşüm, özellikle işletmelerin sürdürülebilirlik sağlamaları ve rekabet avantajı elde etmeleri noktasında çeşitli zorluklar yaratmaktadır. Sürdürülebilir başarı ve rekabet avantajı elde etmenin en önemli unsurlarından biri, örgütlerin sahip olduğu örgütsel insan gücünü nasıl yönettiğine bağlıdır. İnsan kaynağının yürütülüş süreci işletmelerin performansları üzerinde doğrudan etkilidir. Bu yüzden insan gücü faktörünü merkezine alan etkin ve verimli insan kaynakları yönetimine (İKY) sahip olmak işletmeler için kritik rol oynamaktadır. Sadece işe alım, eğitim ve çalışan gelişimi gibi temel süreçleri yönetmekle sınırlı kalmayan insan kaynakları uygulamaları; aynı zamanda çalışanların motivasyonunu artırarak, performanslarını destekleyerek ve kuruma olan bağlılıklarını güçlendirerek, organizasyonun verimliliğine katkı sağlamaktadır[1].

Günümüzde sağlık sektörü, yalnızca teknolojik gelişmelere değil, aynı zamanda insan kaynağının niteliğine de büyük ölçüde bağımlı bir yapı sergilemektedir. Sağlık hizmetlerinin özünde insan odaklı ve emek yoğun bir yapının bulunması, bu alanda çalışan bireylerin bilgi, beceri, yetkinlik ve kişisel özelliklerinin hizmet kalitesi üzerinde belirleyici olmasına neden olmaktadır. Sağlık sektöründe insan kaynakları yönetimi, doğrudan hizmet kalitesini etkileyen stratejik bir faktör olarak görülmektedir. İşe alım süreçleri; hizmetin etkinliği, hasta güvenliğinin sağlanması ve kurumun genel verimliliği açısından hayati bir öneme sahiptir.

Bu çalışma, yoğun süreçlere sahip sağlık hizmetlerinde işe alım kararlarının daha verimli ve etkin bir biçimde yürütülmesini sağlamak amacıyla çok kriterli karar verme (ÇKKV) yöntemleri ile yapay zekâ ve bulanık mantık temelli yaklaşımları bir araya getirerek yenilikçi bir değerlendirme modeli sunmayı amaçlamaktadır. Bu sayede, sağlık sektöründe işe alım süreci daha etkili bir şekilde yönetilerek hizmet kalitesinin artırılması amaçlanmaktadır.

2.GELİŞME

2.1. Sağlık Hizmetlerinde İnsan Kaynakları

Sağlık kurumlarının uzun süreli varlıklarını sürdürebilmeleri için hem kamu hem de özel sektörün kaynaklarını en verimli şekilde yönetmeleri gerekmektedir. Bunun yanı sıra, sağlık hizmetlerinin kalitesine doğrudan etki eden çalışanların teknik bilgi ve bilimsel yetkinliklerinin objektif bir şekilde değerlendirilmesi önemlidir. Bu bağlamda, insan kaynakları yönetimi süreçlerinin etkin bir şekilde uygulanması kritik bir rol üstlenmektedir[2]. İnsan kaynağı seçiminin temel amacı, organizasyon için gereken niteliklere sahip adayların tespit edilmesi ve bu adayların işe yerleştirilmesidir. Farklı seçenekler arasında en uygun adayı belirlemek, titiz bir değerlendirme süreci ve karar verme aşamasını gerektirir[3].

Sağlık kuruluşlarında insan kaynakları planlaması, mevcut ve gelecekteki sağlık hizmetlerinin etkin bir şekilde sunulabilmesi için gerekli olan sağlık personelinin; sayıca yeterli, donanım açısından yetkin, coğrafi olarak dengeli dağılmış, zamanlaması doğru yapılmış ve uygun pozisyonlarda istihdam edilmesini sağlamayı amaçlayan stratejik bir süreçtir. Bu planlama, sağlık hizmetlerinin sürdürülebilirliği açısından kritik öneme sahiptir ve hem toplumun ihtiyaçlarını karşılamaya hem de kurumun verimliliğini artırmaya yönelik bir temel oluşturur[4].

Dünyada olduğu gibi Türkiye'de, kaliteli sağlık hizmetlerine erişmenin temel taşlarından biri olan sağlık personeline yönelik yatırımlar büyük önem taşımaktadır. 2003 yılında uygulamaya konulan Sağlıkta Dönüşüm Programı ile birlikte, 2006 yılından itibaren sağlık çalışanlarının planlamasına sistemli olarak ağırlık verilmiştir. Sağlık insan gücü planlaması, sağlık kurumlarının stratejik hedefleri arasında öncelikli konumda yer almakta; kurumlar, kaynaklarını ve hedeflerini göz önünde bulundurarak etkin bir insan kaynağı planlaması gerçekleştirmeye çaba göstermektedir[5].

Günümüzde, yüksek rekabet ortamında faaliyet gösteren, uzmanlık gerektiren ve karmaşık yapıya sahip sağlık kurumları için nitelikli insan kaynağı temini hem yaşamsal bir önem taşımakta hem de önemli zorluklar oluşturmaktadır. Bu bağlamda, insan kaynakları planlamasının sistematik ve stratejik bir perspektifle ele alınması zorunludur. Etkili bir planlama süreci, kurumun gereksinim duyduğu yetkinliklere sahip personelin tespit edilmesini ve uygun pozisyonlara yerleştirilmesini sağlar. Ayrıca, kurumun mevcut durumunun kapsamlı bir şekilde analiz edilmesi ve geçmiş verilere dayanarak gelecekteki olası değişimlere uyum sağlama stratejilerinin geliştirilmesi, planlama sürecinin başarısı açısından kritik bir rol oynar. Bu yaklaşımla sağlık kurumları hem çalışanların performansını artırabilir hem de sunulan hizmetin kalitesini sürdürülebilir kılabilirler[2].

2.2. Sağlık Hizmetlerinde İşe Alım

İşletmeler açısından stratejik destek işlevleri arasında yer alan en önemli unsurlardan biri insan kaynakları yönetimidir. Bir işletmenin sahip olduğu iş gücünün bilgi, beceri ve yetkinlik düzeyi; benzer yapısal özelliklere ve sektör koşullarına sahip diğer işletmelerle karşılaştırıldığında rekabet avantajı sağlayan ayırt edici bir unsur niteliği taşımaktadır. Bu durum, özellikle insan odaklı faaliyetlerin öne çıktığı hizmet sektöründe çok daha belirgin hale gelmektedir. İnsan kaynağının işletmedeki rolü, faaliyet gösterilen sektöre bağlı olarak farklı biçimlerde değerlendirilmektedir. Örneğin; üretim odaklı işletmeler kalite hedeflerine ulaşabilmek için personelin etkin yönetimine öncelik verirken, hizmet sunumunun merkezde yer aldığı işletmelerde ise nitelikli personel seçimi kritik bir unsur olarak ön plana çıkmaktadır. Özellikle müşteri ile doğrudan etkileşim içinde olan pozisyonlarda görev yapan çalışanların donanımı ve iletişim becerisi, işletmenin başarısı açısından önemli bir rekabet üstünlüğü sağlamaktadır[6].

Bir kurumda çalışanlar tarafından yürütülen tüm görevlerin ayrıntılı olarak incelenmesine iş analizi denir. Bu süreçte, kurum bünyesinde gerçekleştirilen işler hakkında sistematik veri toplama işlemi yapılır, toplanan bilgiler kayıt altına alınır ve analiz edilir. İş analizinin temel amacı belirli bir pozisyona ait görevlerin açık bir şekilde tanımlanması; bu görevlerin etkin biçimde yerine getirilebilmesi için gereken bilgi, beceri, deneyim ve eğitim gibi personel niteliklerinin ortaya konması; ayrıca işin gerçekleştirildiği ortam hakkında bilgi edinilmesidir. İş analizinden elde edilen iş tanımları ve iş gerekleri, insan kaynakları yönetiminin diğer alanları üzerinde doğrudan etkiye sahiptir. İş analizi yapılmadan, hangi pozisyona kaç personel alınacağı, adaylarda aranacak nitelikler, uygulanacak eğitim programları, ücretlendirme politikalarının belirlenmesi, performans değerlendirme yöntemleri ve iş sağlığı ile güvenliği tedbirleri gibi kritik kararların sağlıklı şekilde alınması mümkün değildir. Bu nedenle iş analizi, insan kaynakları yönetimi süreçlerinin temel unsurlarından biri olarak kabul edilmektedir[7].

Kurumların ihtiyaç duydukları iş gücünü temin etme sürecinde başvurabilecekleri yöntemler, temelde kurum içinden ya da kurum dışından sağlanan kaynaklara dayanmaktadır. Kurumlar, mevcut çalışanları arasından uygun adayları değerlendirebilecekleri gibi, dış çevreden de yeni personel arayışına girebilirler. Bu iki yaklaşım, insan kaynağının bulunmasında kullanılan başlıca yöntemleri oluşturmaktadır[8].

Kurumların personel ihtiyaçlarını karşılamak amacıyla başvurdukları iç kaynaklar, genellikle kurum bünyesinde halihazırda görev yapan çalışanlardan oluşmaktadır. Bu kapsamda, mevcut personel içerisinden uygun niteliklere sahip bireylerin seçilerek farklı pozisyonlara atanması yoluyla ihtiyaçlar giderilebilmektedir. Söz konusu uygulamalar kapsamında terfi, görev yeri değişikliği veya pozisyon değişikliği gibi çeşitli personel hareketlilikleri gündeme gelmektedir. Kurum içi personel seçimi için çeşitli yöntemler kullanılır. Bunlardan biri olan gayri-resmî değerlendirme yöntemi, çalışanların gözlemlenerek görev için uygunluğunun tespit edilmesini içerir. Beceri kayıtları yöntemi ise, çalışanların eğitim geçmişleri, iş tecrübeleri, sosyal yetkinlikleri ve önceki performanslarına ilişkin ayrıntılı bilgilerin analiz edilmesine dayanmaktadır. Diğer bir yöntem olan açık pozisyon ilanı ise, kurum içi duyuru panoları veya resmi yazışmalar aracılığıyla çalışanlara başvuru imkânı tanıyarak kurum içinden aday teminini mümkün kılmaktadır[4].

Personel seçim süreci, adayların bireysel özellikleri ile işin gerektirdiği niteliklerin karşılaştırılması esasına dayanır. Bu karşılaştırma neticesinde, pozisyonun gereklilikleri ile en yüksek uyumu gösteren aday tercih edilir. Adayların doğru seçilmesi işletmelerin devamlılığı için hayati önem taşır. Ancak, doğru niteliklere sahip adayın seçimi ve işe yerleştirilmesi karmaşık ve zorlu bir süreçtir. İşletmeler gereksinim duydukları niteliklere sahip adayların belirlenmesi, seçilmesi ve pozisyona uygun şekilde yerleştirilmesi için işe alım aşamaları titizlikle yürütmelidir[6].

Personel işe alım süreci, öncelikle iş başvurularının toplanması ve ön değerlendirme aşamasıyla başlar. Bu ilk adımı, adayların ilgili pozisyonun gerektirdiği niteliklere uygunluğunu belirlemek amacıyla gerçekleştirilen çeşitli değerlendirme araçları ve yeterlilik testleri izler. Söz konusu testlerin ardından, adaylarla yüz yüze mülakatlar gerçekleştirilerek daha derinlemesine bir değerlendirme süreci yürütülür. Mülakatların takiben, başvuru sahiplerinin geçmiş iş deneyimleri ve referansları detaylı şekilde incelenir. Sürecin son aşamasında ise, uygun bulunan adaylara sağlık kontrolleri uygulanarak, görev için en uygun kişi veya kişilerin belirlenmesi sağlanır[9]. Literatürde, adayların yalnızca mesleki yeterliliklerinin değil, aynı zamanda organizasyon kültürüne uyumlarının da dikkate alınması gerektiği vurgulanmaktadır; bu durum, başarılı bir işe alım süreci için son derece kritik bir öneme sahiptir.

2.3. Analitik Hiyerarşi Prosesi (AHP)

İnsanların karşılaştıkları bir sorun için seçtikleri çözüm yolları, genellikle bireysel düşünce ve değerlendirmelerine bağlı olarak farlılık yansıtabilir. Özellikle kişisel görüşlerin karar verme sürecine dâhil edilmesi hem kararın kalitesini hem de alınma şeklini doğrudan şekillendirmektedir. Aynı sorunla ilgili olarak farklı kişiler, değişik kriterlere farklı önem seviyeleri atfedebilir ve seçenekleri farklı şekillerde değerlendirebilirler. Bu tür durumlarda, kararların verimliliğimi artırmak amacıyla sıkça başvurulan yöntemlerden biri Analitik Hiyerarşi Prosesi (AHP) yöntemidir[10].

2.4. Bulanık Analitik Hiyerarşi Prosesi (BAHP)

Karar verme süreçlerinde yaygın olarak kullanılan Analitik Hiyerarşi Prosesi (AHP), kriterler ile seçenekler arasındaki ikili değerlendirmelerde yalnızca belirgin ve sabit sayısal verileri dikkate alması sebebiyle eleştirilere maruz kalmaktadır. Oysa gerçek yaşam problemleri çoğunlukla belirsizlik içeren, netlikten uzak ortamlarda ortaya çıkmakta ve bu durum, karar vericilerin değerlendirmelerinde çoğu zaman kesin sayısal ifadeler yerine öznel yargılara ve dilsel değerlendirmelere başvurmalarına neden olmaktadır. Bu bağlamda, sayısal karşılaştırmaların yetersiz kaldığı, niteliksel ve yoruma dayalı ifadelerin ön plana çıktığı durumlarda bulanık mantık temelli yaklaşımların benimsenmesi gerekir. Bu gereksinim doğrultusunda, belirsizlikleri daha gerçekçi şekilde yansıtan ve karar vericilerin sezgisel değerlendirmelerini sistematik biçimde modele dâhil etmeyi mümkün kılan Bulanık Analitik Hiyerarşi Prosesi (BAHP) geliştirilmiştir[11].

AHP ve Bulanık AHP yöntemleri karşılaştırıldığında, AHP'nin sadece net verilere dayanması sebebiyle belirsizlik durumlarında sınırlı kaldığı anlaşılmaktadır. Buna karşılık, insan karar mekanizmalarında sıkça rastlanan belirsizlikleri ve bulanıklıkları dikkate alma yetisi sayesinde, BAHP'nin daha işlevsel bir yöntem olduğu ortaya çıkmaktadır. Bu doğrultuda, çok kriterli karar verme problemleri ele alınırken klasik AHP'nin aksine bulanıklığı dikkate alan Bulanık AHP metodunun benimsenmesi daha sağlıklı ve isabetli sonuçlar elde edilmesini sağlayacaktır[11].

Bulanık Analitik Hiyerarşi Prosesi (BAHP) yöntemleri, işlem basamakları açısından çeşitlilik göstermektedir ve her bir yöntemin kendine özgü karakteristik yapıları bulunmaktadır. Bu yöntemler arasında, Chang tarafından 1996 yılında geliştirilen BAHP yöntemi, literatürde en yaygın biçimde uygulanan modellerden biri olarak öne çıkmaktadır. Chang'in yaklaşımı, klasik AHP yönteminin temel adımlarını temel almakta ve hesaplama açısından daha az karmaşık olması nedeniyle uygulamada sıklıkla tercih edilmektedir. Karar verme süreçlerinin çoğunlukla belirsizlik içeren durumlar barındırdığı düşünüldüğünde, geleneksel AHP'ye kıyasla Bulanık AHP yönteminin daha tutarlı ve güvenilir sonuçlar sunduğu görülmektedir[12].

BAHP yöntemi ile personel seçim süreci aşamaları şu şekildedir[13].;

1. Aşama: Karar vericilerden oluşan bir ekip oluşturulur.

2. Aşama: Personel seçiminde göz önünde bulundurulacak kriterler ve bu kriterlere bağlı alt kriterler tanımlanarak, hiyerarşik yapıya sahip bir AHP modeli oluşturulur.

3. Aşama: Belirlenen kriter ve alt kriterlerin önem derecelerini belirlemek amacıyla ikili karşılaştırma matrisleri hazırlanır. Bu matrisler üzerinden bulanık geometrik ortalama yöntemiyle, her bir faktör ve alt faktörün bulanık ağırlıkları hesaplanır.

4. Aşama: Elde edilen bulanık ağırlıklar kullanılarak alt kriterlerin genel (global) bulanık ağırlıkları belirlenir. Bu işlem, her alt kriterin kendi bulanık ağırlığı ile bağlı bulunduğu kriterin bulanık ağırlığının çarpılması yoluyla gerçekleştirilir.

5. Aşama: Hesaplanan genel bulanık ağırlıklar kullanılarak aday personeller değerlendirilir. Her bir adayın bulanık öncelik değeri, ilgili alt kriterlerin değerlendirilmesi sonucunda ortaya çıkan bulanık ağırlıkların toplamı alınarak elde edilir.

6. Aşama: Adaylar için hesaplanan bulanık öncelik değerleri durulaştırılır (netleştirilir).

7. Aşama: Durulaştırılmış öncelik değerleri normalize edilir ve her aday için nihai öncelik sıralaması yapılır. En yüksek öncelik değerine sahip aday, terfi ettirilecek kişi olarak seçilir.

2.5. Uygulama

ANA KRİTERLER	ALT KRİTERLER
ÖN DEĞERLENDİRME	Yaş, Çalışma saatlerine uyum, Lokasyona uyum, Referanslar, Ücret beklentisi
MESLEKİ DONANIM	Mesleki eğitim geçmişi, Mesleki bilgi ve uzmanlık, Bilgisayar bilgisi, Deneyim, Görev tanımına hakimiyet
KİŞİSEL ÖZELLİKLER	Fiziksel görünüm, Özgüven, Kendini ifade edebilme, Değişime açıklık, Problem çözme becerisi
YÖNETİM BECERİSİ	Organizasyon ve planlama becerisi, Liderlik, Takım yönetimi, Zaman yönetimi, Kriz yönetimi
BİLİŞSEL VE SOSYAL BECERİLER	Analitik düşünme, Kavrama ve algı yeteneği, Stratejik düşünme, Takım çalışmasına yatkınlık, İletişim becerisi

Paydaş	SAYI
AKADEMİSYEN	3
AKTİF ÇALIŞAN	6
LİSANSÜSTÜ ÖĞRENCİ	8
TOPLAM	17

Bu çalışmanın uygulama aşamasında öncelikle kapsamlı bir literatür taraması gerçekleştirilmiş ve sağlık sektörüne özgü olarak işe alımda dikkate alınması gereken ana ve alt kriterler belirlenip bulunan kriterler zamansal sınırlılıklar sebebi ile kısıtlanmıştır. Bu kriterler Arsu'nun çalışması temel alınarak beş ana başlık altında toplanmış (ön değerlendirme, mesleki donanım, kişisel özellik, yönetim becerisi ve bilişsel-sosyal beceriler) ve her biri alt kriterleriyle birlikte yapılandırılmıştır[14]. Ardından bu kriterler AHP (Analitik Hiyerarşi Süreci) yöntemi çerçevesinde anket formuna dönüştürülerek katılımcılara sunulmuş, ilgili toplam 17 paydaşın (3 akademisyen, 6 sağlıkta aktif çalışan, 8 lisansüstü öğrenci) bu kriterleri puanlamaları istenmiştir. Bu kriterlerin göreli önem düzeyleri Chang'in önerdiği bulanık hiyerarşi prosesi kullanılarak analiz edilmiştir.

2.6. Uygulama Bulguları

ANA KRİTER	ALT KRİTER	Wi
Ön değerlendirme	Çalışma saatlerine uyum	0,086583
Mesleki donanım	Deneyim	0,076143
Yönetim becerisi	Kriz yönetimi	0,065916
Mesleki donanım	Mesleki bilgi ve uzmanlık	0,062969
Yönetim becerisi	Zaman yönetimi	0,062086
Bilişsel ve sosyal beceri	İletişim becerisi	0,060665
Yönetim becerisi	Takım yönetimi	0,060539
Bilişsel ve sosyal beceri	Kavrama ve algı yeteneği	0,060056
Kişisel özellik	Problem Çözme Be	0,05407
Yönetim becerisi	Liderlik	0,053102
Bilişsel ve sosyal beceri	Takım çalışmasına yatkınlık	0,052606
Mesleki donanım	Görev tanımına hakimiyet	0,042456
Bilişsel ve sosyal beceri	Stratejik düşünme	0,038654
Kişisel özellik	Kendini İfade E	0,037316
Kişisel özellik	Değişime Açıklık	0,037234
Mesleki donanım	Bilgisayar bilgisi	0,030504
Ön değerlendirme	Referanslar	0,02785
Mesleki donanım	Mesleki eğitim geçmişi	0,022838
Bilişsel ve sosyal beceri	Analitik düşünme	0,021424
Kişisel özellik	Özgüven	0,017278
Kişisel özellik	Fiziksel görünüm	0,00993
Ön değerlendirme	Lokasyona uyum	0,009083
Yönetim becerisi	Organizasyon ve planlama becerisi	0,005711
Ön değerlendirme	Yaş	0,002825
Ön değerlendirme	Ücret beklentisi	0,002165

ANA KRİTER	Wİ	CR	ALT KRİTER	Lokal Ağırlık	CR	Genel Ağırlık
Ön Değerlendirme	0,128505424	0,01	Yaş	0,021984	0,02	0,002825
			Çalışma saatlerine uyum	0,67377		0,086583
			Lokasyona uyum	0,070679		0,009083
			Referanslar	0,216724		0,02785
			Ücret beklentisi	0,016844		0,002165
Mesleki donanım	0,234909561		Mesleki eğitim geçmişi	0,09722	0,02	0,022838
			Mesleki bilgi ve uzmanlık	0,268057		0,062969
			Bilgisayar bilgisi	0,129853		0,030504
			Deneyim	0,324136		0,076143
			Görev tanımına hakimiyet	0,180734		0,042456
Kişisel özellik	0,1558275		Fiziksel görünüm	0,063722	0,03	0,00993
			Özgüven	0,110876		0,017278
			Kendini İfade E	0,239472		0,037316
			Değişime Açıklık	0,238942		0,037234
			Problem Çözme Be	0,346988		0,05407
Yönetim becerisi	0,24735355		Organizasyon ve planlama becerisi	0,023087	0,008	0,005711
			Liderlik	0,214682		0,053102
			Takım yönetimi	0,244745		0,060539
			Zaman yönetimi	0,251003		0,062086
			Kriz yönetimi	0,266483		0,065916
Bilişsel ve sosyal beceri	0,233403965		Analitik düşünme	0,091789	0,003	0,021424
			Kavrama ve algı yeteneği	0,257303		0,060056
			Stratejik düşünme	0,16561		0,038654
			Takım çalışmasına yatkınlık	0,225386		0,052606
			İletişim becerisi	0,259913		0,060665

Uygulamanın bulgularına göre, kriterlerin ağırlıkları hesaplanarak elde eden tutarlılık oranı 0,01 olarak bulunmuştur. Alt kriterlerin kendi içinde ki değerlendirmeleri tutarlı sonuçlar vermiştir. Lokal ağırlık ve ana kriterin ağırlığı çarpılarak elde edilen genel ağırlık sonucuna göre en üst sırada; ön değerlendirme ana kriterinin çalışma saatine uyum alt kriteri işe alımlarda en önemli kriter olduğu ortaya çıkmıştır. Mesleki donanım ana kriterinin deneyim alt kriteri ikinci sırada, yönetim becerisi ana kriterinin kriz yönetimi alt kriteri de üçüncü sırada yer almaktadır. Ön değerlendirme, mesleki donanım, yönetim becerisi, bilişsel ve sosyal beceriler kriterlerinin homojen olarak dağıldığını görülmüştür. Buna en önemli kanıt ön değerlendirme ana kriterinin en alt ve en üst sırada olmasıdır. Ön değerlendirme ana kriterinin çalışma saatlerine uyum alt kriteri en üst düzeyde iken en altta yaş ve ücret beklentisi olduğu ortaya çıkmıştır.

3. SONUÇ

Sağlık sektörü, hizmet sunumunun doğası gereği, yalnızca fiziksel altyapı ve teknolojik gelişmelere değil, aynı zamanda insan kaynağının kalitesine ve iş gücünün niteliğine yüksek derecede bağımlı bir yapıya sahiptir. Bu çalışmada, işe alım süreçlerinin nesnel, sistematik ve çok boyutlu bir değerlendirme ile yürütülmesine olanak tanıyan yapay zekâ destekli ve bulanık mantık temelli bir yaklaşım önerilmiştir. Özellikle karar alma sürecinde belirsizlik içeren unsurların dikkate alınabilmesini sağlayan Bulanık Analitik Hiyerarşi Prosesi (BAHP) yöntemi, geleneksel yöntemlere kıyasla daha gerçekçi ve güvenilir sonuçlar sunmaktadır.

Analiz sonuçları, sağlık sektöründe işe alım süreçlerinde belirleyici olan unsurların yalnızca teknik yeterliliklerle sınırlı olmadığını ortaya koymuştur. Özellikle "Çalışma saatlerine uyum", "deneyim", "kriz yönetimi", "mesleki bilgi ve uzmanlık" ile "zaman yönetimi" gibi alt kriterlerin yüksek önem düzeyine sahip olması, sağlık çalışanlarının yoğun iş temposuna ve ani gelişen durumlara karşı hazırlıklı olmalarının gerekliliğine işaret etmektedir. İnsan kaynakları uzmanlarının işe alım kararlarında adayların yalnızca eğitim durumuna değil, aynı zamanda adayların işleyişe uygunluğu ve yönetsel becerilerinin de dikkate alınması gerekmektedir.

Ayrıca, bu çalışma adayların bireysel özellikleri ile zihinsel yetkinliklerinin de göz ardı edilmemesi gerektiğini ortaya koymuştur. Sağlık sektörü gibi yüksek stresli ve sürekli değişim gerektiren bir alanda hizmet sunumu yapacak bireylerin duygusal zekâ, etkili iletişim ve takım çalışması gibi becerilerinin güçlü olması hizmet kalitesini doğrudan etkilemektedir. İletişim, liderlik ve zaman yönetimi gibi yetkinliklerin ön planda tutulması, sağlık kuruluşlarının yalnızca teknik donanımı yüksek personel değil, aynı zamanda yönetsel kabiliyetleri gelişmiş ve stratejik düşünme yetisine sahip bireylere olan gereksinimini vurgulamaktadır.

Çalışma kapsamında geliştirilen değerlendirme modeli, insan kaynakları uzmanlarının işe alım sürecinde kişisel önyargılardan arındırılmış, bilimsel temelli karar mekanizmalarını benimsemeleri gerektiğine işaret etmektedir. Yapay zekâ ve bulanık mantık temelli yöntemlerin insan kaynakları yönetiminde kullanımının artırılması, değerlendirme süreçlerinin hem nesnelliğini hem de doğruluğunu önemli ölçüde iyileştirecektir. Ayrıca, bu yaklaşımlar sayesinde işe uygun personelin belirlenme süreci hızlanacak; kurumlar, kriz dönemlerinde daha dayanıklı, değişimlere daha uyum sağlayabilen ve hasta memnuniyetine daha duyarlı çalışan profilleri ile hizmet verme kapasitesine sahip olacaktır.

Sonuç olarak, sağlık sektöründe insan kaynağının niteliği yalnızca bir operasyonel unsur değil, doğrudan kurumun stratejik başarısını belirleyen temel bir faktördür. Bu nedenle, işe alım süreçlerinin bilimsel verilere dayalı, şeffaf ve kurumsal hedeflerle uyumlu şekilde yürütülmesi için süreçlerin çok kriterli ve bilimsel yöntemlerle yapılandırılması, sektörde sürdürülebilir kalite yönetimi açısından vazgeçilmez bir gerekliliktir. Bu çalışma gerek teorik altyapısı gerekse uygulamalı yönü ile sağlık hizmetlerinde insan kaynakları yönetimine yeni bir bakış açısı kazandırmakta ve karar vericilere rehberlik edecek özgün bir model sunmaktadır.

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SUSTAINABLE DEVELOPMENT GOALS AND MIDWIFERY SERVICES

ABSTRACT

The Sustainable Development Goals (SDGs), adopted by the United Nations in 2015, include global goals such as eliminating poverty, reducing inequalities and protecting the environment by 2030. The quality, accessibility and inclusiveness of health services also have an important place among these goals. In this context, midwifery services directly contribute to the third goal of the SDG, "Healthy Individuals". Midwifery is a multidimensional health discipline that is not limited to supporting birth; it also includes pre-pregnancy care, post-natal follow-up, newborn care, reproductive health counseling and family planning services. In this context, midwifery services play a critical role in reducing maternal and infant mortality and contribute to increasing the level of social health. Reports published by the World Health Organization (WHO) and the International Confederation of Midwives (ICM) show that employing a sufficient number of qualified midwives can significantly reduce preventable deaths related to childbirth. Indeed, investments in midwifery services have strategic importance in achieving sustainable development goals in terms of both strengthening health systems and ensuring gender equality. On the other hand, the roles of midwives in the health system in many countries have not been sufficiently defined or supported. This situation makes it difficult for women to access qualified prenatal and postnatal care and deepens health inequalities. In this context, the midwifery profession needs to be strengthened, the professional qualifications of midwives should be increased, continuous education opportunities should be provided and their active participation in decision-making mechanisms should be encouraged for the success of the SDGs. As a result, midwifery services have a central role in achieving sustainable development goals. Supporting midwifery services is an inevitable necessity for the efficiency of health systems, improving maternal and child health indicators and increasing social welfare. In this context, it is important to reshape health policies with a perspective that focuses on midwifery services.

Keywords: Midwifery, midwifery services, sustainable development goals.

SÜRDÜRÜLEBİLİR KALKINMA AMAÇLARI VE EBELİK HİZMETLERİ

ÖZET

Birleşmiş Milletler tarafından 2015 yılında kabul edilen Sürdürülebilir Kalkınma Amaçları (SKA), 2030 yılına kadar yoksulluğun ortadan kaldırılması, eşitsizliklerin azaltılması ve çevrenin korunması gibi küresel hedefleri içermektedir. Bu amaçlar arasında sağlık hizmetlerinin niteliği, ulaşılabilirliği ve kapsayıcılığı da önemli bir yer tutmaktadır. Bu çerçevede, ebelik hizmetleri SKA'nın özellikle 3. amacı olan "Sağlıklı Bireyler" hedefine doğrudan katkı sunmaktadır. Ebelik, yalnızca doğum eylemini desteklemekle sınırlı olmayan; gebelik öncesi bakım, doğum sonrası izlem, yenidoğan bakımı, üreme sağlığı danışmanlığı ve aile planlaması hizmetlerini de içeren çok boyutlu bir sağlık disiplinidir. Bu kapsamda, ebelik hizmetleri anne ve bebek ölümlerinin azaltılmasında kritik bir rol oynamakta, toplumsal sağlık düzeyinin yükseltilmesine katkı sağlamaktadır. Dünya Sağlık Örgütü (DSÖ) ve Uluslararası Ebeler Konfederasyonu (ICM) tarafından yayımlanan raporlar, yeterli sayıda nitelikli ebenin istihdam edilmesinin, doğumla ilişkili önlenebilir ölümlerin büyük ölçüde azaltılabileceğini ortaya koymaktadır. Nitekim, ebelik hizmetlerine yapılan yatırımlar, hem sağlık sistemlerinin güçlendirilmesi hem de cinsiyet eşitliğinin sağlanması açısından sürdürülebilir kalkınma hedeflerine ulaşmada stratejik bir öneme sahiptir. Öte yandan, pek çok ülkede ebelerin sağlık sistemi içindeki rolleri yeterince tanımlanmamış ya da desteklenmemiştir. Bu durum, kadınların nitelikli doğum öncesi ve sonrası bakıma erişimini zorlaştırmakta ve sağlıkta eşitsizlikleri derinleştirmektedir. Bu bağlamda, SKA'ların başarısı için ebelik mesleğinin güçlendirilmesi, ebelerin mesleki yeterliliklerinin artırılması, sürekli eğitim olanaklarının sağlanması ve karar alma mekanizmalarına aktif katılımlarının teşvik edilmesi gerekmektedir. Sonuç olarak, sürdürülebilir kalkınma hedeflerine ulaşmada ebelik hizmetlerinin merkezi bir rolü bulunmaktadır. Sağlık sistemlerinin etkinliği, anne ve çocuk sağlığı göstergelerinin iyileştirilmesi ve toplumsal refahın artırılması için ebelik hizmetlerinin desteklenmesi kaçınılmaz bir gerekliliktir. Bu bağlamda, sağlık politikalarının ebelik hizmetlerini merkeze alan bir perspektifle yeniden şekillendirilmesi önem arz etmektedir.

Anahtar kelimeler: Ebelik, ebelik hizmetleri, sürdürülebilir kalkınma amaçları.

GİRİŞ

Kalkınma, bireylerin, toplumların ve devletlerin sosyoekonomik refah düzeylerinin ilerletilmesini hedefleyen, çok boyutlu ve dinamik bir süreçtir. Türk Dil Kurumu'na göre bu kavram; bir durumun aşamalı olarak iyileştirilmesi, gelişme ve zenginleşme yönünde ilerleme şeklinde tanımlanmaktadır. Ancak kalkınma artık yalnızca ekonomik büyüme göstergeleriyle sınırlı tutulmamakta, çevresel sürdürülebilirlik, ekolojik denge ve toplumsal refah unsurlarını da kapsayan bütüncül bir çerçevede ele alınmaktadır (1,2).

Kalkınma olgusunun nicel büyümenin ötesine taşınarak, niteliksel gelişmeyi de içerecek şekilde yeniden tanımlanması süreci, ilk kez 1972 yılında yayımlanan "The Limits to Growth" (Büyümenin Sınırları) başlıklı rapor ile bilimsel gündeme taşınmıştır. Bu rapor, çevresel kaynakların sınırlılığı, nüfus artışı ve sanayileşmenin olumsuz etkileri bağlamında küresel ekosistemin sürdürülebilirliğine dikkat çekmiş; insanlığın temel ihtiyaçlarını karşılayacak şekilde, ani ve yıkıcı krizlerin önüne geçilmesi gerektiğini vurgulamıştır (3,4). Bu bağlamda sürdürülebilirlik, doğal kaynakların kendini yenileme kapasitesine uygun biçimde yönetilmesini zorunlu kılan bir kavram olarak tanımlanmıştır.

Bu yaklaşımın daha da geliştirilmesi, 1987 yılında Dünya Çevre ve Kalkınma Komisyonu tarafından yayımlanan Brundtland Raporu ile mümkün olmuştur. Raporda sürdürülebilir kalkınma, "mevcut kuşakların gereksinimlerini karşılarken, gelecek nesillerin kendi ihtiyaçlarını karşılama yeteneklerinden ödün vermeyen bir kalkınma biçimi" olarak tanımlanmış ve bu tanım uluslararası düzeyde kabul görmüştür (5).

Sürdürülebilir kalkınma yaklaşımı, çevresel kaynakların yalnızca ekonomik verimlilik amacıyla değil, aynı zamanda ekolojik denge, sosyal adalet ve insan sağlığı açısından da korunması gerekliliğini vurgular. Bu perspektif, 2000 yılında Birleşmiş Milletler tarafından kabul edilen Binyıl Kalkınma Hedefleri (BKH) ile küresel ölçekte daha somut bir politika çerçevesine kavuşmuştur. BKH'lerin devamı niteliğinde olan ve 2015 yılında ilan edilen "2030 Sürdürülebilir Kalkınma Gündemi" kapsamında, 17 ana hedef, 169 alt hedef ve toplam 247 gösterge tanımlanmıştır (6). Bu göstergelerden 215'i Türkiye tarafından hesaplanmakta olup, 20'si doğrudan sağlıkla ilgilidir; sağlıkla bağlantılı göstergeler, tüm kategoriler içinde en geniş alanı kapsamaktadır (7).

Ayrıca sağlık göstergeleri, diğer sürdürülebilir kalkınma hedeflerinin yaklaşık %38'i tarafından etkilenmekte ve %13'ünü doğrudan etkilemektedir. Bu durum, sağlığın sürdürülebilir kalkınma bağlamında merkezi bir konumda yer aldığını ortaya koymaktadır. Sürdürülebilir kalkınmanın sosyal boyutları, özellikle kadınlar, aile yapıları ve toplumsal dinamikler açısından hayati önem taşımaktadır. Bu bağlamda, birinci basamak sağlık hizmetlerinin temel taşı olan ebelik hizmetleri, kadın sağlığı ve toplum sağlığı açısından kritik bir role sahiptir (8,9).

Türkiye'nin sürdürülebilir kalkınma politikalarında sağlıkla ilgili hedefler, kadınların güçlendirilmesi, toplumsal cinsiyet eşitliğinin sağlanması ve genel halk sağlığının iyileştirilmesi yönünde stratejik bir öneme sahiptir. 2023 yılı itibarıyla Türkiye, 156 ülke arasında 72. sırada yer almakta ve OECD ülkeleri arasında yalnızca Kolombiya ve Meksika'nın önünde bulunmaktadır (10).

SÜRDÜRÜLEBİLİR KALKINMA AMAÇLARININ KÜRESEL GÖRÜNÜMÜ

2015 yılında gerçekleştirilen Birleşmiş Milletler Sürdürülebilir Kalkınma Zirvesi'nde kabul edilen 2030 Gündemi, yalnızca gelişmekte olan ülkelere değil, tüm ülkelere yönelik küresel bir sorumluluk çerçevesi sunmuştur. Bu gündem doğrultusunda belirlenen Sürdürülebilir Kalkınma Amaçları (SKA'lar), "hiç kimseyi geride bırakmamak" ilkesi etrafında şekillenmiştir ve evrensel kapsayıcılık ilkesiyle tasarlanmıştır. SKA'lar, yalnızca sağlık ve eğitim gibi temel insan haklarını kapsamakla kalmayıp, ekonomik büyüme, çevre koruma, iklim değişikliği ile mücadele, altyapı gelişimi ve eşitsizliklerin azaltılması gibi birçok kesişen alanı içermektedir. Bu hedefler yasal olarak bağlayıcı olmasa da, tüm devletlerin gönüllü olarak uygulamaya koymaları ve izleme mekanizmaları aracılığıyla ilerlemeyi raporlamaları beklenmektedir (11).

SÜRDÜRÜLEBİLİR KALKINMA HEDEFLERİ BAĞLAMINDA EBELİK HİZMETLERİNİN ROLÜ

Sürdürülebilir Kalkınma Hedefleri (SKH), küresel kalkınma sürecinin 2015-2030 yılları arasındaki 15 yıllık yol haritasını çizen, bütüncül ve insan odaklı bir çerçeve sunmaktadır. Bu hedeflerin temel dayanaklarını; yoksulluk ve açlıkla mücadele, doğal kaynakların sürdürülebilir şekilde yönetilmesi, insan haklarına saygı temelinde sosyal adaletin sağlanması, şiddet ve korkudan arındırılmış bir yaşamın tesis edilmesi ve tüm bu ilkeleri gerçekleştirecek küresel iş birliği ile çok paydaşlı yönetişim anlayışı oluşturmaktadır (12).

2030 yılına kadar gerçekleştirilmesi öngörülen 17 ana hedef ve 169 alt hedefin büyük bölümü, kadınların ekonomik ve sosyal yönden güçlendirilmesi ile doğrudan ilişkilidir. Kadının Statüsü Genel Müdürlüğü (2018) ve SDG (2020) verileri, sürdürülebilir kalkınma süreçlerinde kadınların karar alma mekanizmalarında etkin rol üstlenmelerinin, bireysel hak ve özgürlüklere erişimlerinin ve toplumsal katkılarının artırılmasının, ülkelerin sürdürülebilir kalkınma liginde yer alabilmeleri açısından vazgeçilmez olduğunu ortaya koymaktadır (13,14). Kadının güçlendirilmesi, yalnızca bireysel refahın artırılması anlamına gelmeyip; kadınların yaşamları üzerinde söz sahibi olma, stratejik kararlar alabilme ve sosyal yapının tüm katmanlarında aktif katılım gösterebilme kapasitesine ulaşmalarıdır. Bu süreçte; eğitime erişim, farkındalık düzeyinin yükseltilmesi, toplumsal cinsiyet temelli ayrımcılığın ortadan kaldırılması, özgüvenin pekiştirilmesi, sağlık ve ekonomik kaynaklara ulaşımın kolaylaştırılması kritik unsurlar arasında yer almaktadır (15,16). Sağlık hizmetleri, sürdürülebilir kalkınmanın ekonomik, çevresel ve sosyal boyutlarının kesişme noktasında konumlanmakta; bireyin yaşam kalitesi ile doğrudan ilişkilendirilen bir göstergedir. Bu bağlamda, hem Binyıl Kalkınma Hedefleri'nde (BKH) hem de Sürdürülebilir Kalkınma Hedefleri'nde (SKH), sağlık alanı öncelikli müdahale sahalarından biri olarak tanımlanmıştır. Özellikle "çocuk ölümlerinin azaltılması", "anne sağlığının iyileştirilmesi" ve "bulaşıcı hastalıklarla mücadele" başlıkları, sürdürülebilir kalkınmanın sağlık boyutunun temelini oluşturmaktadır. 2030 hedefleri arasında yer alan "Her yaşta sağlıklı ve kaliteli yaşamı güvence altına almak" ilkesi, doğrudan halk sağlığı politikalarının geliştirilmesini zorunlu kılmaktadır (13).

Bu bağlamda, ebelik hizmetlerinin önemi daha da belirginleşmektedir. Ebeler; yalnızca doğum sürecini yöneten sağlık profesyonelleri değil, aynı zamanda birey ve toplum sağlığını koruyan, özellikle kadınların güçlenmesinde önemli rol oynayan sosyal aktörlerdir. Ebelik uygulamaları, kontraseptif danışmanlık, gebelik takibi, doğum ve lohusalık dönemlerinde

bireye özgü bakım sunumu gibi kapsamlı hizmetlerle, hem kadınların üreme sağlığı hakkını hem de toplumsal sağlık düzeyini doğrudan etkilemektedir. Bu yönüyle ebeler, sürdürülebilir kalkınma hedefleri doğrultusunda birer "değişim ajanı" olarak değerlendirilmelidir (17,18).

EBELİK HİZMETLERİNİN STRATEJİK ROLÜ

Ebelik, sadece klinik hizmet sunumu ile sınırlı kalmayıp; bireylerin, özellikle de kadınların, sağlık okuryazarlığını artıran, üreme sağlığı haklarını koruyan, aile planlamasına katkı sunan çok yönlü bir disiplindir. Kontrasepsiyonel bakım hizmetlerinin, toplumsal cinsiyet eşitliği hedeflerine katkı sunması ve uzun vadede sürdürülebilir toplum yapısına temel oluşturması, ebelerin rolünü yalnızca sağlık alanında değil, sosyal kalkınma ekseninde de stratejik hâle getirmektedir. Bu doğrultuda, ebelik hizmetlerine yapılan yatırım, yalnızca kısa vadeli sağlık çıktıları değil, uzun vadede kuşaklar arası refah artışını da beraberinde getirecektir (19). Ebelik eğitiminin güçlendirilmesi, mesleki özerkliklerinin artırılması, toplumsal farkındalığın yükseltilmesi ve sağlık politikalarında karar verici aktörler olarak tanımlanmaları, sürdürülebilir kalkınma hedeflerinin gerçekleşmesinde önemli bir ivme sağlayacaktır (20).

SONUÇ

Sürdürülebilir Kalkınma Amaçları, kalkınmayı yalnızca ekonomik büyüme olarak değil, insan haklarına saygılı, doğayla uyumlu ve toplumsal eşitliği önceleyen çok boyutlu bir süreç olarak ele almaktadır. Bu hedefler; özellikle kadınların güçlendirilmesi, toplumsal cinsiyet eşitliği ve sağlığa erişimin artırılması açısından büyük önem arz etmektedir. Kadınların güçlendirilmesi, onların sağlık hizmetlerine erişimlerinin artması, eğitim düzeylerinin yükseltilmesi ve sosyal karar alma süreçlerine katılımlarının teşvik edilmesi ile mümkündür (21,15). Bu bağlamda sağlık sistemi içerisinde stratejik öneme sahip olan ebelik hizmetleri, hem bireysel hem de toplumsal sağlık göstergelerinin iyileştirilmesinde temel bir rol üstlenmektedir. Ebelik yalnızca doğum ve doğum öncesi/sonrası bakım hizmeti sunmakla sınırlı kalmayıp, aynı zamanda anne ve yenidoğan sağlığının korunması, üreme sağlığının desteklenmesi ve toplumsal refahın artırılmasına katkı sağlamaktadır (22).

Ebelik hizmetlerinin sürdürülebilir kalkınma hedefleriyle entegrasyonu, yalnızca sağlık göstergelerinde değil, aynı zamanda cinsiyet eşitliği, eğitim ve sosyal katılım alanlarında da ilerleme sağlamaya olanak tanımaktadır. Bu nedenle, ebelerin yetkinliklerinin güçlendirilmesi, hizmet alanlarının genişletilmesi ve sağlık politikaları içerisinde aktif roller üstlenmeleri, sürdürülebilir kalkınma vizyonunun gerçekleştirilmesi adına stratejik bir zorunluluktur (23,24). Sürdürülebilir Kalkınma Hedefleri, dünya çapında yoksullukla mücadele, doğal kaynakların sürdürülebilir yönetimi ve insan haklarına dayalı bir kalkınma anlayışını benimsemektedir. 2030 yılına kadar gerçekleştirilmesi planlanan bu hedeflerin çoğu, özellikle kadınların ekonomik ve sosyal güçlenmesiyle doğrudan ilişkilidir. Kadınların güçlendirilmesi, onların yaşamları üzerinde daha fazla kontrol sahibi olmalarını ve stratejik seçimler yapabilmelerini sağlamaktadır. Bu süreçte, eğitim ve farkındalık artışı, kendine güvenin güçlendirilmesi, kadınların kaynaklara erişimlerinin iyileştirilmesi önemli birer araçtır (25,15). Sağlık, sürdürülebilir kalkınmanın iktisadi, çevresel ve sosyal boyutlarının kesişim noktasında yer alırken, "Sağlıklı ve kaliteli yaşamı güvence altına almak" hedefi, sürdürülebilir kalkınmanın sağlık boyutuna dair temel vurguyu yapmaktadır. Ebelik

hizmetleri, bu hedefin gerçekleştirilmesinde önemli bir rol üstlenmektedir. Ebelik, yalnızca sağlıkla ilgili bir hizmet değil, aynı zamanda toplumsal gelişime katkı sağlayan, gelecekteki nesillerin haklarını koruyan bir mekanizmadır. Dolayısıyla, ebelerin, sürdürülebilir kalkınma hedeflerinin geliştirilmesi ve sürdürülebilirliğinin sağlanmasında etkin bir rol oynaması gerekmektedir (26,27).

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SUSTAINABILITY AND HUMAN RESOURCES MANAGEMENT IN THE CONTEXT OF THE UNITED NATIONS SUSTAINABLE DEVELOPMENT GOALS

ABSTRACT

Objective: Human resources management in the health sector is considered as a strategic element that directly affects service quality. Healthcare services are highly dependent on employee quality due to its human-oriented structure. In this context, recruitment processes in healthcare services are critical for service effectiveness, patient safety and organizational efficiency. The aim of this study is to make an evaluation based on artificial intelligence and fuzzy logic with multi-criteria decision-making methods in order to make recruitment strategies more efficient in healthcare services. At the same time, the secondary objective is to provide a decision support mechanism for human resources specialists in recruitment processes.

Material and Method: In this study, five main criteria (pre-assessment, professional qualification, personal characteristics, management skills and cognitive-social skills) and sub-criteria of these criteria were determined. These criteria were transformed into a questionnaire form within the framework of the Analytic Hierarchy Process (AHP) method and applied to three different stakeholder groups in the field of health management (academicians of the faculty of health sciences, active employees in the sector, health management graduate students). The data obtained will be analysed with Fuzzy AHP (Analytic Hierarchy Process), which is one of the fuzzy multi-criteria decision-making methods used in the solution of real life problems, and the priorities of the criteria will be calculated.

Findings: As a result of the analysis, the main criteria of management skills, professional equipment and cognitive and social skills have the highest weight. When all sub-criteria were evaluated together with the main criteria, the top three were the sub-criteria of compliance with working hours belonging to the main criterion of pre-assessment, the sub-criterion of

experience belonging to the main criterion of professional equipment and the sub-criterion of crisis management belonging to the main criterion of management skills.

Conclusion: Considering the most important criteria in the recruitment processes of human resources in the health sector, the sector expects its employees to be experienced, to comply with working hours meticulously, and to manage crises well.

Keywords: Health services, Human Resources Management, Recruitment Strategies, Fuzzy Multi-Criteria Decision Making.

SÜRDÜRÜLEBİLİRLİK BAĞLAMINDA İNSAN KAYNAKLARI YÖNETİMİ VE BİRLEŞMİŞ MİLLETLER SÜRDÜRÜLEBİLİR KALKINMA AMAÇLARI

ÖZET:

Amaç: Sağlık sektöründe insan kaynakları yönetimi, hizmet kalitesini doğrudan etkileyen stratejik bir unsur olarak değerlendirilmektedir. Sağlık hizmetleri, insan odaklı yapısı nedeniyle çalışan niteliğine son derece bağımlıdır. Bu bağlamda, sağlık hizmetlerinde işe alım süreçleri hizmetin etkinliği, hasta güvenliği ve kurum verimliliği açısından kritik öneme sahiptir. Bu çalışmanın amacı, sağlık hizmetlerinde işe alım stratejilerini daha verimli hale getirmek amacıyla çok kriterli karar verme yöntemleri ile yapay zekâ ve bulanık mantık temelli bir değerlendirme yapılmasıdır. Aynı zamanda insan kaynakları uzmanlarına işe alım süreçlerinde karar destek mekanizması sunmak ta ikincil amaçtır.

Materyal ve Yöntem: Bu çalışmada beş ana kriter (ön değerlendirme, mesleki donanım, kişisel özellik, yönetim becerisi ve bilişsel-sosyal beceri) ve bu kriterlere ait alt kriterler belirlenmiştir. Belirlenen bu kriterler Analitik Hiyerarşi Prosesi (AHP) yöntemi çerçevesinde bir anket formuna dönüştürülerek sağlık yönetimi alanındaki üç farklı paydaş grubuna (sağlık bilimleri fakültesi akademisyenleri, sektörde aktif çalışanlar, sağlık yönetimi yüksek lisans öğrencileri) uygulanmıştır. Elde edilen veriler gerçek hayat problemlerinin çözümünde kullanılan bulanık çok kriterli karar verme yöntemlerinden olan Bulanık AHP (Analitik Hiyerarşi Prosesi) ile analiz edilerek kriterlerin öncelikleri hesaplanacaktır.

Bulgular: Analiz sonucunda yönetim becerisi, mesleki donanım ile bilişsel ve sosyal beceri ana kriterleri en yüksek ağırlığa sahiptir. Ana kriterlerle birlikte tüm alt kriterler değerlendirildiğinde ilk üç te ön değerlendirme ana kriterine ait çalışma saatlerine uyum alt kriteri, mesleki donanım ana kriterine ait deneyim alt kriterli ile yönetim becerisi ana kriterine ait kriz yönetimi alt kriteri bulunmuştur.

Sonuç: Sağlık sektöründe insan kaynaklarını işe alım süreçlerinde en önemli kriterler dikkate alındığında sektör çalışanlarının deneyimli, çalışma saatlerine titizlikle uymasını, krizleri iyi yönetebilmesini beklemektedir.

Anahtar Kelimeler: Sağlık hizmetleri, İnsan Kaynakları Yönetimi, İşe Alım Stratejileri, Bulanık Çok Kriterli Karar Verme.

1. GİRİŞ

Küresel kalkınma sorunlarının artan karmaşıklığı karşısında, sürdürülebilir kalkınma yaklaşımı hem kamu hem özel sektörün sorumluluklarını yeniden tanımlamaktadır. Birleşmiş Milletler tarafından 2015 yılında ilan edilen Sürdürülebilir Kalkınma Amaçları (SKA), yoksullukla mücadeleden sağlıklı yaşam koşullarının sağlanmasına, eğitimden çevresel korumaya kadar geniş bir yelpazede hedefler belirleyerek, dünya genelinde sürdürülebilir bir dönüşüm süreci başlatmıştır. Bu hedeflere ulaşılabilmesi için yalnızca devlet politikalarının değil, işletmelerin kurumsal yapılarının da insan odaklı ve sürdürülebilirlik eksenli hale gelmesi gerekmektedir.

Bu noktada, kurumsal işleyişin temel unsurlarından biri olan insan kaynakları yönetimi (İKY), sürdürülebilir kalkınma hedeflerinin gerçekleştirilmesinde kilit bir rol üstlenmektedir.

Bu çalışma, insan kaynakları yönetimi ilkeleri ile SKA'lar arasındaki bütüncül ilişkiyi irdelemekte; özellikle "Yoksulluğa Son" (SKA 1), "Açlığa Son" (SKA 2), "Sağlık ve Kaliteli Yaşam" (SKA 3) ve "Nitelikli Eğitim" (SKA 4) başlıkları çerçevesinde, kurumların sosyal sorumluluklarını nasıl yerine getirebileceklerine ışık tutmaktadır. İKY'nin temel ilkeleri olan verimlilik, insancıl davranış, eşitlik, güvence, açıklık ve halef yetiştirme, sadece çalışan refahını artırmakla kalmamakta, aynı zamanda daha adil ve kapsayıcı bir toplumun inşasına katkıda bulunmaktadır. Bu bağlamda, çalışma hem kurumsal başarı hem de toplumsal gelişim açısından insan kaynakları politikalarının stratejik önemini vurgulamakta; işletmelerin ekonomik kârın ötesinde sosyal ve çevresel sorumluluk bilinciyle hareket etmesinin gerekliliğini ortaya koymaktadır.

2. GELİŞME (İNSAN KAYNAKLARI YÖNETİMİ ve SKA)

2.1.İNSAN KAYNAKLARI YÖNETİMİ VE İLKELERİ

İnsan kaynakları yönetimi (İKY), çalışanların işe alımından performans değerlendirmesine, eğitimden kariyer planlamasına kadar birçok süreci kapsayan stratejik bir yönetim alanıdır (Dessler, 2020). Modern örgütlerde insan kaynağı yalnızca üretim faktörü değil, aynı zamanda rekabet avantajı sağlayan temel bir unsurdur.

İKY'nin temel ilkeleri arasında liyakat, eşitlik, şeffaflık ve çalışan memnuniyeti yer alır. Bu ilkeler, örgütsel verimliliği artırmakla kalmaz, aynı zamanda sürdürülebilir başarıyı destekler (Tüzüner, 2022). Dijitalleşme ve küreselleşme gibi gelişmeler, İKY'yi operasyonel bir işlev olmaktan çıkarıp stratejik bir role dönüştürmüştür (Armstrong & Taylor, 2023).

Sonuç olarak, insan kaynakları yönetimi ilkeleri, sadece personel yönetimini değil, aynı zamanda örgüt kültürünü ve uzun vadeli başarıyı şekillendiren temel bir çerçeve sunar.

İKY'nin temel ilkeleri şunlardır:

2.1.1. Verimlilik İlkesi

Verimlilik ilkesi, örgütlerde çalışanların üretkenliğini ve çıktısını maksimize etmek amacıyla iş süreçlerinin rasyonel ve etkili biçimde düzenlenmesini ifade eder. Armstrong (2020), insan kaynakları yönetiminin temel hedeflerinden birinin çalışanlardan alınan çıktıyı artırmak olduğunu, bunun da ancak iyi yapılandırılmış sistemler, açık performans ölçütleri ve sürekli

gelişimle sağlanabileceğini vurgulamaktadır. Bu bağlamda, verimlilik sadece niceliksel üretim artışı değil, aynı zamanda kalite, maliyet ve zaman boyutlarının da iyileştirilmesini kapsar (Eren, 2017).

2.1.2. İnsancıl Davranış İlkesi

İnsancıl yaklaşım, çalışanların sadece üretim aracı olarak değil, duygusal, sosyal ve psikolojik ihtiyaçları olan bireyler olarak değerlendirilmesini gerektirir. Maslow'un ihtiyaçlar hiyerarşisi kuramından hareketle, bireyin kendini gerçekleştirmesi için güvenli ve destekleyici bir iş ortamına gereksinim duyduğu görülmektedir (Dessler, 2020). Ulrich ve arkadaşları (2008), modern insan kaynakları yönetiminin başarısını, çalışanlara saygı gösterme, empati kurma ve psikolojik güvenlik sağlamaya dayandırmaktadır.

2.1.3. Eşitlik İlkesi

Eşitlik ilkesi, çalışanlar arasında ayrımcılığa yer vermeyen, liyakate dayalı ve adil uygulamaları esas alır. Bu çerçevede işe alım, ücretlendirme, kariyer gelişimi gibi süreçlerde fırsat eşitliği sağlanması ön plandadır. TİSK'in (2022) yayımladığı ilkeler belgesinde belirtildiği gibi, toplumsal cinsiyet eşitliği ve engellilik gibi farklılıklar gözetilerek, dezavantajlı gruplara pozitif destekler sağlanması kurumsal sorumluluğun bir parçasıdır.

2.1.4. Güvence İlkesi

İş güvencesi ve sosyal güvenlik, çalışanların örgütle kurdukları ilişkinin sürdürülebilirliği açısından kritik öneme sahiptir. Armstrong (2020), çalışan bağlılığının en güçlü belirleyicilerinden birinin "örgütsel güven" olduğunu ifade etmektedir. Bu güven, kariyer yollarının açık olması, işten çıkarılma risklerinin düşük olması ve kurumun çalışanına yatırım yapması ile inşa edilir. Güvence ilkesi, aynı zamanda çalışanların motivasyonunu artırarak iş performansını dolaylı biçimde olumlu etkiler (Dessler, 2020).

2.1.5. Açıklık (Şeffaflık) İlkesi

Şeffaflık ilkesi, karar alma mekanizmalarının ve uygulamaların tüm paydaşlara açık, anlaşılır ve izlenebilir olmasını ifade eder. TİSK (2022), açıklık ilkesini "hesap verebilirlik, katılım ve kurumsal güven inşasının temeli" olarak tanımlar. Açık performans değerlendirme sistemleri, net görev tanımları ve çalışanlara düzenli geribildirim sağlanması, şeffaflık ilkesinin somut örneklerindendir.

2.1.6. Halef Yetiştirme İlkesi

Kurumsal süreklilik ve liderlik başarısı, halef yetiştirme süreçlerinin niteliğiyle doğrudan ilişkilidir. Ulrich ve arkadaşları (2008), stratejik insan kaynakları planlamasının temel bileşenlerinden birinin "geleceğin liderlerini bugünden yetiştirmek" olduğunu belirtmektedir. Etkin bir halefiyet planlaması, sadece ani pozisyon değişimlerinde kriz yönetimi sağlamakla kalmaz, aynı zamanda kurumsal belleğin korunmasına da katkı sağlar.

2.2.SÜRDÜRÜLEBİLİR KALKINMA AMAÇLARI

Sürdürülebilir Kalkınma Amaçları, 2015 yılında Birleşmiş Milletler tarafından belirlenen ve 2030 yılına kadar ulaşılması hedeflenen **17 evrensel amaçtan oluşan** bir yol haritasıdır. Amaç, yoksulluğu sona erdirmek, gezegeni korumak ve herkes için barış ve refahı sağlamaktır.

Bu amaçlar arasında **eğitim, sağlık, cinsiyet eşitliği, temiz enerji, ekonomik büyüme, iklim eylemi** gibi konular yer alır. Tüm ülkeler için geçerli olan bu hedefler, sosyal, ekonomik ve çevresel sürdürülebilirliği birlikte gözetir.

Kısacası, SKA'lar dünyayı daha adil, yaşanabilir ve sürdürülebilir hale getirmeyi amaçlayan küresel bir eylem planıdır. İlk 4 amaç aşağıdaki gibidir;

2.2.1. Yoksulluğa Son

Yoksulluğun her biçimini ve her yerde tamamen ortadan kaldırmak hedefleniyor. Bu kapsamda:

- Aşırı yoksulluğun 2030'a kadar sona erdirilmesi,
- Yoksulluk oranlarının yarı yarıya azaltılması,
- Sosyal koruma sistemlerinin yaygınlaştırılması,
- Yoksulların ekonomik kaynaklara ve hizmetlere eşit erişiminin sağlanması,
- Afetler ve krizlere karşı dayanıklılığın artırılması amaçlanıyor.

2.2.2. Açlığa Son

Gıda güvenliğini sağlamak, iyi beslenmeyi desteklemek ve sürdürülebilir tarımı yaygınlaştırmak temel odaktır. Alt başlıklar arasında:

- Açlığın tamamen sona erdirilmesi,
- Yetersiz beslenmenin tüm biçimlerinin ortadan kaldırılması,
- Küçük üreticilerin gelirlerinin artırılması ve kaynaklara eşit erişiminin sağlanması,
- Dayanıklı ve doğa dostu tarım uygulamalarının teşviki bulunur.

2.2.3. Sağlık ve Kaliteli Yaşam

Herkes için sağlıklı bir yaşam ve refah hedefleniyor:

- Anne ve çocuk ölümlerinin azaltılması,
- Bulaşıcı ve bulaşıcı olmayan hastalıkların önlenmesi,
- Uyuşturucu ve alkol bağımlılığıyla mücadele,
- Evrensel sağlık hizmetlerine erişimin sağlanması gibi maddeleri içerir.

2.2.4. Nitelikli Eğitim

Herkes için kapsayıcı, adil ve kaliteli eğitimi güvence altına almak:

- Ücretsiz ve eşit temel eğitime erişimin sağlanması,
- Okul terk oranlarının azaltılması,
- Mesleki ve teknik eğitimin yaygınlaştırılması,
- Eğitimde cinsiyet eşitliğinin sağlanması,
- Dijital okuryazarlık gibi becerilerin geliştirilmesi hedefleniyor.

	Verimlilik İlkesi	İnsancıl Davranış İlkesi	Eşitlik İlkesi	Güvence İlkesi	Açıklık İlkesi	Halef Yetiştirme İlkesi
1. Yoksulluğa Son: Yoksulluğun tüm biçimlerini her yerde sona erdirmek	Verimlilik ilkesi; bireylerin eğitim, sağlık, istihdam, toprak ve mülk edinimi gibi temel hizmetlere ve ekonomik kaynaklara eşit erişimini sağlayarak, özellikle yoksul ve kırılgan grupların üretkenliğini artırmayı, çok boyutlu yoksulluğun azaltılmasını, afetlere karşı dayanıklılığın güçlendirilmesini ve gelişmekte olan ülkelerde kalkınma iş birlikleriyle kaynakların etkin kullanılmasını güvence altına alarak sürdürülebilir kalkınma hedeflerine doğrudan katkı sunar.	Aşırı yoksulluğun ortadan kaldırılması, bireylerin temel ihtiyaçlarını karşılayabilmesini sağlayarak, eşitlikçi ve adaletli bir yaklaşımı destekler; bu süreç, sosyal koruma sistemlerinin güçlendirilmesi ve kırılgan gruplara eşit haklar sağlanarak toplumsal dayanışmayı artırır, insan onuru, toplumsal güvenlik ve sürdürülebilir kalkınma hedeflerine ulaşılmasına katkıda bulunur.	Yoksulluğun tüm biçimlerinin ortadan kaldırılması, eşitlik ve sosyal adalet temelinde yapılandırılmış politikalarla, kırılgan grupların güçlendirilmesi ve kaynaklara adil erişim sağlanarak sürdürülebilir kalkınmanın gerçekleştirilmesini amaçlar.	Aşırı yoksulluğun ortadan kaldırılması, herkesin eşit fırsatlarla temel hizmetlere, ekonomik kaynaklara ve haklara erişimini güvence altına alarak sosyal adaletin sağlanmasını ve kırılgan grupların güçlendirilmesini amaçlar.	Açıklık ilkesi, kurumların ücretlendirme, sosyal yardımlar, fırsat eşitliği ve kriz yönetimi gibi alanlarda şeffaflık sağlayarak çalışanların güvenliğini ve adil katılımını güçlendirir; böylece sosyal koruma sistemlerine olan güveni artırır, gelir adaletsizliğini azaltır ve yoksulluğun tüm biçimlerini sona erdirmeye yönelik politikaların etkin biçimde uygulanmasını mümkün kılar.	Yoksulluğun tüm biçimlerini sona erdirmeyi amaçlayan kurumlar, halef yetiştirme ilkesiyle dezavantajlı bireylerin liderlik pozisyonlarına erişimini destekleyerek gelir eşitsizliğini azaltır, sosyal koruma politikalarının devamlılığını sağlar ve sürdürülebilir kalkınmaya duyarlı, stratejik düşünebilen liderler aracılığıyla kapsayıcı ve dirençli kurumsal yapılar inşa eder
2. Açlığa Son: Açlığı bitirmek, gıda güvenliğine ve iyi beslenmeye ulaşmak ve sürdürülebilir tarımı desteklemek	2030 yılına kadar açlığın sona erdirilmesi ve herkesin yeterli, besleyici gıdaya erişiminin sağlanması, bireylerin fiziksel ve zihinsel gelişimlerini destekleyerek üretkenliklerini artırır; özellikle küçük ölçekli gıda üreticilerinin toprağa, suya, teknolojiye ve finansal hizmetlere eşit erişiminin sağlanması, tarımsal verimliliği artırarak kaynakların etkin kullanımını ve çevresel sürdürülebilirliği destekler.	Güvenli ve yeterli besine erişim, sağlıklı yaşamı güvence altıyarak toplumsal eşitlik ve insancıl değerleri savunur; küçük üreticilerin desteklenmesi ve sürdürülebilir tarım uygulamaları, adil kalkınma ve insan haklarına saygıyı teşvik eder.	Gıda güvenliği ve beslenme politikaları, toplumsal eşitlik ve sürdürülebilir kalkınma ilkeleri doğrultusunda, özellikle kırılgan grupların güvenli ve besleyici gıdaya eşit erişimini, küçük üreticilerin güçlendirilmesini ve tarımda adil, kapsayıcı bir dönüşümün sağlanmasını amaçlayan bütüncül bir yaklaşımla tasarlanmalıdır.	Yoksulluğa karşı güçlü kalkınma stratejileri, toplumsal cinsiyet eşitliği ve kırılgan grupların dayanıklılığını artırarak, küçük çiftçilerin ve yerli halkların eşit erişimini sağlayan, sürdürülebilir gıda üretim sistemlerini güçlendirir.	Açıklık ilkesi, kurumların yemek politikalarından hassas gruplara yönelik desteklere, eğitim ve kaynak paylaşımından sürdürülebilir tarım ve tedarik zinciri uygulamalarına kadar tüm süreçleri şeffaf biçimde yönetmesini sağlayarak gıda güvenliğini artırır, adil beslenme olanakları sunar ve açlığın her biçiminin sona erdirilmesine kurumsal düzeyde katkı sunar.	Halef yetiştirme ilkesi doğrultusunda sağlık, çevre, adil ticaret ve sürdürülebilir tarım vizyonuna sahip liderlerin yetiştirilmesi; gıda tedarik zincirlerinin adil ve dayanıklı biçimde yönetilmesini, çalışanların beslenme ve sağlık ihtiyaçlarına duyarlı politikalar geliştirilmesini ve kırsal kalkınmayı destekleyerek açlığın sona erdirilmesine kurumsal katkı sağlar.
Sağlık ve Kaliteli Yaşam: Sağlıklı ve kaliteli yaşamı her yaşta güvence altına almak	Sağlık hizmetlerine erişimin artırılması, bulaşıcı ve bulaşıcı olmayan hastalıkların önlenmesi, çevresel faktörlerin kontrolü, trafik güvenliği önlemleri ve bağımlılıkla mücadele gibi stratejiler, bireylerin fiziksel ve zihinsel sağlıklarını iyileştirerek iş gücü verimliliğini artırır ve sürdürülebilir kalkınmayı destekler.	Bireylerin temel haklarına, eşitliğe ve adil muameleye dayalı bir yaklaşım, sağlık hizmetlerine eşit erişimi garanti altına alarak, toplumsal eşitlik, insan onuru ve refahı savunur, bulaşıcı ve bulaşıcı olmayan hastalıklarla mücadele, bağımlılıkların önlenmesi ve sağlık güvencesinin sağlanması gibi insancıl değerlerle uyumlu bir şekilde toplumsal dayanışmayı güçlendirir.	Sürdürülebilir kalkınma hedefleri kapsamında sağlık politikaları, herkesin eşit, erişilebilir ve kaliteli sağlık hizmetlerinden yararlanmasını sağlayarak toplumsal refahı ve yaşam hakkını güvence altına almayı amaçlamaktadır.	Tüm bireylerin, cinsiyet, yaş veya sosyoekonomik durumdan bağımsız olarak, kaliteli sağlık hizmetlerine güvenli ve eşit erişimini sağlayarak, üreme sağlığı hizmetlerine ve eğitimine evrensel erişim temin eder, çevresel faktörlerin yol açtığı hastalıkları önler ve sağlık krizlerine karşı toplulukları daha dirençli hale getirir.	Açıklık ilkesi doğrultusunda sağlık izinlerinden aşı politikalarına, ruh sağlığı hizmetlerinden iş güvenliği uygulamalarına kadar tüm kurumsal sağlık politikalarının şeffaf biçimde duyurulması; çalışanların fiziksel ve ruhsal sağlıklarını korur, toplumsal bulaşları önler, kadın ve çocuk sağlığını destekler ve her yaşta sağlıklı ve kaliteli yaşamı güvence altına alır.	Halef yetiştirme ilkesi doğrultusunda toplumsal cinsiyet eşitliği, kriz yönetimi, ruhsal ve fiziksel sağlık, bağımlılıkla mücadele, iş güvenliği, adil sağlık erişimi ve sürdürülebilir sağlık politikaları konusunda donanımlı liderlerin yetiştirilmesi, her yaşta sağlıklı ve kaliteli yaşamı kurumsal düzeyde güvence altına alır.
Nitelikli Eğitim: Kapsayıcı ve hakkaniyete dayanan nitelikli eğitimi sağlamak ve herkes için yaşam boyu öğrenim fırsatlarını teşvik etmek	Eğitime yapılan yatırımlar; erken çocukluk döneminden yükseköğretime kadar her aşamada bireylerin bilgi, beceri ve yetkinliklerini artırarak nitelikli ve üretken iş gücü oluşturur, öğretmen eğitimi ve mesleki gelişimle öğrenme çıktılarının kalitesini artırır, böylece kurumsal verimlilikten ekonomik büyümeye, istihdamdan sürdürülebilir kalkınma hedeflerine kadar çok boyutlu stratejik kazanımlar sağlar.	Ücretsiz ve hakkaniyetli eğitim hakkı, her bireyin potansiyelini gerçekleştirmesine olanak tanırken, toplumsal cinsiyet eşitliği, insan hakları, fırsat eşitliği ve insancıl değerler temelinde, özellikle kırılgan gruplara yönelik eşit fırsatlar sunarak daha adil, kapsayıcı ve sürdürülebilir bir toplum yapısı oluşturmayı amaçlar.	Eğitimde eşitlik ilkesi, tüm bireylerin sosyoekonomik durumdan bağımsız olarak kapsayıcı, nitelikli ve erişilebilir öğrenme fırsatlarına ulaşmasını hedefleyerek, bireysel potansiyelin gelişimini, toplumsal adaleti ve sürdürülebilir kalkınmayı destekleyen bütüncül bir yaklaşımı ifade eder.	Her bireyin, cinsiyet, sosyoekonomik durum, engel durumu veya sosyal kimliği ne olursa olsun eğitim hakkına eşit erişimini güvence altına alarak, fırsat eşitliği sağlar, toplumsal cinsiyet eşitliğini destekler ve sürdürülebilir kalkınma için daha kapsayıcı bir toplum inşa eder.	Açıklık ilkesi doğrultusunda eğitim haklarının, gelişim planlarının, burs ve destek programlarının şeffaf biçimde sunulması; ayrımcılık karşıtı politikaların açıkça ilan edilmesi ve kapsayıcı öğrenme ortamlarının desteklenmesi, herkes için yaşam boyu öğrenim fırsatlarını teşvik eden hakkaniyetli ve nitelikli bir eğitim kültürü oluşturur.	Eğitim odaklı, eşitliği önceleyen, sürekli öğrenmeyi teşvik eden ve bilgi paylaşımına açık haleflerin yetiştirilmesi; kurum içinde kapsayıcı, hakkaniyetli ve yaşam boyu öğrenimi destekleyen nitelikli eğitim kültürünün yerleşmesini sağlar.

Bu çalışmanın uygulama aşamasında, insan kaynakları yönetimi ilkeleri ile sürdürülebilir kalkınma amaçları arasında kurulan ilişkiler, görsel bir tablo aracılığıyla sistematik olarak değerlendirilmiştir. Hazırlanan tabloda, yatay eksende İKY'nin temel ilkeleri; düşey

eksende ise Birleşmiş Milletler tarafından belirlenen 17 sürdürülebilir kalkınma amacından ilk dört tanesi yer almaktadır.

Her bir hücre, ilgili İKY ilkesi ile SKA hedefi arasındaki olası ilişkiyi, ortak paydada buluşan değer ve uygulamalar üzerinden analiz etmektedir. Bu yapı, sadece teorik değil aynı zamanda uygulamaya dönük bir perspektifle insan kaynakları süreçlerinin sürdürülebilirlik hedeflerine nasıl entegre edilebileceğini ortaya koymaktadır.

Örneğin, **E3 hücresinde**, *güvence* ilkesi ile SKA 3 olan *Sağlık ve Kaliteli Yaşam* hedefi ilişkilendirilmiştir. Bu hedef, tüm bireylerin cinsiyet, yaş ya da sosyoekonomik durumdan bağımsız olarak sağlık hizmetlerine eşit ve güvenli erişimini sağlamayı; üreme sağlığı hizmetleri ve eğitiminin evrensel düzeyde erişilebilir olmasını; çevresel faktörlerin yol açtığı hastalıkların önlenmesini ve sağlık krizlerine karşı dayanıklı toplumların oluşturulmasını amaçlamaktadır. Bu bağlamda, çalışanların sağlık güvencelerinin sağlanması ve iş yerinde sağlık destek sistemlerinin kurulması gibi İKY uygulamaları, doğrudan bu hedefe hizmet etmektedir.

Başka bir örnekte, *halef yetiştirme* ilkesi ile SKA 4 olan *Nitelikli Eğitim* hedefi eşleştirilmiştir. Kurum içerisinde bilgi aktarımı, mentorluk, kariyer planlaması ve sürekli öğrenmeye teşvik gibi uygulamalar, nitelikli eğitimi destekleyen ve sürdürülebilir kurum kültürünün gelişimini sağlayan temel unsurlar arasında yer almaktadır.

Hazırlanan bu tablo, insan kaynakları yönetimi ile sürdürülebilir kalkınma amaçları arasındaki stratejik ilişkinin hem teorik düzeyde hem de uygulamada ne şekilde şekillenebileceğini açık bir şekilde ortaya koymaktadır. İlgili eşleştirmeler, kurumlara sadece kendi çalışan politikalarını sürdürülebilirlik çerçevesinde yeniden yapılandırmaları için yol göstermekle kalmaz, aynı zamanda toplumsal kalkınmaya katkı sağlama potansiyelini de artırır.

3. SONUÇ

Sürdürülebilir kalkınma, küresel ölçekte karşı karşıya olduğumuz çevresel, sosyal ve ekonomik sorunlara bütüncül çözümler sunmayı amaçlayan bir yaklaşım olarak hem kamu hem de özel sektör için temel bir stratejik öncelik hâline gelmiştir. Bu süreçte insan kaynakları yönetimi (İKY), sadece bir operasyonel işlev olmaktan çıkmış, kurumların sürdürülebilirlik hedeflerine ulaşmasında kritik bir rol üstlenen stratejik bir yapı taşına dönüşmüştür.

Mevcut literatürde sürdürülebilir kalkınma amaçları (SKA) ile insan kaynakları yönetimi ilkeleri arasında bazı bağlantılar kurulmaya çalışılmış, bu iki alanın ilişkisi çeşitli yönleriyle ele alınmıştır. Ancak yapılan incelemelerde, SKA'ların alt hedefleri ile İKY ilkelerini doğrudan ve sistematik biçimde eşleştiren kapsamlı akademik çalışmalara henüz rastlanmamıştır. Bu durum, hem teorik bilgi birikiminde bir boşluk olduğunu hem de uygulamaya yönelik somut rehberlerin eksikliğini göstermektedir.

Bu doğrultuda hazırlanan çalışmamızda, literatürdeki bu eksikliği gidermek ve sürdürülebilir kalkınma ile insan kaynakları yönetimi arasında daha somut bağlar kurmak amacıyla, SKA alt hedefleri ile İKY ilkeleri arasında doğrudan eşleştirmeler yapılmıştır. Her bir SKA hedefinin kendi iç dinamikleri dikkate alınarak, insan kaynakları yönetiminin temel ilkeleriyle nasıl örtüştüğü detaylı biçimde analiz edilmiştir. Bu eşleştirmeler, sadece teorik

bir katkı sunmakla kalmamış, aynı zamanda uygulayıcılar için pratik bir yol haritası işlevi de görmeyi hedeflemiştir.

Gelecek çalışmalarımızda, tüm 17 sürdürülebilir kalkınma amacı ve bunların alt hedefleri ile insan kaynakları yönetiminin tüm temel ilkeleri arasındaki ilişkiyi daha kapsamlı biçimde ele almayı planlamaktayız. Bu tür bir haritalandırmanın, kurumların kendi insan kaynakları politikalarını sürdürülebilirlik ekseninde yeniden şekillendirmelerine katkı sağlayacağına inanıyoruz. Ayrıca bu yaklaşım, hem çalışan memnuniyeti ve bağlılığını artıracak, hem de sosyal sorumluluk, eşitlik, kapsayıcılık ve çevresel duyarlılık gibi alanlarda kurumsal performansın iyileşmesine destek olacaktır.

Sonuç olarak, sürdürülebilir kalkınma ile insan kaynakları yönetimi arasındaki bu bütüncül ilişki, gelecekteki akademik çalışmalar açısından önemli bir araştırma alanı sunmaktadır. Bu çalışmanın, söz konusu iki disiplin arasında köprü kurmaya yönelik girişimlere ilham vereceğini ve sürdürülebilirlik odaklı insan kaynakları politikalarının gelişimine katkı sağlayacağını umuyoruz.

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ANTIFUNGAL EFFECT of CELL-FREE SUPERNATANTS of *Lactobacillus delbrueckii* subsp. *bulgaricus* on *CANDIDA* spp.

ABSTRACT

Introduction: Today, it is known that not only the live forms of probiotics but also the metabolites they secrete have important effects on host health. Cell-free supernatants containing these metabolites attract attention with their antimicrobial effects. In recent years, studies have shown that these antimicrobial effects observed on bacterial pathogens may also be valid against *Candida* species, which are opportunistic fungal pathogens.

Objective: The aim of this study was to evaluate the antifungal effects of live and inactivated cell-free supernatants (CFS) from *Lactobacillus delbrueckii subsp. bulgaricus* (*L.bulgaricus*) on *Candida albicans* (*C. albicans*) ATCC 10231 and *Candida parapsilosis* (*C. parapsilosis*) ATCC 22019 strains.

Methods: In this study, antifungal susceptibility of *C. albicans* and *C. parapsilosis* was evaluated according to the CLSI M27-A3 microdilution method (CLSI, 2008). Live and inactivated CFS samples were tested against yeast suspension ($1.5x10^3$ CFU/mL) after dilution between 0.39-100%. Microplates were incubated at 35°C for 24 hours and growth inhibition was visually assessed. Minimum inhibitory concentration (MIC) and minimum fungicidal killing concentration (MFK) were determined. For MIC, samples at MIC and higher concentrations were plated on Sabouraud Dextrose Agar (SDA) plates and incubated at 35°C for 48 hours. Fluconazole (FLC) and voriconazole (VOR) were used as reference antifungals.

Results: In the results of this study, the MIC and MFC values of LBL supernatant were found to be 25% for both *C. albicans* strains, while the MIC and MFC values of LBI supernatant were found to be 6.25% for both *C. parapsilosis* strains. In *C. parapsilosis* strain, MIC and MFC values of both LBL and LBI supernatants were determined as 50% for both. For *C. albicans* strain, fluconazole (FLC) MIC value was 4 µg/mL and MFC value was 8 µg/mL; for *C. parapsilosis* strain, voriconazole (VOR) MIC value was 0.0625 µg/mL and MFC value was 0.125 µg/mL.

Conclusion: The results of the study show that *L. bulgaricus* CFSs show antifungal activity against *Candida* species and especially LBIs may be effective at lower concentrations. In tests on *C. albicans* and *C. parapsilosis* strains, it was observed that inactivated CFSs were more effective than LBL, especially on *C. albicans*. These findings suggest that the method of preparation of supernatants may play a decisive role in biological activity.

Keywords: *Lactobacillus delbrueckii* subsp. *bulgaricus*, Probiotics, Cell-free supernatant, Antifungal, *Candida*.

Lactobacillus delbrueckii subsp. *bulgaricus* HÜCRESİZ SÜPERNATANTLARININ *CANDİDA* spp.'ler ÜZERİNE ANTİFUNGAL ETKİSİ

ÖZET

Giriş: Günümüzde probiyotiklerin yalnızca canlı formları değil, salgıladıkları metabolitlerin de konak sağlığı üzerinde önemli etkiler gösterdiği bilinmektedir. Bu metabolitleri içeren hücresiz süpernatantlar, antimikrobiyal etkileriyle dikkat çekmektedir. Son yıllarda, bakteriyel patojenler üzerinde gözlemlenen bu antimikrobiyal etkilerin, fırsatçı fungal patojenler olan *Candida* türlerine karşı da geçerli olabileceği, yapılan çalışmalarda gösterilmektedir.

Amaç: Bu çalışmada, *Lactobacillus delbrueckii subsp. bulgaricus* (*L.bulgaricus*) kaynaklı canlı ve inaktive hücresiz süpernatantların (CFS), *Candida albicans* (*C. albicans*) ATCC 10231 ve *Candida parapsilosis* (*C. parapsilosis*) ATCC 22019 suşları üzerindeki antifungal etkilerinin değerlendirilmesi amaçlanmıştır.

Yöntem: Bu çalışmada, *C. albicans* ve *C. parapsilosis*'in antifungal duyarlılığı, CLSI M27-A3 mikrodilüsyon yöntemine göre değerlendirilmiştir (CLSI, 2008). Canlı ve inaktive CFS örnekleri, %0,39–100 arasında seyreltildikten sonra maya süspansiyonuna ($1.5x10^3$ CFU/mL) karşı test edilmiştir. Mikroplaklar 35°C'de 24 saat inkübe edilip, büyüme inhibisyonu görsel olarak değerlendirilmiştir. Minimum inhibitör konsantrasyonu (MİK) ve minimum fungisidal öldürme konsantrasyonu (MFK) belirlenmiştir. MFK için, MİK ve daha yüksek konsantrasyonlardaki örnekler Sabouraud Dextrose Agar (SDA) plaklarına ekilip 35°C'de 48 saat inkübe edilmiştir. Referans antifungaller olarak flukonazol (FLC) ve vorikonazol (VOR) kullanılmıştır.

Bulgular: Bu çalışma sonuçlarında *C. albicans* suşunda, LBC süpernatantının MİK ve MFK değerleri her ikisi içinde %25; LBI süpernatantının MİK ve MFK değerleri ise her ikisi için %6,25 olarak tespit edilmiştir. *C. parapsilosis* suşunda hem LBC hem de LBI süpernatantlarının MİK ve MFK değerleri her ikisinde de %50 olarak belirlenmiştir. *C. albicans* suşu için flukonazol (FLC) MİK değeri 4 µg/mL, MFK değeri 8 µg/mL; *C. parapsilosis* suşu için vorikonazol (VOR) MİK değeri 0,0625 µg/mL, MFK değeri ise 0,125 µg/mL olarak bulunmuştur.

Sonuç: Çalışma sonucunda, *L. bulgaricus* CFS'lerinin *Candida* türlerine karşı antifungal etki gösterdiğini ve özellikle LBI'lerin daha düşük konsantrasyonlarda etkili olabileceğini göstermektedir. *C. albicans* ve *C. parapsilosis* suşları üzerinde yapılan testlerde, inaktive CFS'lerin özellikle *C. albicans* üzerinde LBC'ye göre daha etkili olduğu gözlemlenmiştir. Bu bulgular, süpernatantların hazırlanma yönteminin biyolojik etkinlik üzerinde belirleyici bir rol oynayabileceğini düşündürmektedir.

Anahtar Kelimeler: ***Lactobacillus delbrueckii* subsp. *bulgaricus***, Probiotikler, Hücresiz süpernatant, Antifungal, *Candida*.

GİRİŞ

Probiyotik mikroorganizmalar, özellikle laktik asit bakterileri (LAB), insan sağlığı üzerinde gösterdikleri olumlu etkiler nedeniyle son yıllarda bilimsel araştırmalarda yoğun ilgi görmektedir. Bu mikroorganizmaların yalnızca canlı formları değil, aynı zamanda salgıladıkları metabolitleri içeren hücresiz süpernatantların (CFS) yapıları da biyolojik aktiviteleri açısından dikkat çekmektedir. CFS'ler; laktik, asetik asit gibi organik asitler, bakteriyosinler, hidrojen peroksit ve çeşitli enzimler gibi antimikrobiyal bileşenleri içermekte olup, canlı hücre içermeden biyolojik etki gösterebilmektedir (Hill ve ark., 2014; Aguilar-Toalá ve ark., 2018; Żółkiewicz ve ark., 2020).

Son yıllarda yapılan çalışmalar, CFS'lerin özellikle bakteriyel patojenlere karşı antimikrobiyal etkiler sergilediğini ortaya koymakta; buna ek olarak, bu etkinin fırsatçı fungal patojenler olan *Candida* türleri üzerinde de gözlemlenebileceği bildirilmektedir (Tejero-Sariñena ve ark., 2012; Somashekaraiah ve ark., 2019; Tenea ve ark., 2023). *C. albicans* ve *C. parapsilosis*, bağışıklığı baskılanmış bireylerde sistemik enfeksiyonlara neden olabilen önemli patojenler arasında yer almakta ve giderek artan antifungal direnç nedeniyle tedavide zorluklar yaşanmaktadır (Mayer ve ark., 2013; Guinea, 2014; Arendrup ve Patterson, 2017). Bu durum, doğal antifungal ajanlara olan ihtiyacı artırmaktadır.

Laktik asit bakterilerinden elde edilen CFS'lerin antifungal etkileri üzerine yapılan araştırmalar, bu süpernatantların hem *Candida* türlerinin çoğalmasını hem de biyofilm oluşumunu baskılayabildiğini göstermektedir (Angmo ve ark., 2016; Suchodolski ve ark., 2021; Andrade ve ark., 2022). Özellikle *Lactobacillus delbrueckii* subsp. *bulgaricus* gibi GRAS (Genel Olarak Güvenli Olarak Tanınan) statüsüne sahip süt kökenli türlerin, gıda ve sağlık alanında yaygın kullanımı bu suşlardan elde edilen biyolojik ürünleri ön plana çıkarmaktadır (FAO/WHO, 2001).

Bu çalışmada, *L. bulgaricus*'un canlı (LBC) ve ısı ile inaktive edilmiş (LBI) CFS örneklerinin, klinik öneme sahip iki tür olan *C. albicans* ve *C. parapsilosis* üzerindeki antifungal etkilerinin karşılaştırmalı olarak değerlendirilmesi amaçlanmıştır. Özellikle süpernatantların hazırlanma yöntemlerinin biyolojik etkinlik üzerindeki etkilerinin ortaya konması, gelecekte geliştirilmesi olası yeni antifungal ajanlara yönelik önemli bilgiler sağlayabilir.

GEREÇ VE YÖNTEM

Probiyotik Bakteri CFS'lerinin Hazırlanması

Bu çalışmada kullanılan probiyotik bakteri izolatı, öncelikle De Man, Rogosa ve Sharpe (MRS) agar besiyerinde kültüre edilmiştir. Ardından tek koloni seçilerek MRS sıvı besiyerine inoküle edilmiş ve 37 °C'de 24 ila 48 saat inkübasyona bırakılmıştır. Bakteriyel çoğalmanın ardından, bir kısmı 100 °C'de 30 dakika süreyle su banyosunda ısıyla inaktive edilmiştir. Canlı ve inaktive bakteri kültürlerinden hücresiz süpernatantların (CFS) elde edilmesi amacıyla kültürler 4500 rpm'de 20 dakika santrifüjlenmiştir (Sadeghi-Aliabadi ve ark., 2014). Elde edilen süpernatantlar, 0.22 µm gözenek çapına sahip PES membran filtrelerden geçirilerek sterilize edilmiş ve analizlerde kullanılmıştır. Isı ile inaktivasyonun etkinliğini doğrulamak amacıyla santrifüj sonrası elde edilen pelet yeniden süspanse edilmiş,

MRS agar üzerine ekilerek inkübasyona alınmış ve mikrobiyal üremenin olup olmadığı gözlemlenmiştir (Karimi Ardestani ve ark., 2019).

Antifungal Duyarlılık Testi

Bu çalışmada, *Candida* türlerine karşı antifungal duyarlılığı belirlemek amacıyla, Clinical and Laboratory Standards Institute (CLSI) M27-A3 yönergelerine uygun olarak mikrodilüsyon yöntemiyle *in vitro* duyarlılık testi uygulanmıştır (CLSI, 2008). Deneylerde standart mikroorganizmalar olarak *C. albicans* ATCC 10231 ve *C. parapsilosis* ATCC 22019 suşları kullanılmıştır.

Her bir canlı ve inaktive CFS'lerin %100-0,39 arasında değişen konsantrasyonlarda seri dilüsyonları hazırlanmıştır. Maya süspansiyonu 1,5 × 10^3 CFU/mL olacak şekilde hazırlanmış ve her mikrotitre plak kuyucuğuna 10 µL olacak şekilde eklenmiştir. Her testte pozitif ve negatif kontrol grupları da dahil edilmiştir. Mikroplaklar, 35 °C'de 24 saat inkübasyona bırakılmış ve fungal büyüme veya inhibisyon durumu görsel olarak değerlendirilmiştir. Her bir suş için minimum inhibitör konsantrasyon (MİK) ve minimum fungisidal konsantrasyon (MFK) değerleri belirlenmiştir. MFK tayini için, MİK değeri ile MİK'in iki ve üç katı olan konsantrasyonlardaki kuyucuklardan 10 µL örnek alınarak Sabouraud Dekstroz Agar (SDA) besiyerine ekilmiş ve 35 °C'de 48 saat inkübe edilmiştir. İnkübasyon sonrasında koloni oluşumu gözlemlenmiş, üremenin olmadığı en düşük konsantrasyon MFK değeri olarak kaydedilmiştir. Referans antifungal ajanlar olarak flukonazol (FLC) ve vorikonazol (VOR) kullanılmıştır.

BULGULAR

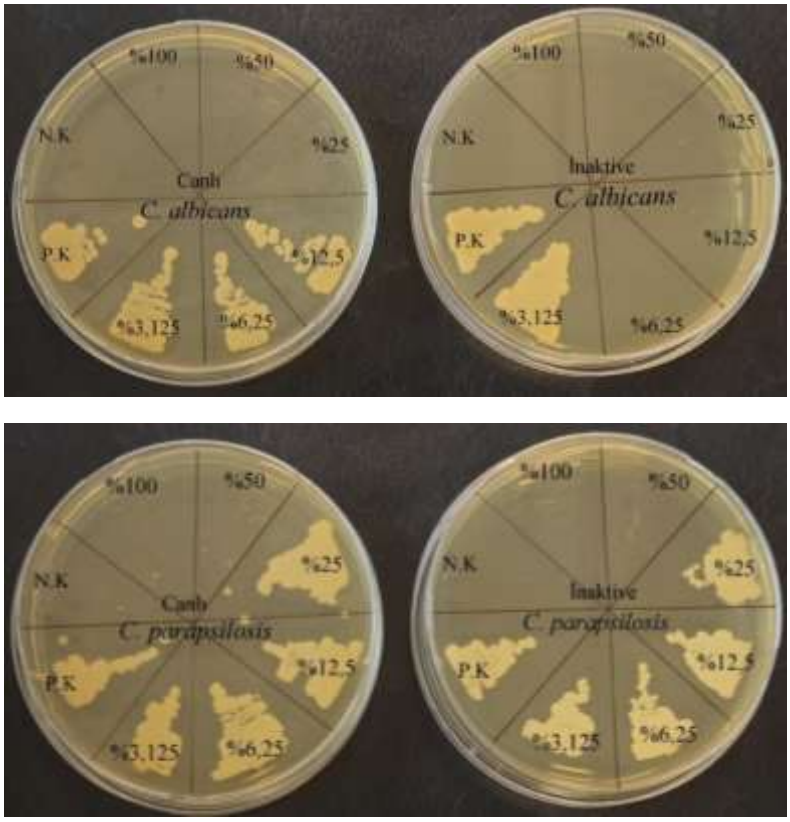
Hücresiz süpernatantların, *Candida* türlerine karşı antifungal aktivitelerini değerlendirmek amacıyla broth mikrodilüsyon yöntemi uygulanmıştır. Referans antifungal ajanlar olarak *C. albicans* ve *C. parapsilosis* için sırasıyla MİK ve MFK değerleri flukonazol (FLC, 4-8 µg/mL) ve vorikonazol (VOR, 0,0625-0,125 µg/mL) tespit edilmiştir. CFS örneklerinin *C. albicans* ve *C. parapsilosis* suşlarına karşı gösterdiği MİK ve MFK değerleri Tablo 1 ve Şekil 1'de sunulmuştur.

Çalışma bulgularına göre, *C. albicans* suşu üzerinde uygulanan LBC için hem MİK hem de MFK değerleri %25 olarak belirlenmiştir. Aynı suş üzerinde LBİ kullanıldığında ise her iki değer de %6,25 konsantrasyonunda gözlemlenmiştir. *C. parapsilosis* suşu üzerinde yapılan analizlerde hem LBC hem de LBİ süpernatantlarının MİK ve MFK değerleri %50 olarak tespit edilmiştir. Elde edilen bulgular, özellikle inaktive süpernatantların *C. albicans* suşuna karşı daha düşük konsantrasyonlarda antifungal etkili olabileceğini göstermektedir.

Tablo 1: Canlı ve inaktive *L. bulgaricus* CFS'lerin *Candida* spp.'ye karşı antifungal aktivitesi

Mantar Suşları	Canlı (%)		İnaktive (%)		FLC (µg/ml)		VOR (µg/ml)	
	MİK	MFK	MİK	MFK	MİK	MFK	MİK	MFK
***Candida albicans* ATCC 10231**	25	25	6,25	6,25	4	8	n. d	n. d
***Candida parapsilosis* ATCC 22019**	50	50	50	50	n. d	n. d	0,0625	0,125

n.d: zon yok; MİK: Minimum İnhibitör Konsantrasyon; MFK: Minimum Fungisidal Konsantrasyon; FLC: fluconazole; VOR: voriconazole.



Şekil 1: Canlı ve inaktive *L. bulgaricus* CFS'lerinin MFK petri görüntüleri

TARTIŞMA

Son yıllarda probiyotik mikroorganizmalar, yalnızca gastrointestinal sistem sağlığını destekleyici rolleriyle değil, aynı zamanda antimikrobiyal aktiviteleriyle de dikkat

çekmektedir. Özellikle maya ve küf gibi fungal patojenlere karşı geliştirdikleri biyolojik etkiler, bu mikroorganizmaları potansiyel antifungal ajanlar arasında ön plana çıkarmaktadır. Fermente süt ürünlerinden elde edilen *L. bulgaricus*, bu bağlamda önemli bir probiyotik suş olarak değerlendirilmektedir. Yapılan araştırmalar, bu bakterinin ürettiği metabolitlerin çeşitli fungal patojenlere karşı antifungal etki gösterebildiğini ortaya koymaktadır.

Bu çalışmada, *L. bulgaricus*'a ait canlı ve ısı ile inaktive edilmiş CFS'lerin antifungal potansiyeli değerlendirilmiş olup, elde edilen bulgular bazı *C.albicans* ve *C. parapsilosis* türleri üzerinde anlamlı düzeyde inhibitör etki gösterdiğini ortaya koymuştur.

Lactobacillus delbrueckii subsp. *bulgaricus*'un antifungal etkinliğine dair literatürde çeşitli bulgular yer almaktadır. Örneğin, Teneva ve ark. (2015), *L. bulgaricus* B1 ve TAB2 suşlarının *Candida albicans* NBIMCC 74 üzerindeki etkilerini incelemiş ve her iki suşun da ko-kültür koşullarında *C. albicans*'ın büyümesini anlamlı ölçüde baskıladığını bildirmişlerdir. Bu inhibisyonun büyük ölçüde laktik asit üretimi ile ilişkili olduğu vurgulanmıştır. Benzer şekilde, Spaggiari ve ark. (2022), tarafından yürütülen bir çalışmada, *L. delbrueckii*'nin vulvovajinal kandidiyazis modelinde güçlü antifungal etki gösterdiği ve bu etkinin epitel bariyer fonksiyonunun korunması ve inflamasyonun azaltılması yoluyla gerçekleştiği ifade edilmiştir. Li ve ark. (2019) ise, *L. delbrueckii*'nin *C. albicans*'ın virülansını azaltma ve konak bağışıklık sistemini modüle etme yoluyla antifungal etki gösterdiğini rapor etmişlerdir.

Bu bulguları destekleyen bir diğer çalışma da Vázquez-Muñoz ve ark. (2021) tarafından gerçekleştirilmiş olup, araştırmacılar *Lactobacillus* türlerinin antifungal etkilerini; hücre duvarı ve membran bütünlüğünü bozma, organik asit ve antimikrobiyal metabolit üretimi ile bağışıklık sistemini aktive etme mekanizmaları üzerinden açıklamışlardır. Özellikle *L. bulgaricus*'un *Candida* türlerine karşı bu çok yönlü etkilerinden dolayı doğal antifungal ajan adayı olabileceği ifade edilmiştir.

Bizim çalışmamızda da *L. bulgaricus*'a ait LBC ve LBİ formlarının *C. albicans* ve *C. parapsilosis* suşları üzerindeki antifungal etkileri değerlendirilmiştir. Broth mikrodilüsyon yöntemiyle elde edilen verilere göre, *C. albicans* suşunda LBC'nin MİK ve MFK değerleri %25 olarak tespit edilmiştir. Aynı suş üzerinde LBİ süpernatantı uygulandığında bu değerler %6,25'e düşmüştür. *C. parapsilosis* suşu için ise hem LBC hem de LBİ süpernatantlarının MİK ve MFK değerleri %50 olarak belirlenmiştir. Bu sonuçlar, özellikle inaktive süpernatantların *C. albicans* suşuna karşı daha düşük konsantrasyonlarda antifungal etkili olabileceğini göstermektedir.

Çalışmanın bazı sınırlılıkları mevcuttur. Öncelikle, test edilen *Candida* türlerinin ve klinik izolat sayısının sınırlı olması, sonuçların genellenebilirliğini kısıtlamaktadır. Ayrıca, elde edilen bulgular yalnızca *in vitro* analizlere dayandığından, bu etkinin *in vivo* koşullarda da geçerli olup olmadığını ortaya koymak için hayvan deneyleri ve klinik çalışmalar gerekmektedir.

SONUÇ

Çalışmanın sonucunda, *Lactobacillus delbrueckii* subsp. *bulgaricus*'a ait CFS'lerin, *Candida* türlerine karşı antifungal aktivite gösterdiği belirlenmiştir. Özellikle inaktive edilmiş

süpernatantların canlı süpernatantlara kıyasla daha düşük konsantrasyonlarda etkili olduğu gözlemlenmiştir. *C. albicans* ve *C. parapsilosis* suşları üzerinde yapılan değerlendirmelerde, inaktive edilmiş süpernatantların özellikle *C. albicans* üzerinde LBC'ye göre daha yüksek antifungal etki gösterdiği saptanmıştır.

Bu bulgular, CFS'nin antifungal etkinliğinde süpernatantın hazırlanma yönteminin belirleyici olabileceğini göstermektedir. Dolayısıyla, probiyotik kaynaklı süpernatantların antifungal potansiyellerinin değerlendirilmesinde, üretim ve inaktivasyon yöntemlerinin dikkatle optimize edilmesi gerekmektedir. Bu doğrultuda, ileri çalışmalarla süpernatant bileşenlerinin karakterizasyonu yapılarak, antifungal etkinlikten sorumlu biyoaktif bileşiklerin tanımlanması ve mekanizmalarının aydınlatılması, mikrobiyal kaynaklı doğal antifungal ajanların geliştirilmesine katkı sağlayacaktır.

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COLOSTRUM MANAGEMENT STRATEGIES IN CATTLE FARMS

ABSTRACT

In cattle farming, the health of neonatal calves is critically dependent on the efficacy of passive immune transfer, wherein the timely provision of colostrum—of sufficient quantity and appropriate quality—is of paramount importance. Colostrum serves as the principal source of passive immunity for calves, due to its high concentrations of immunoglobulins (particularly IgG), antimicrobial proteins, growth factors, and antioxidant components. The preservation of its immunological integrity requires hygienic collection immediately post-milking, storage under controlled temperatures, and administration via optimized protocols. Moreover, environmental conditions encountered during heat treatment, freezing, thawing, and extended storage can significantly influence both the microbial load and the integrity of biological components. In this context, colostrum management emerges as a critical practice that necessitates the scientific and systematic handling of all stages from production to consumption. This review examines the definition, significance, and quality parameters of colostrum, while emphasizing colostrum-centered management strategies designed to enhance postnatal survival and vitality in calves.

Keywords: Colostrum Management, Passive Immunity, Calf Health, Vitality

SIĞIRCILIK İŞLETMELERİNDE KOLOSTRUM YÖNETİM STRATEJİLERİ

ÖZET

Sığırcılıkta neonatal buzağı sağlığı, pasif transferin etkinliği ile doğrudan ilişkilidir ve bu süreçte kolostrumun zamanında, yeterli miktarda ve uygun kalitede temini hayati önem taşımaktadır. Kolostrum; yüksek konsantrasyonda immünoglobulinler (özellikle IgG), antimikrobiyal proteinler, büyüme faktörleri ve antioksidan bileşenler içermesi nedeniyle buzağının pasif bağışıklık kazanmasında birincil kaynaktır. Ancak kolostrumun immünolojik kalitesinin korunması; sağımdan itibaren hijyenik koşullarda toplanması, uygun sıcaklıkta saklanması ve optimal yöntemlerle uygulanmasıyla mümkündür. Ayrıca, kolostrumun ısıl işlemle muamele edilmesi, dondurulması, çözdürülmesi ve muhafaza süresi boyunca maruz kaldığı çevresel koşullar; hem mikrobiyal yük hem de biyolojik bileşenler üzerinde önemli etkiler göstermektedir. Bu bağlamda, kolostrum yönetimi; üretimden tüketime kadar olan tüm aşamaların bilimsel temelli ve sistematik biçimde yürütülmesini gerektiren kritik bir uygulamadır. Bu çalışmada, kolostrumun tanımı, önemi ve kalitesi ele alınmış; ayrıca doğum sonrası buzağıların yaşama şansını artırmaya yönelik kolostruma dayalı yönetimsel yaklaşımlar üzerinde durulmuştur.

Anahtar Kelimeler: Kolostrum Yönetimi, Pasif Bağışıklık, Buzağı Sağlığı, Yaşama Gücü

1. GİRİŞ

Ruminantlarda gebelik esnasında anneden yavruya antikor geçişi olmadığı için, pasif bağışıklık öğelerinden immunoglobulinlerin buzağılara aktarılmasının tek yolu kolostrumdur. Kolostrum, buzağının doğumdan sonraki ilk birkaç saatte aldığı bağışıklık sistemini destekleyen ve büyüme için gerekli besin öğeleriyle zengin olan ilk sütüdür. Bu madde, immünoglobulinler başta olmak üzere büyüme faktörleri, antimikrobiyal proteinler, hücresel bileşenler, vitaminler, mineraller ve enerji sağlayıcı besin maddeleri açısından oldukça zengindir. Bu yönüyle, buzağıların enfeksiyonlara karşı korunmasında, bağışıklık sisteminin gelişiminde ve genel sağlığının sürdürülebilirliğinde temel bir role sahiptir [1–5]. Ticari süt çiftliklerinin sürdürülebilirliği için yıl boyunca yeterli miktarda yüksek kaliteli kolostrum tedarik etmek önemli bir sorundur. Çünkü kolostrum verimi ve bileşimi bireysel, sürüsel ve mevsimsel faktörlere göre önemli değişiklikler gösterebilmektedir. Bu sebeple doğru bir kolostrum yönetim stratejisinin geliştirilmesi gerekmekte olup, sığırcılıkta kolostrum yönetimi, sağlıklı ve güçlü bir buzağı yetiştirebilmek için kritik bir unsur olarak değerlendirilmektedir [1,4,6,7]. Kolostrum yönetiminin doğru ve etkili bir şekilde uygulanması sadece buzağıların sağlıklı bir şekilde büyümesini sağlamakla kalmaz, aynı zamanda genel sürü sağlığını da doğrudan etkiler [6–9].

1.1. Kolostrumun Verilme Zamanı ve Miktarı

Buzağılarda yaşamın ilk saatleri, bağışıklık sisteminin gelişimi açısından kritik bir öneme sahiptir. Doğumla birlikte pasif bağışıklığın kazanılması, kolostrumun zamanında, yeterli miktarda ve uygun kalitede verilmesine bağlıdır. Doğumdan hemen sonra buzağının aldığı kolostrumlarda bulunan immunoglobulinlerin büyük bir kısmı kan dolaşımına katılırken, 24 saatten sonra emilim kapasitesi neredeyse tamamen kaybolur. Bu nedenle, kolostrumun gecikmeden ve doğru şekilde uygulanması yaşama gücünü doğrudan etkiler. Verilecek kolostrum miktarı da en az zamanlaması kadar önemlidir. İdeal olarak yeni doğan bir buzağıya doğumdan sonraki ilk 6 saat içinde ilk öğünde vücut ağırlığının yaklaşık %5'i kadar ve ilk günde ise 3-4 öğünde vücut ağırlığının %10'u kadar kolostrum verilmesi gereklidir [7,10–12].

1.2. Kolostrum Kalitesinin Değerlendirilmesi

Kolostrumun kalitesi büyük ölçüde içerdiği immünoglobulin G (IgG) konsantrasyonuna bağlıdır. Yetersiz kalitedeki kolostrumun verilmesi durumunda, buzağıların bağırsak yoluyla yeterli miktarda IgG absorbe edememesi söz konusu olabilir. Bu durum, pasif transfer başarısızlığı olarak tanımlanır ve neonatal mortalite oranlarının artışı, gelişim geriliği ve hastalıklara duyarlılıkla ilişkilidir. Ayrıca bu hayvanlar yaşamlarının ilerleyen dönemlerinde de hedeflenen döl ve süt verim seviyesine ulaşamazlar [2,5,7,12–14]. Kolostrumun kalitesinin değerlendirilmesi aynı zamanda işletme düzeyinde yönetimsel kararların alınmasında da kritik bir araçtır. Düzenli kalite kontrol uygulamaları sayesinde, düşük kaliteli kolostrumun zamanında tespiti ve bertarafı sağlanabilirken; yüksek kaliteli kolostrum, dondurularak ileride kullanım için saklanabilir. Bu tür stratejik uygulamalar, sürü sağlığının korunmasına ve ekonomik kayıpların azaltılmasına doğrudan katkı sağlar [3,15]. Kolostrum kalitesinin belirlenmesi için hem biyokimyasal analizlerle, hem de saha koşullarında uygulanabilen değişik metotlar kullanılır. Günümüzde bu değerlendirmelerin pratik ölçüm yöntemleriyle desteklenmesi, sürdürülebilir büyükbaş yetiştiriciliğinin temel gerekliliklerinden biri haline gelmiştir [7,12,16–19].

1.2.1. Kolostrum Kalitesinin Görsel Muayene Yöntemi ile Belirlenmesi

Kolostrumdaki yüksek antikor yoğunluğu, genellikle toplam kuru madde oranının fazlalığıyla ilişkilidir. Bu nedenle, görsel değerlendirmeler kolostrumun kalitesi hakkında önemli ipuçları verebilir. Bağışıklık maddeleri bakımından zengin ve kaliteli bir kolostrum, genellikle yoğun yapılı ve krema kıvamındadır. Buna karşılık, sulu ve açık renkli kolostrum, yeni doğan bir buzağı için uygun bir ilk besin değildir. Çünkü bu tür kolostrumlar, kuru madde, protein, yağ ve özellikle bağışıklık sağlayan maddeler açısından yetersizdir. Bu yöntemin en büyük avantajı herhangi bir ekipman veya maliyet gerektirmemesidir. Fakat yoğun kıvamlı ve koyu renkli her kolostrum, bağışıklık maddelerini yeterince içermeyebilir. Bu nedenle yanılma payı vardır [20–22].

1.2.2. Kolostrum Kalitesinin Özgül Ağırlık Tespiti ile Belirlenmesi

Özgül ağırlık (yoğunluk), bir sıvının birim hacminin ağırlığıdır. Kolostrumda özgül ağırlık, içerdiği kuru madde, özellikle immünoglobulin G (IgG) yoğunluğu ile doğrudan ilişkilidir. Bu sebeple kolostrumun özgül ağırlığı, kalitesinin nesnel göstergesi olarak ölçülebilir. Kolostrumun özgül ağırlığını ölçen alete kolostrometre adı verilmektedir. Kolostrometre ile yapılan ölçüm yaygın olarak kullanılan, pratik ve maliyeti düşük bir yöntemdir [17–20].

1.2.3. Kolostrum Kalitesinin Refraktometre ile Belirlenmesi

Refraktometreler, sıvı malzemelerin içindeki katı madde miktarını ve kırılma indislerini ölçen cihazlardır. Kolostrum gibi sıvılarda, yoğunluk arttıkça, kırılma indeksi de yükselir. Bu, sütün içeriğinde daha fazla immünoglobulin (IgG) olduğu anlamına gelir. Refraktometre ölçümleri, genellikle Brix olarak ifade edilir. Brix değeri %22 veya daha fazla olan kolostrumlar yüksek kaliteli, %18-%22 arasındakiler orta kaliteli ve %18'in altındakler ise düşük kaliteli olarak değerlendirilir [18,23,24].

1.2.4. Kolostrum Kalitesinin İmmunoglobulin Seviyesine Göre Belirlenmesi

Kolostrum kalitesini etkileyen en önemli faktör içerdiği immunoglobulin miktarıdır. Kolostrumlarda bulunan immunoglobulinlerin % 85'lik kısmını IgG oluşturduğu için, kalite sınıflandırılması yapılırken genellikle bu antikorun seviyesi baz alınır. Buzağılarda immunite ile ilgili yapılan çalışmalar sonucunda, yeterli pasif immunitenin sağlanması için verilecek kolostrumun 1 litresinde en az 50 gram IgG bulunması gerektiği sonucuna varılmıştır. Kolostral IgG konsantrasyonu radyal immünodifüzyon (RID), ELISA (Enzyme-Linked Immunosorbent Assay) ve türbidimetrik immün testi (TIA) gibi yöntemler ile belirlenebilir. Bu analizlerin güvenilirliği oldukça yüksek olsa da, zaman alıcı ve maliyetlidir. Ayrıca ticari süt üreticileri için uygulanabilirliği de zordur [5,14,16,21,25,26].

1.3. Kolostrumda Bakteriyel ve Patojen Kontaminasyonun Önemi ve Önlenmesi

Buzağı sağlığını ve pasif bağışıklığın etkinliğini koruyabilmek için kolostrumun mikrobiyal kalitesi büyük önem taşımaktadır. Kolostrumdaki bakteri ve patojen kontaminasyonu, immünoglobulin emilimini azaltmakla kalmayıp aynı zamanda buzağıları hastalık yapıcı mikroorganizmalara maruz bırakmaktadır. Bu bağlamda kolostrumun üretiminden buzağıya verilmesine kadar geçen süreçte hijyen uygulamaları titizlikle yürütülmelidir [27,28]. Endüstri standartlarına göre toplam bakteri sayısı (<100.000 cfu/mL) ve koliform bakteri sayısı (<10.000 cfu/mL) sınırlamaları getirilmiş olsa da [15], yakın dönem araştırmalar bu sınırların çoğu çiftlikte aşılmakta olduğunu göstermektedir. Örneğin, Çekya'da yapılan bir çalışmada

kolostrum örneklerinin yalnızca %28,4'ü toplam bakteri sayısı açısından standartların altında bulunmuştur [29].

Kolostrum kontaminasyonu genellikle sağım, depolama ve buzağılara verilme aşamalarda meydana gelmektedir. Kolostrum örneklerinin büyük çoğunluğunda çevresel, dışkısal ve deri/mukoza kaynaklı mikroorganizmalar tespit edilmiştir. Bu bulgular, sadece meme sağlığına değil, aynı zamanda çevresel hijyene de odaklanılması gerektiğini ortaya koymaktadır. Bu kapsamda, kolostrumun elde edilmesinden sonra hızlıca soğutulması, uygun koşullarda saklanması ve kullanılan tüm ekipmanların etkili bir şekilde temizlenip dezenfekte edilmesi büyük önem arz etmektedir [28,30].

1.4. Kolostrumda Isıl İşlem Uygulamaları

Kolostrumda mikrobiyal yükün azaltılması amacıyla başvurulan yöntemlerden birisi ısıl işlem uygulamasıdır. Isıl işlemin etkinliği, doğrudan kolostrumun başlangıçtaki mikrobiyal yüküyle ilişkilidir [31]. Bu bağlamda, ısıl işlem uygulanacak dahi olsa, kolostrumun sağım, depolama ve transfer süreçlerinde kontamine olmasının önlenmesi temel bir öncelik olmaya devam etmelidir. Isıl işlem uygulaması, ideal sıcaklık ve süre koşullarında gerçekleştirildiğinde immünoglobulin G (IgG) düzeyinde kayba neden olmadan bakteri kontaminasyonunu önemli ölçüde azaltabilmektedir. Yürütülen bir çalışmada, deneysel olarak kontamine edilen kolostrum örneklerinde 60°C'de 60 dakika uygulanan ısıl işlemin; Mycoplasma bovis (10^8 cfu/mL), Listeria monocytogenes (10^6 cfu/mL), Escherichia coli (10^6 cfu/mL) ve Salmonella enteritidis (10^6 cfu/mL) gibi enfeksiyöz ajanları etkili bir şekilde ortadan kaldırdığı belirlenmiştir [32]. Isıl işlem, bakteriyel yükü azaltmak için etkili bir strateji olarak kabul edilse de, son dönem araştırmalar bu işlemin yalnızca mikrobiyal kontaminasyonu değil, aynı zamanda kolostrumun fonksiyonel ve biyolojik özelliklerini de etkileyebileceğini ortaya koymuştur [31,33–35]. Ayrıca, ısıl işlem; reaktif oksijen ve azot türlerini azaltmakta veya tamamen ortadan kaldırmakta [36], bağışıklık sisteminin aktif bileşenlerinden olan lökositlerin varlığını azaltmakta ve alternatif kompleman yolunun aktivitesini düşürmektedir [37]. Bu sonuçlar ısıl işlem uygulamasının potansiyel faydaları kadar olası olumsuz etkilerinin de dikkate alınması gerektiğini ortaya koymaktadır.

1.5. Kolostrumun Depolanması

Kolostrum verimi, kompozisyonu ve IgG konsantrasyonu doğum mevsimine göre değişkenlik göstermektedir. Kolostrumun çiftlik koşullarında uygun şekilde depolanması, hem içerdiği immünoglobulin G (IgG) başta olmak üzere biyolojik bileşenlerin korunması, hem de mevsimsel üretim dalgalanmalarına karşı yeterli miktarda kolostrumun temin edilebilmesi açısından kolostrum yönetim sistemlerinin temel bir unsurudur [7,12]. Taze kolostrum hemen tüketime sunulmayacaksa, hızla soğutularak buzdolabında (4°C) ya da uzun süreli saklama için derin dondurucuda (−20°C) muhafaza edilmelidir. Taze kolostrumun koruyucu madde kullanılmadan buzdolabında en fazla 2 gün, potasyum sorbat ilavesiyle ise en fazla 4 gün süreyle saklanması önerilmektedir [12,38]. Uzun süreli saklama gereksinimlerinde ise kolostrumun −20°C'de dondurularak muhafaza edilmesi tavsiye edilmektedir [39–41]. Ancak, uzun dönemli donmuş kolostrum saklamasına ilişkin sınırlı literatürlerde birbirinden son derece farklı veriler mevcuttur. Yürütülen bir çalışmada, kolostrumun 3 ay boyunca dondurulmuş şekilde saklanmasının IgG ve IgM konsantrasyonlarını etkilemediği; ancak 6 aylık saklama süresinin ardından bu değerlerin sırasıyla %14,6 ve %60,5 oranında azaldığı belirlenmiştir [42]. Başka bir çalışmada ise, taze kolostrumun -20 °C de muhafaza edildiği taktirde 15 yıl boyunca kalitesinde herhangi bir bozulma olmadan saklanabildiğini ifade etmişlerdir [43].

2. SONUÇ

Buzağı yetiştiriciliğinde neonatal dönem, immün sistemin henüz tam olarak gelişmediği ve çevresel stres faktörlerine duyarlılığın yüksek olduğu bir evredir. Bu dönemde buzağılar, immünolojik olarak savunmasız olmaları nedeniyle enfeksiyöz ve non-enfeksiyöz hastalıklara karşı yüksek risk altındadır. Son yıllarda buzağı bakım ve yönetim uygulamalarında önemli gelişmeler sağlanmış olmasına rağmen, neonatal mortalite oranlarının halen yüksek oranlarda seyrettiği bilinmektedir. Kolostrum yönetimi, neonatal buzağılarda pasif bağışıklığın etkin bir şekilde sağlanabilmesi açısından kritik öneme sahip olup, sürü sağlığı yönetiminin temel bileşenlerinden birini oluşturur. Yetersiz veya hatalı kolostrum uygulamaları, bağışıklık sisteminin yetersiz gelişmesine, büyüme performansında düşüşe ve enfeksiyonlara yol açabilir. Buzağılarda kolostral bağışıklığın optimal düzeyde sağlanabilmesi için zamanlama, miktar, kalite ve hijyen gibi birçok unsurun doğru yönetilmesi gerekir. Bu nedenle her çiftlik, kendi koşullarına uygun, ölçülebilir ve takip edilebilir bir kolostrum yönetim sistemi kurmalıdır.

3. KAYNAKLAR

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RELATIONSHIP BETWEEN STRESS AND BEHAVIOR IN DAIRY CATTLE FARMING

ABSTRACT

Stress in dairy cattle farming has a significant impact on animal health and welfare. Modern farming systems introduce stress factors that can alter the physiological and behavioral responses of animals. This study examines the relationship between stress and behavior in dairy cattle. Stress can arise from environmental factors and human-animal interactions, influencing animals' coping strategies. Cattle may develop active (proactive) or passive (reactive) coping strategies when faced with stress. Factors such as pain, illness, and thermal stress can lead to changes in cattle behavior. Furthermore, human-animal interactions can determine stress responses. Positive interactions reduce stress, while negative interactions can increase stress levels. Thermal stress can cause health issues such as reduced milk yield, reproductive problems, and weakened immune function. The aim of this study is to understand the effects of stress factors on dairy cattle behavior.

Keywords: Behavior, Temperament, Stress, Dairy Cattle

SÜT SIĞIRI YETİŞTİRİCİLİĞİNDE STRES VE DAVRANIŞ İLİŞKİSİ

ÖZET

Süt sığırı yetiştiriciliğinde stres, hayvanların sağlığı ve refahı üzerinde önemli bir etkiye sahiptir. Modern yetiştirme sistemlerinde karşılaşılan stres faktörleri, hayvanların fizyolojik ve davranışsal tepkilerini değiştirebilir. Bu çalışma, süt sığırlarında stres ve davranış arasındaki ilişkiyi incelemektedir. Stres, çevresel faktörler ve insan-hayvan etkileşimleri gibi bir dizi faktörden kaynaklanabilir ve hayvanların başa çıkma stratejilerini etkileyebilir. Hayvanlar, stresle başa çıkarken aktif (proaktif) veya pasif (reaktif) stratejiler geliştirebilirler. Örneğin, ağrı, hastalık ve sıcaklık stresi gibi faktörler, süt sığırlarının davranışlarında değişikliklere yol açabilir. Ayrıca, insan-hayvan etkileşimleri de hayvanların stres tepkilerini belirleyebilir. Olumlu etkileşimler, hayvanların daha az stres göstermesini sağlarken, olumsuz etkileşimler stres seviyelerini artırabilir. Sıcaklık stresi, süt veriminde azalma, üreme problemleri ve bağışıklık fonksiyonunun zayıflaması gibi sağlık sorunlarına yol açabilir. Bu çalışmanın amacı, stres faktörlerinin süt sığırlarının davranışları üzerindeki etkilerini anlamaktır.

Anahtar Kelimeler: Davranış, Mizaç, Stres, Süt Sığırı

1. GİRİŞ

Süt sığırı yetiştiriciliği, geleneksel ekstansif sistemlerden teknoloji ve sürü yönetim uygulamalarının entegre edildiği entansif ve yarı-entasif sistemlere dönüşmüştür[1]. Bu yeni ortamlar, ideal bir sürü yönetimi için tasarlanmış olsa da, hayvanlarda strese yol açabilecek potansiyel zorluklar yaratabilir. Bu da hayvanların sağlık ve refahını olumsuz etkileyebilir[2].

Stres, zararlı çevresel faktörlere maruz kalmanın bir sonucu olarak ortaya çıkar ve bağışıklık baskılanmasından büyüme ve üreme azalmasına kadar geniş bir etki yelpazesinde, adaptif mekanizmaların başarısız olması durumunda ölüme yol açabilen spesifik olmayan bir fizyolojik tepkiyi tetikler[3–5]. Stres, iki farklı şekilde ortaya çıkabilir. İlk olarak, sempatik-adrenal-medullar eksenin aktivasyonu ile bir savaş ya da kaç tepkisi oluşur; bu vücutta hızlı bir enerji kaynağı kullanımına yol açar[6]. Diğer bir durum ise "genel adaptasyon sendromu"dur ve metabolik etkileri uzatmak için kortikosteroidlerin salınımını tetikleyen adrenokortikotropik hormon salınımı ile hormonal değişikliklerle karakterizedir[7]. Stres, doğal bir fizyolojik tepki olsa da, uzun süreli stres, özellikle kronik yüksek kortizol seviyeleri, bağışıklık baskılanması ve doku atrofisi gibi zararlı etkilere yol açabilir[8].

Sütçü sığırlarının davranışlarını anlamak, başarılı bir yetiştirme ve iyi bir sürü yönetimi için kritik öneme sahiptir. Strese karşı bireysel davranışsal tepkiler, mizaç olarak tanımlanır[9]. Yoğun ticari yetiştiricilikte, çiftlik hayvanları olumsuz bir durumla karşılaştığında kaçma, uzaklaşma, arama, bekleme gibi çeşitli davranışlar sergileyebilir. Araştırmalar, bu tür durumlarda hayvanların aktif (savaş ya da kaç) ve pasif (koruma-geri çekilme) başa çıkma stratejileri gösterdiğini bildirmiştir[10]. Aktif tepki (proaktif), bölgesel kontrol ve saldırganlık ile karakterizedir, pasif tepki (reaktif) ise hareketsizlik, idrara çıkma, dışkılama ve düşük düzeyde saldırganlık gibi tepkilerle tanımlanır[10]. Son yıllarda yapılan çalışmalarda, süt sığırlarında başa çıkma stratejileri ve mizaçtaki bireysel farklılıklar araştırılmış ve birçok çalışma, stres faktörü olarak insan maruziyetine odaklanarak fizyolojik ve davranışsal tepkileri değerlendirmiştir[11,12].

Bu çalışmanın amacı, süt sığırlarında stres faktörleri ile davranışlar arasındaki ilişkinin değerlendirilmesidir. Bu kapsamda, süt sığırı yetiştiriciliğinde yaygın olarak karşılaşılan ağrı, hastalık, sıcaklık stresi, insan-hayvan etkileşimleri, barınak içi çevresel koşullar, yetersiz konfor düzeyi ve sosyal stres gibi stres etmenlerinin hayvan davranışları üzerindeki etkileri ele alınmıştır. Ayrıca, süt sığırlarının bu stres faktörlerine karşı geliştirdikleri davranışsal olarak başa çıkma mekanizmaları incelenmiştir.

1.6. Strese Karşı Davranışsal Tepkilerin Önemi

Bir hayvanın stres faktörlerine verdiği tepkinin temel amacı, fizyolojik ve davranışsal düzenlemelerle dengeyi (allostaz) korumaktır. Bu tepkiler, hayvanların gelecekteki zorlukları tahmin etmelerine ve bu zorluklarla başa çıkmalarına yardımcı olarak çevresel stres faktörlerine uyum sağlamalarını destekler[13].

Stres tepkileri, hayvanların stres faktörlerini nasıl algıladıkları ve bu faktörlere nasıl tepki verdiklerine bağlıdır. Weiss ve ark. (50), stres faktörünün etkisinin, bu faktörün fiziksel özelliklerinden ziyade, hayvanın bu faktörü tahmin etme ya da kontrol etme yeteneğiyle bağlantılı olduğunu bulmuşlardır[14]. Hayvanlar, genellikle uygun davranışlar sergileyerek bu kontrolü sağlar ve farklı bireyler aynı stres faktörlerine farklı tepkiler verebilir. Örneğin, aktif ve saldırgan yapıya sahip hayvanlar kaçma davranışı gösterirken, pasif hayvanlar hareketsiz kalarak geri çekilme tepkisi verir[15].

Baş etme stratejileri, proaktif ve reaktif başa çıkma olarak iki ana tipe ayrılabilir[13]. Proaktif başa çıkma, daha önceki stres faktörleriyle mücadele etmek için geliştirilen alışkanlık ve davranışları kullanmayı içerirken, reaktif başa çıkma yeni zorlukları ele almak için davranışları değiştirmeyi gerektirir[16]. Bu başa çıkma stilleri, fizyolojik ve nöroendokrin süreçlerde farklılıklar yaratır. Sığırlar, stresle başa çıkma biçimleri bakımından bireysel farklılıklar gösterir ve bu özellikler zamanla tutarlı olabilir[17].

1.7. Süt Sığırlarında Farklı Stres Etmenlerine Davranışsal Tepkiler

Süt sığırları, barınma, yetiştiricilik ve sağlık koşullarıyla ilgili çeşitli stres faktörlerine maruz kalmaktadır. Bu stres faktörleri arasında yüksek yerleşim sıklığı, sıcaklık stresi, hastalık veya topallıktan kaynaklanan ağrı, insanlarla etkileşimler ve sağım yer alır. Bu stres faktörleri, uzun süre ayakta durma, yatış sürelerinin azalması, anormal yürüyüş, aktivite azalması, geviş getirme ve insanlardan kaçınma gibi belirli davranışsal tepkilere yol açar [13].

1.2.1. Ağrı ve Hastalıkların Davranış Üzerindeki Etkileri

Süt sığırlarında ağrı, özellikle hayvanlar tekrar ağrılı koşullara maruz kaldığında stres tepkilerine neden olabilir. Böğürmek ,sırt kamburlaştırmak ve etkilenen vücut bölgelerine dikkat etmek gibi ağrının davranışsal göstergeleri, ağrı seviyelerini değerlendirmek için yaygın olarak kullanılır [18]. Araştırmalarda, kulak küpesi takma, sıcak demirle boynuz alma ve boynuz kesme gibi ağrılı hayvancılık prosedürlerinin davranışsal etkileri incelenmiş ve ağrıya yanıt olarak artan huzursuzluk ve kaçma-kaçınma tepkileri gözlenmiştir[19,20].

Ayrıca, buzağılamadan sonra hasta inekler buzağılardan ayrılma ve beslenme süresinin azalması gibi davranışlar sergilemiş ve bu durumun ağrı veya rahatsızlığa işaret ettiği sonucuna varılmıştır[21]. Örneğin, ilk doğum yapan metritisli bir inek aktivitesini azaltır veya yatma süresini artırır, bu da ağrıyla ilişkili kaçınma davranışının göstergesidir[22,23]. Mastitis ve topallık gibi sağlık sorunları da önemli davranış değişikliklerine yol açar. Mastitisli inekler sağım sırasında daha huzursuz hale gelir, yatma süresini azaltır ve yatma pozisyonlarını değiştirir[24,25]. Kronik ağrının kaynağı olan topallık, hareketin azalmasına, ağırlık dağılımının değişmesine ve sağımhaneden kaçınmaya neden olur[26,27]. Topallık ayrıca agresif davranışları artırabilir ve topal ineklerde diğerlerine göre daha fazla saldırganlık görülebilir[28].

Ketozis ve asidoz gibi subklinik durumlar, geviş getirme süresinin azalması ve çiğneme aktiviteleri gibi daha hafif düzeyde davranış değişikliklerine yol açar[29,30]. Bu küçük davranış değişiklikleri, hassas hayvancılık teknolojileriyle tespit edilebilir ve sağlık sorunlarının erken teşhis edilmesi potansiyelini vurgular[13].

1.2.2. İnsan - Hayvan Etkileşimleri ve Davranış Üzerindeki Etkileri

İnsan-sığır etkileşimleri dört ana kategoride incelenebilir: insan varlığı, yaklaşım, temas ve kısıtlama[31]. Bu etkileşimler, sığırların stres seviyelerini ve genel davranışlarını önemli ölçüde etkiler. Sığırların mizaçları, başa çıkma stratejileri ve bakım ile kısıtlamalara verdikleri davranışsal tepkiler, bu etkileşimlerin kalitesine göre şekillenir[11]. Etkileşimlerin şekli ve şiddeti, hayvanın stres ya da korku yaşayıp yaşamadığını belirleyebilir; olumlu etkileşimler insan-sığır ilişkisini güçlendirirken, olumsuz etkileşimler stresi artırabilir[12,32].

Özellikle rutin bakım görevlerinde, hayvan bakıcısının tutumu önemli bir rol oynamaktadır. Yoğun süt yetiştiriciliği sistemlerinde, insan-sığır etkileşimleri genellikle görsel temasla sınırlı olsa da, sığırları hafif temasla yönlendirmek gibi dokunsal etkileşimler de yaygındır.

Sosyal bağ kurma ve sakin sözlü iletişim gibi yumuşak etkileşimler, sığırların insanlardan korkmasını ve kaçınma mesafelerini azaltabilir[33]. Bu etkileşimler, örneğin fırçalama veya sürekli olarak çalışma alanlarından geçirme gibi alışma protokolleri ile geliştirilebilir; böylece, düveler daha olumlu davranışsal tepkiler gösterebilir[34].

Olumlu insan-hayvan etkileşimleri, daha yüksek süt üretimi ve daha iyi refah sonuçları ile ilişkilidir[35], ancak olumsuz etkileşimler korku davranışlarına, süt veriminin azalmasına ve meme sağlığı sorunlarına yol açabilir[36,37]. Araştırmalar, bağırma veya vurma gibi sert bakım uygulamalarının ineklerde korku yarattığını, besleme gibi olumlu pekiştirme yöntemlerinin ise motivasyonu ve iş kolaylığını artırdığını göstermektedir[38]. Sığırların insanlar tarafından sert muamele görmesi, insan-sığır ilişkisini olumsuz etkileyebilir ve kaçınma mesafesinin artmasına yol açabilir[39]. Örneğin, sıklıkla olumsuz bakıma maruz kalan inekler, minimal insan etkileşimiyle sağılan ineklere göre daha yüksek stres belirteçleri, örneğin sempatik aktivite ve kortizol seviyeleri gösterir[40]. Bu durum, olumsuz etkileşimlerin sığır davranışları üzerinde uzun süreli etkiler bırakabileceğini, ancak bu tür anıların süresinin kesin olarak belirlenemediğini göstermektedir. Olumlu etkileşimler ise kaçınma davranışını uzun süre boyunca azaltabilir, bu da olumlu etkileşimlerden kalıcı faydaların sağlanma potansiyelini göstermektedir[33].

1.2.3. Sıcaklık Stresinin Refah ve Davranış Üzerindeki Etkileri

Sütçü sığırlar, homeotermik yapıda olup, fizyolojik olarak dar bir termal aralıkta işlev görmek üzere adapte olmuştur. Sıcaklık stresi, iç metabolik ısının ve çevresel sıcaklıkların birleşik etkisiyle bu dengeyi bozar[41]. Sıcaklık stresinin ana etkilerinden biri, besin alımındaki azalma olup, bu durum üretkenlik ve sağlık üzerinde olumsuz etkilere yol açar. Süt veriminde azalma, üreme problemleri, oksidatif stres, ketozis, protein ve mikro besin eksiklikleri ve zayıflamış bağışıklık fonksiyonu gibi sonuçlar ortaya çıkabilir; bu da hastalıklara karşı duyarlılığı artırır[42]. Ayrıca, rumen fonksiyonu bozulur ve bu da rumen asidozu gibi sağlık komplikasyonlarına yol açabilir[43].

Sıcaklık stresi, termoregülasyon için davranışsal değişikliklere yol açar. İnekler, su alımını artırır, yem alımını azaltır, daha uzun süre ayakta durur ve geviş getirmeyi azaltır[44,45]. Değişen içme davranışları, daha sık ama kısa süreli su içme seansları ve suya erişim için artan rekabeti içerir; zayıf ve pasif inekler, yüksek rekabet ortamlarından kaçınmak için su içme düzenlerini değiştirir[46]. Gölge arama davranışı da yaygındır; gölge yoksa, inekler vücut ısısını dengelemek için ayakta durmayı tercih eder[47]. Yüksek sıcaklıklar, ayakta durmanın hava akışına daha fazla maruz kalan vücut yüzeyini artırması nedeniyle yatarak geçirilen süreyi %30'a kadar azaltabilir[48]. Uzun süreli sıcaklık stresi, aktivite seviyelerini artırır ve dinlenme düzenlerini bozar. Araştırmalar, dinlenme süresindeki azalmaların, tek başına artan aktiviteden daha güvenilir bir sıcaklık stresi göstergesi olabileceğini ortaya koymuştur[49]. Buzağılarda sıcaklık stresi, yatma süresini değiştirir; ancak ek gölgeleme, özellikle sıcak günlerde yatma süresini önemli ölçüde etkilemese de toplamda yatma süresini azaltabilir[50].

1.2.4. Sağım Uygulamalarından Kaynaklanan Stres ve Davranış Üzerindeki Etkileri

Sağım uygulamaları, çeşitli seviyelerde strese yol açabilir ve bu stres genellikle davranışsal tepkilerle değerlendirilir. Bazı araştırmalar, robotik sağım sistemlerinin daha yüksek stresle ilişkilendirildiğini belirtirken[51], diğer çalışmalarda ise bu sistemlerin balık sırtı sağımhanelere kıyasla daha düşük huzursuzluk davranışları sergilediği gözlemlenmiştir[52]. Sağım sırasında sosyal hiyerarşi, davranışsal stres üzerinde önemli bir etkiye sahiptir. İlk

doğum yapan inekler, sürüdeki alt statüleri nedeniyle daha fazla saldırganlık sergileyebilir ve daha uzun bekleme süreleri yaşayabilirler[53,54]. Benzer şekilde, daha çekingen mizaçlı inekler, sağım robotlarına erişim için daha uzun süre bekleyebilirler[55].

Sağımdan hemen sonra, özellikle istemsiz çıkışların olduğu sağımhanelerde artan adımlama oranları gibi davranışsal göstergeler, stresin belirgin bir işareti olabilir[56]. Döner sağım sistemleri, inekler arasında sürekli görsel temas sayesinde geviş getirmeyi teşvik ederek ve fiziksel ağrıyı azaltarak sabit sistemlere göre stresi daha etkili bir şekilde azaltabilir[57]. Ancak, bekleme alanlarında geçirilen süre, bilinen bir stres faktörü olmaya devam etmektedir[58]. Sağım sırasında süt ineklerinin stres yanıtlarını etkileyen faktörlerden biri de bireysel çiftlik uygulamaları, inek deneyimi ve insan-hayvan etkileşimlerinin kalitesidir[59].

1.2.5. Yetersiz Konfor, Yerleşim Sıklığı ve Sosyal Stresin Davranış Üzerindeki Etkileri

Çevresel ve sosyal faktörler, süt ineklerinin refahını ve davranışlarını önemli ölçüde etkiler. Özellikle konforla ilgili davranışlar, yatma süresi, zemin tipi, yatak malzemesi ve ahır tasarımı gibi unsurlardan büyük ölçüde etkilenir. Araştırmalar, ineklerin beton zeminler veya kalitesiz şilteler yerine odun yongaları veya talaş gibi daha yumuşak yüzeyleri tercih ettiğini ve bunun yatma süresini artırarak genel konforu yükselttiğini göstermektedir[60]. Öte yandan, düşük kaliteli yüzeylere, örneğin destek altlıklarına uzun süre maruz kalmak, yatma davranışını olumsuz yönde etkileyebilir[61].

Fiziksel konforun yanı sıra, sosyal stres faktörleri de inek davranışlarını etkiler. Hayvan yoğunluğu ve yeniden gruplaşma gibi unsurlar, sığırların davranışlarını değiştirebilir. Yüksek yerleşim sıklığı, yatma ve beslenme sürelerinin kısalmasına, agresif etkileşimlerin artmasına ve beslenme sırasında daha fazla yer değiştirme eylemine yol açabilir[62,63]. Özellikle yerleşim sıklığı %130'dan fazla olduğunda, ineklerin konforu azalır ve geviş getirme süreleri kısalabilir[62,63].

Ahır tasarımına yapılacak müdahaleler, örneğin kafa kilitleri, bariyerler veya bireysel yem durakları, beslenme alanlarındaki rekabeti ve saldırganlığı azaltabilir[64]. Ayrıca, sosyal hiyerarşi, baskın ineklerin TMR (Total Mixed Ration) ile yapılan beslenmeye daha fazla zaman ayırmasına neden olabilir. Bu da kaynak erişimini karmaşıklaştırarak besin alımını etkileyebilir[63,65]. Süt sığırcılığı yönetiminde yaygın olarak uygulanan yeniden gruplandırma, beslenme ve dinlenme kalıplarını bozsa da, tanıdık bireylerin yeniden gruplara entegre edilmesi bu olumsuz etkileri hafifletebilir[66].

1.8. Süt Sığırcılığında Stresi Yönetme Stratejileri

Süt çiftçiliğinde etkili stres azaltma stratejileri, çevresel ve yönetimsel müdahalelere odaklanır. En kapsamlı şekilde incelenen stres faktörlerinden biri olan sıcaklık stresi, ahırdaki mikro iklimi düzenleyerek ve vücut yüzeyini ıslatarak, ardından fan havalandırması gibi tekniklerle ısı dağılımını artırarak hafifletilebilir[67]. Ayrıca, beslenme düzenlemeleri (besleme zamanlarını daha serin saatlere kaydırmak ve Toplam Karma Rasyon (TMR) veya Kısmen Karma Rasyon (PMR) kullanmak gibi) baskın ineklerin yem alımını artırarak ve yem seçimini sınırlayarak stres dayanıklılığını daha da destekleyebilir. Canlı maya ve probiyotikler (DFM'ler) gibi yem katkı maddeleri, termal stres sırasında rumen verimliliğini artırarak da yardımcı olabilir[68].

Sosyal stresi yönetmek için uygun yerleşim sıklığını korumak oldukça önemlidir. Bu, ahır kapasitesini beslenme, içme ve dinlenme için yeterli alan sağlayacak şekilde planlamayı ve mümkünse ilk ve çok doğum yapmış inekler için ayrı barınaklar sağlamayı içerir[69]. Sosyal

uyumu sağlamak için, minimum düzeyde yeniden gruplaşma yaparak ve gerektiğinde saldırganlığı azaltmak amacıyla birkaç yeni hayvanı birden getirerek istikrarlı gruplar oluşturulabilir[69]. Öngörülebilir bir sosyal ve fiziksel ortam, stresle başa çıkmada daha etkili olabilir.

Ayrıca, akıllı aydınlatma sistemleri gibi yenilikler de faydalı olabilir. İneklerin sirkadiyen ritimlerini bozmadan, hem dinlenme hem de gerekli aktivitelerini desteklemek için kırmızı ışık içeren, 16 saat ışık ve ardından 8 saat karanlık olacak şekilde bir aydınlatma programı uygulanabilir[70]. Davranışsal ihtiyaçlarını karşılamak için kaşınma fırçaları gibi çevresel zenginleştirmeler kullanılabilir.

Sonuç olarak, iyi yönetim uygulamaları esastır. Aşırı kalabalıklık, özellikle hassas dönemlerde (geçiş dönemi gibi) önlenmeli ve ahırlar nominal kapasitelerinin %80'inden fazla doldurulmamalıdır. Ayrıca, dinlenme alanlarının yanı sıra yemlik ve suluklara yeterli erişim sağlanmalıdır, çünkü bu kaynaklar uygun yerleşim sıklığı seviyelerinin belirlenmesinde büyük öneme sahiptir[13].

2. SONUÇ

Süt sığırlarının strese karşı verdikleri davranışsal değişiklikler, bu hayvanların birincil ve en acil tepkileridir ve olumsuz koşullarla başa çıkabilmek için uyarlanabilir bir mekanizma olarak görev yapar. Yapılan araştırmalar, yoğun ticari barınma sistemlerinde ağrı, hastalık, termal yük, teknolojik müdahaleler ve sosyal baskılar gibi bir dizi stres faktörünü ortaya koymuş ve her biri farklı davranışsal tepkilere yol açmıştır. Bu değişikliklerin yetiştiriciler ve veteriner hekimler tarafından zamanında tanınması, etkili bir stres yönetimi için kritik öneme sahiptir. Hayvanların refah seviyelerini iyileştirmede erken müdahale, hayati bir rol oynamaktadır.

Hassas hayvancılık teknolojileri, özellikle davranışsal sensörler, akut stres tepkilerini gerçek zamanlı olarak belirleme konusunda umut vaat etmektedir. Bununla birlikte, yetiştiricilikte kronik stres genellikle tekrarlayan akut stres ataklarından kaynaklanmaktadır[13]. Ancak, kronik olarak stresli sığırların akut stres olaylarına nasıl tepki verdiği konusunda ampirik veri eksikliği devam etmektedir ve bu durum daha fazla araştırma yapılması gerektiğini göstermektedir. Otomatik sistemler aracılığıyla beslenme ve yatma davranışlarının izlenmesi, kronik stresin erken tespitini artırabilir ve bunun sonucunda hem hayvan refahını hem de sürü üretkenliğini iyileştirebilir.

Davranışsal stres tepkilerini değerlendirirken, hayvanların mizaç ve başa çıkma tarzlarındaki farklılıklar göz önünde bulundurulmalıdır. Ayrıca, veteriner hekimler ve yetiştiriciler arasındaki ağrı algısı ve yönetimi konusunda var olan tutarsızlıklar[13], davranışsal tepkilerin önemini vurgulamaktadır. Gelecekte, doğrulanmış davranışsal değerlendirmelerin başa çıkma stratejileriyle birleştirilmesi, süt sığırlarında stres ve refah anlayışını geliştirmede önemli bir adım olacaktır.

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THE POSSIBLE IMMUNOSUPPRESSIVE EFFECT OF MIR375 AND MIR223 IN PREGNANCY AND IN CANCER

ABSTRACT

Introduction: Since tumor and trophoblast cells have similar immunosuppressive mechanisms, there has been interest in the molecular connections between pregnancy and cancer in recent years. Immunosuppression, which allows the fetus to develop during pregnancy, causes cancer progression in cancer patients. It has been shown that microRNAs (miRNAs) that can remain stable in many fluids such as plasma and play a role in many biological functions such as immune response. Therefore, in the current study, the expression levels of miRNAs, MIR375 and MIR223, that thought to be related to maternal immune response, were examined in the plasma of healthy pregnant women.

Material and Method: 152 healthy pregnant women from different trimesters and 48 healthy non-pregnant women were included in the study. Expression levels of MIR375 and MIR223 in maternal plasma were determined using real-time polymerase chain reaction (RT-PCR). miRNA expression data were calculated using log2-delta delta CT ($2^{-\Delta\Delta Ct}$) analysis. Statistical significance of miRNA expression was determined using one-way ANOVA test.

Results: No significant difference was observed between pregnant and non-pregnant women in terms of expression levels of MIR375 and MIR223 ($p>0.05$). However, after grouping pregnant women according to their trimesters, it was observed that the expression level of maternal MIR223-3p increased in the second trimester and in the first half of the third trimester, and the expression level of MIR375-3p increased in the first trimester and in the second half of the third trimester ($p=0.046$ and $p=0.033$, respectively).

Conclusion: Our findings indicate that the expression levels of MIR375-3p and MIR223-3p change during healthy pregnancy. Analysis of maternal cancer-associated miRNAs during

healthy pregnancy may shed light on the dynamic interactions between cancer immunity and similar biological processes.

Keywords: Gebelik, kanser, MIR375, MIR223, RT-PCR

MIR375 VE MIR223'ÜN GEBELIKTE VE KANSERDE OLASI BAĞIŞIKLIK BASKILAYICI ETKİSİ

ÖZET

Giriş: Tümör ve trofoblast hücrelerinin benzer immünosüpresif mekanizmaları olduğundan, son yıllarda gebelik ve kanser arasındaki moleküler bağlantılara ilgi duyulmaktadır. Gebelikte fetusun gelişmesine fırsat veren immüosüpresyon, kanser hastalarında kanserin ilerlemesine sebep olmaktadır. Plazma gibi birçok sıvıda stabil kalabilen mikroRNA (miRNA)'ların immün yanıt gibi birçok biyolojik işlevde görev aldığı gösterilmiştir. Bu nedenle, mevcut çalışmada, sağlıklı gebe kadınların plazmasında, maternal immün yanıtla ilişkili olduğu düşünülen miRNA'lar olan MIR375 ve MIR223'ün ifade düzeylerine bakılmıştır.

Materyal ve Metod: Çalışmaya farklı trimesterlerden 152 sağlıklı gebe kadın ve 48 sağlıklı gebe olmayan kadın dahil edilmiştir. Maternal plazmada, MIR375 ve MIR223'ün ifade düzeyleri, gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) kullanılarak belirlenmiştir. miRNA ifade verileri log2-delta delta CT ($2^{-\Delta\Delta Ct}$) analizi kullanılarak hesaplanmıştır. miRNA ifadesinin istatistiksel önemi, one-way ANOVA testi kullanılarak belirlenmiştir.

Bulgular: MIR375 ve MIR223'ün ifade düzeyleri açısından, gebe ve gebe olmayan kadınlar arasında anlamlı bir fark gözlenmemiştir ($p>0,05$). Fakat, gebe kadınlar trimesterlerine göre gruplandırıldıktan sonra, maternal MIR223-3p'nin ifade düzeyinin ikinci trimesterde ve üçüncü trimesterin ilk yarısında, MIR375-3p'nin ifade düzeyinin ise birinci trimesterde ve üçüncü trimesterin ikinci yarısında arttığı gözlemlenmiştir (sırasıyla $p=0,046$ ve $p=0,033$).

Sonuç: Bulgularımız, MIR375-3p ve MIR223-3p'nin ifade düzeylerinin sağlıklı gebelik sırasında değiştiğini göstermektedir. Sağlıklı gebelik sırasında maternal kanserle ilişkili miRNA'ların analiz edilmesi, kanser bağışıklığı ve benzer biyolojik süreçler arasında meydana gelen dinamik etkileşimlere ışık tutabilir.

Anahtar Kelimeler: Gebelik, kanser, MIR375, MIR223, RT-PCR

1. INTRODUCTION

A mother's tightly regulated biological mechanisms enable mother to tolerate the semi-allogeneic fetus for a predetermined period of time throughout pregnancy, which is an immunological event. The primary mechanism behind this process is the placental syncytiotrophoblast cells' ability to regulate migration and invasion into the maternal decidua while simultaneously fostering immunological tolerance, even though the precise mechanisms are still unclear (Goldman-Wohl and Yagel, 2002).

Pregnancy and cancer are similar in that they both begin with individual cells that divide, infiltrate, and regulate the immune system in similar ways. Since tumor and trophoblast cells have similar immunosuppressive mechanisms, there has been interest in the molecular connections between pregnancy and cancer in recent years (Holtan et al., 2009; Manzo, 2019). Immunosuppression, which allows the fetus to develop during pregnancy, causes cancer progression in cancer patients.

It has been shown that microRNAs (miRNAs) can remain stable in many fluids such as plasma and can play roles in many biological functions such as immune response (Png et al., 2011; Zhou et al., 2012). MIR375 and MIR223 has been widely reported in a range of immunological activities in recent years, indicating that they are critical regulators of cell differentiation and may be involved in immune system regulation (Jiao et al. 2021, Liu et al., 2021; Yuan et al. 2021).

In the current study, the expression levels of miRNAs, MIR375 and MIR223, that thought to be related to maternal immune response, were examined in the plasma of healthy pregnant women.

2. MATERIAL AND METHOD

2.1. Research Participants

This study involved 152 healthy pregnant women in different trimesters (34 in the first trimester, 38 in the second trimester, 33 in the first half of the third trimester, and 47 in the second half of the third trimester) and 48 healthy non-pregnant women who applied to the Gynecology and Obstetrics outpatient clinic at Tokat Gaziosmanpasa University Medical Faculty. Our study was accepted as ethically feasible on May 5, 2020 by the Dean's Office of the Clinical Research Ethics Committee of Tokat Gaziosmanpasa University, Faculty of Medicine (Decision no: 20-KAEK-275).

2.2. Sample Preparation and Real-Time PCR (RT-PCR) Examination

Mother blood samples of five milliliters were put in EDTA tubes and centrifuged for 10 minutes at 3000 rpm. After centrifugation, the plasma was stored at -80°C in microcentrifuge tubes. miRNAs were extracted from these plasma samples using the SanPrep Column microRNA Mini-Preps Kit (Biobasic). cDNA conversion was made by using the cDNA synthesis mix that comes with the Single miRNA qPCR Assay kit (Atlas Biotechnologies, Türkiye). The real-time polymerase chain reaction (RT-PCR) was used to measure the expression levels of MIR375 and MIR223 in maternal plasma. The Ct values of the target gene and the reference gene (Rnu-6) used for normalization were used in the calculations.

2.3. Statistical Analysis

To calculate the miRNA expression data, log2-delta delta CT ($2^{-\Delta\Delta Ct}$) analysis was used. The one-way ANOVA test was utilized to ascertain the statistical significance of miRNA expression. A p-value of less than 0.05 was considered statistically significant, and all p-values were two-tailed.

3. RESULTS

No significant difference was observed between pregnant and non-pregnant women in terms of expression levels of MIR375-3p and MIR223-3p (p>0.05) (Table 1).

Table 1. Expression levels of MIR223-3p, and MIR375-3p in the plasma of pregnant and non-pregnant women

miRNA	Group	N	Expression level ($2^{-\Delta\Delta Ct}$)	p value
MIR223-3p	Pregnant women	152	2.44±2.479	0.195
	Non-pregnant women	48	1.93±1.946	
MIR375-3p	Pregnant women	152	2.08±2.314	0.200
	Non-pregnant women	48	1.63±1.477	

However, after grouping pregnant women according to their trimesters, it was observed that the expression level of maternal MIR223-3p was increased in the second trimester and in the first half of the third trimester, and the expression level of MIR375-3p was increased in the first trimester and in the second half of the third trimester (p=0.046 and p=0.033, respectively) (Table 2).

Table 2. Expression levels of MIR223-3p, and MIR375-3p, in different trimesters of pregnant women and in non-pregnant women

miRNA	Group	N	Expression level ($2^{-\Delta\Delta Ct}$)	p value
MIR223-3p	1. Trimester (1-14 weeks)	34	1.90±1.906	**0.046**
	2. Trimester (15-27 weeks)	38	3.11±2.687	
	3. Trimester (28-33 weeks)	33	2.91±2.807	
	3. Trimester (34-40 weeks)	47	1.96±2.304	
	Non-pregnant women	48	1.93±1.946	
MIR375-3p	1. Trimester (1-14 weeks)	34	2.45±2.486	**0.033**
	2. Trimester (15-27 weeks)	38	1.68±1.866	
	3. Trimester (28-33 weeks)	33	1.39±1.819	
	3. Trimester (34-40 weeks)	47	2.63±2.678	
	Non-pregnant women	48	1.63±1.477	

4. DISCUSSION

miRNAs, single-stranded, short (19–25 nucleotides), nonprotein-coding RNAs, has the potential to create an additional category of molecular markers. miRNAs function in a variety of biological processes, including immune response (Baehrecke, 2003; Calin et al.,

2005). A number of miRNAs have been demonstrated to exist in body fluids and other extracellular spaces, including plasma, in a constant cell-free form (Kibel, 2009; Alečković and Kang, 2015).

In recent years, MIR375 has been widely reported in a range of immunological activities, indicating that it is a critical regulator of cell differentiation and may be involved in immune system regulation (Liu et al., 2021). In our investigation, we found that pregnant women's plasma had increased levels of MIR375-3p, particularly during the first trimester and the second half of the third trimesters of pregnancy, when the immunological response is crucial for the mother's immune system to accept the fetus. MIR375 has been found to be a tumor suppressor in numerous gain-of-function and loss-of-function studies in cancer cells, per related papers (Liu et al., 2021).

MIR223 may be crucial for immunological tolerance and can change cytokine signaling (Bhati et al., 2023). Numerous investigations have revealed that MIR223 is dysregulated in infectious illnesses and can influence inflammation by targeting multiple immune-related genes (Jiao et al. 2021, Yuan et al. 2021). Problems during pregnancy may be associated with irregular MIR223 expression (Song et al., 2024). It is noteworthy that a similar study discovered that the serum levels of MIR223 were abnormally elevated in patients with gestational diabetes (Dinesen et al. 2023). Another study discovered that the placentas of patients with pregnancy-induced hypertension express MIR223 less frequently (Xu et al. 2014). MIR223 levels were discovered to be higher in biological fluids (mostly serum or plasma) in some malignancies compared to healthy people or people with lower-risk situations (Barbagallo et al., 2024). In healthy pregnant women, we observed elevated plasma levels of MIR223 during the second trimester and the first half of the third trimester. Differences in sample selection could be one reason for the discrepancies in the results.

In conlusion, our findings indicate that the expression levels of MIR375-3p and MIR223-3p change during healthy pregnancy. Analysis of maternal cancer-associated miRNAs during healthy pregnancy may shed light on the dynamic interactions between cancer immunity and similar biological processes.

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THE SIMILAR PROLIFERATIVE EFFECT OF MIR451A AND MIR141 IN PREGNANCY AND CANCER

ABSTRACT

Introduction: Molecular connections between cancer and pregnancy have recently attracted attention due to the comparable proliferative pathways of tumor and trophoblast proliferation. MicroRNAs (miRNAs) that can be found in stable form in many fluids including plasma have been shown to play a role in various biological pathways such as oncogenesis, differentiation, development, and apoptosis. The present study aimed to determine the expression levels of cell cycle-related miRNAs MIR451A and MIR141 in the plasma of healthy pregnant women.

Material and Method: 48 healthy non-pregnant women and 152 healthy pregnant women from different trimesters were included in the study. Real-time polymerase chain reaction (RT-PCR) method was used to analyze the expression levels of MIR451A and MIR141 isolated from maternal blood. Log2−delta delta CT ($2^{-\Delta\Delta Ct}$) analysis was performed to calculate miRNA expression data. One-way ANOVA test was used to evaluate the statistical significance of miRNA expression.

Results: A statistically significant difference was found in the expression levels of MIR451A between pregnant and non-pregnant women (p=0.004). After classifying pregnant women according to their trimesters, maternal MIR451A expression levels in plasma were found to be high in all trimesters (p=0.027), while MIR141-3p expression levels were high in the second trimester and the first half of the third trimester (p=0.000).

Conclusion: According to our findings, the expression levels of MIR451A and MIR141-3p change throughout healthy pregnancy. By analyzing miRNAs, associated with cancer proliferation, during healthy pregnancy, dynamic relationships between cancer metastasis and pregnancy can be understood due to comparable biological pathways.

Keywords: Pregnancy, cancer, MIR451, MIR141-3p, RT-PCR

MIR451A VE MIR141'İN GEBELİK VE KANSERDE BENZER PROLİFERATİF ETKİSİ

ÖZET

Giriş: Kanser ve gebelik arasındaki moleküler bağlantılar, tümör ve trofoblast çoğalmasının karşılaştırılabilir proliferatif yolları nedeniyle son zamanlarda dikkat çekmektedir. Plazma dahil pekçok sıvıda kararlı halde bulunabilen mikroRNA (miRNA)'ların, onkogenez, farklılaşma, gelişim ve apoptoz gibi çeşitli biyolojik yolaklarda rol oynadığı gösterilmiştir. Mevcut çalışma ile, sağlıklı gebe kadınların plazmasında, hücre döngüsü ile ilişkili miRNA'lar olan MIR451A ve MIR141'in ifade seviyelerinin belirlenmesi amaçlanmıştır.

Materyal ve Metod: Çalışmaya 48 sağlıklı gebe olmayan kadın ve farklı trimesterlerden 152 sağlıklı gebe kadın dahil edilmiştir. Maternal kandan izole edilen MIR451A ve MIR141'in ifade seviyelerini analiz etmek için gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) yöntemi kullanılmıştır. miRNA ifade verilerini hesaplamak için Log2−delta delta CT ($2^{-\Delta\Delta Ct}$) analizi yapılmıştır. miRNA ifadesinin istatistiksel önemini değerlendirmek için one-way ANOVA testi kullanılmıştır.

Bulgular: Gebe ve gebe olmayan kadınlar arasında, MIR451A'nın ifade seviyelerinde istatistiksel olarak anlamlı bir fark bulunmuştur (p=0.004). Gebe kadınların, trimesterlerine göre sınıflandırılmasının ardından, plazmadaki maternal MIR451A ifade seviyelerinin tüm trimesterlerde yüksek olduğu bulunmuştur (p=0,027), MIR141-3p ifade seviyeleri ise ikinci trimesterde ve üçüncü trimesterin ilk yarısında yüksek çıkmıştır (p=0,000).

Sonuç: Bulgularımıza göre, MIR451A ve MIR141-3p'nin ifade seviyeleri sağlıklı gebelik boyunca değişmektedir. Sağlıklı gebelik sırasında, kanser çoğalmasıyla ilişkili miRNA'lar analiz edilerek, karşılaştırılabilir biyolojik yollardan dolayı kanser metastazı ile gebelik arasındaki dinamik ilişkiler anlaşılabilir.

Anahtar Kelimeler: Gebelik, kanser, MIR451, MIR141-3p, RT-PCR

1. INTRODUCTION

Pregnancy is an immunological event in which the mother's closely controlled biological processes allow her to tolerate the semi-allogeneic fetus for a predefined amount of time. Although the exact mechanisms are yet unknown, the main mechanism underlying this process is the placental syncytiotrophoblast cells ability to control migration and invasion into the maternal decidua while at the same time promoting immunological tolerance (Goldman-Wohl and Yagel, 2002). Similar to this, cancerous tumor cells generate their invasive, immunosuppressive, and proliferative traits by "trophoblast-like" biological processes. Molecular connections between cancer and pregnancy have recently attracted attention due to the comparable proliferative pathways of tumor and trophoblast proliferation (Holtan et al., 2009; Manzo, 2019). During the first trimester of pregnancy, the growth of a fetus and the proliferation of tumor cells are nearly the same.

MicroRNAs (miRNAs) that can be found in stable form in many fluids including plasma have been shown to play a role in various biological pathways such as oncogenesis, differentiation, development, and apoptosis (Png et al., 2011; Zhou et al., 2012). MIR451A and MIR141 are important carcinogens that regulate invasion, apoptosis, cell differentiation, and the cell cycle by acting as a tumor supressor gene and an oncogene, respectively (Bai and Wu, 2019; Yang et al., 2022). It has been demonstrated that MIR141 plasma levels increase during pregnancy and cancer (Mouillet et al., 2010; Mak et al., 2017).

The present study aimed to determine the expression levels of cell cycle-related miRNAs, MIR451A and MIR141, in the plasma of healthy pregnant women.

2. MATERIAL AND METHOD

2.1. Research Participants

152 healthy pregnant women in various trimesters (34 in the first trimester, 38 in the second trimester, 33 in the first half of the third trimester, and 47 in the second half of the third trimester) and 48 healthy non-pregnant women who applied to the Gynecology and Obstetrics outpatient clinic at Tokat Gaziosmanpaşa University Medical Faculty participated in this study.

The Dean's Office of the Clinical Research Ethics Committee of Tokat Gaziosmanpaşa University Faculty of Medicine certified our study as ethically feasible on May 5, 2020 (Decision no: 20-KAEK-275).

2.2. Sample Preparation and Real-Time PCR (RT-PCR) Examination

Five milliliters of mother blood samples were placed in EDTA tubes and centrifuged at 3000 rpm for ten minutes. Following centrifugation, the plasma was kept in microcentrifuge tubes at -80°C. These plasma samples were treated with the SanPrep Column microRNA Mini-Preps Kit (Biobasic) to extract miRNAs. The cDNA synthesis mix included in the Single miRNA qPCR Assay kit (Atlas Biotechnologies, Türkiye) was used to convert the cDNA. The expression levels of MIR451A and MIR141 in maternal plasma were assessed using the real-time polymerase chain reaction (RT-PCR). The Ct values of the target gene and the reference gene (Rnu-6) used for normalization were used in the calculations.

2.3. Statistical Analysis

The miRNA expression data were computed using log2-delta delta CT (2-ΔΔCt) analysis. The statistical significance of miRNA expression was determined using the one-way ANOVA test. All p-values were two-tailed, and a p-value of less than 0.05 was regarded as statistically significant.

3. RESULTS

A statistically significant difference was found in the expression levels of MIR451A between pregnant and non-pregnant women (p=0.004) (Table 1).

Table 1. Expression levels of MIR451A, and MIR141-3p in the plasma of pregnant and non-pregnant women

miRNA	Group	N	Expression level ($2^{-\Delta\Delta Ct}$)	p value
MIR451A	Pregnant women	152	2.78±2.221	**0.004**
	Non-pregnant women	48	1.73±1.986	
MIR141-3p	Pregnant women	152	2.10±2.079	0.182
	Non-pregnant women	48	1.65±1.721	

After classifying pregnant women according to their trimesters, maternal MIR451A expression levels in plasma were found to be high in all trimesters (p=0.027), while MIR141-3p expression levels were high in the second trimester and the first half of the third trimester (p=0.000) (Table 2).

Table 2. Expression levels of MIR451A, and MIR141-3p, in different trimesters of pregnant women and in non-pregnant women

miRNA	Group	N	Expression level ($2^{-\Delta\Delta Ct}$)	p value
MIR451A	1. Trimester (1-14 weeks)	34	2.62±2.305	**0.027**
	2. Trimester (15-27 weeks)	38	3.20±2.490	
	3. Trimester (28-33 weeks)	33	2.89±2.191	
	3. Trimester (34-40 weeks)	47	2.47±1.945	
	Non-pregnant women	48	1.73±1.986	
MIR141-3p	1. Trimester (1-14 weeks)	34	1.06±1.294	**0.000**
	2. Trimester (15-27 weeks)	38	2.40±2.225	
	3. Trimester (28-33 weeks)	33	3.08±2.407	
	3. Trimester (34-40 weeks)	47	1.92±1.841	
	Non-pregnant women	48	1.65±1.721	

4. DISCUSSION

The single-stranded, short (19–25 nucleotides), nonprotein-coding RNAs known as miRNAs have the capacity to generate a new class of molecular markers. Proliferation is one of the many biological processes in which miRNAs are involved (Baehrecke, 2003; Calin et al., 2005). It has been shown that certain miRNAs are consistently found in a cell-free form in

bodily fluids and other extracellular spaces, such as plasma (Kibel, 2009; Alečković and Kang, 2015).

In cancer, MIR451A has been shown to act as a tumor suppressor gene (Bai and Wu, 2019). Overexpression of MIR451A led to increased apoptosis, decreased proliferation, and changed cell cycle distribution (Mamoori et al., 2019). When Vidal et al. (2018) compared the miRNA profiles of embryonic tissues and cancer cell lines, they discovered that MIR451A was strongly expressed in placental tissues but dramatically downregulated in cancer cell lines. However, MIR451A was shown to be present in significant concentrations in pregnant women's plasma throughout all trimesters in our investigation. It's possible that the varied materials under analysis are the cause of this diversity.

It has been demonstrated that MIR141 plasma levels increase during pregnancy (Mouillet et al., 2010). MIR141 plasma levels in the third trimester were reported to be at least five times higher than those in the corresponding placenta tissue. In the initial half of the third trimester, we also found that normal pregnant women had higher maternal plasma levels of MIR141-3p ($p=0.000$). An earlier study found that MIR141 is also a key carcinogen that regulates invasion, apoptosis, cell differentiation, and the cell cycle. According to Mak et al. (2017), it is associated with a poor prognosis, a high rate of lymph node metastases, and distant metastases.

In conclusion, according to our findings, the expression levels of MIR451A and MIR141-3p change throughout healthy pregnancy. By analyzing miRNAs, associated with cancer proliferation, during healthy pregnancy, dynamic relationships between cancer metastasis and pregnancy can be understood due to comparable biological pathways.

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MODERN ASPECTS OF STUDYING THE ISSUE OF DIAGNOSTICS OF INTESTINAL INFECTIONS AMONG CHILDREN

ABSTRACT

In the study of the patterns of development of epidemics of infectious diseases, environmental epidemiology is becoming increasingly important, the main subject of which is the establishment of cause-and-effect relationships between environmental factors and human health. Paraclinic research methods can help in solving the issues of differential diagnosis of viral and bacterial diarrhea: leukocytosis in the general blood analysis is a classic sign of bacterial infection; Detection of leukocytes during coprocytoscopy also indirectly confirms the diagnosis of bacterial/invasive diarrhea (sensitivity of this method 0.73, specificity 0.84) [21]. However, in the early stages of the examination, the registration of moderate leukocytosis, relative neutrophilia is possible even with viral diarrhea, which is often the main reason for the unjustified appointment of antibacterial therapy. In developed countries, the method of determining fecal lactoferrin is widely used (sensitivity of the method is 0.92, specificity is 0.79).

Keywords: acute intestinal infections, children, research, diagnostic

Acute intestinal infections, as the most common infectious diseases in humans, are second in frequency only to acute respiratory viral infections. Changes in the structure of nutrition, water consumption, production technologies, storage and sale of food products are accompanied by changes in the population of microorganisms, their virulence and resistance, the spread of pathogens with multiple resistance to antimicrobial drugs. One of the consequences is the widespread dissemination of dysbiotic disorders in the intestine among the population. A decrease in the colonization resistance of the intestine contributes to the suppression of the functions of the body's immune system, which, in turn, provokes an increase in the incidence of chronic diseases of the digestive tract. All of these processes ultimately lead to a change in the previously prevailing pathogens of acute intestinal infections [1]. Among acute intestinal infections of established etiology, salmonella and shigella are increasingly rare, giving way to viral diarrhea and intestinal opportunistic flora. Previously, pathogenic flora was considered as part of the normal microflora as commensals, now this group of microorganisms is considered the etiological cause of infectious diarrhea.

In the study of the patterns of development of epidemics of infectious diseases, environmental epidemiology is becoming increasingly important, the main subject of which is the establishment of cause-and-effect relationships between environmental factors and human health.

The issues of improving the diagnosis and optimizing the treatment of acute intestinal infections in childhood do not lose their relevance. In recent years, there has been a steady trend towards an increase in the incidence of acute intestinal infections with an average annual growth rate of 6-7% [2].

All acute intestinal infections in children are divided into groups:

1) bacterial intestinal infections: bacterial dysentery (shigellosis), salmonellosis, typhoid fever and paratyphoid fever, escherichiosis (coli infection), cholera, botulism, campylobacteriosis and other intestinal infections caused by anaerobic pathogens;

2) intestinal infections caused by staphylococcus and opportunistic microorganisms (Klebsiella, Citrobacter, Pseudomonas aeruginosa, Proteus).

In recent years, there has been an increase in intestinal infections. In children with a complicated premorbid background, diseases often occur in the form of generalized variants;

3) viral intestinal infections: rotaviruses, noroviruses, sapoviruses, astroviruses, adenoviruses, coronaviruses, enteroviruses;

4) intestinal infections of unknown etiology;

5) combined intestinal infections (mixed infections); 6) intestinal invasions: intestinal amebiasis (amoebic dysentery), giardiasis.

Most often, several pathogenetic mechanisms are realized in intestinal infections, for example, a combination of invasive and secretory in salmonellosis, osmotic and secretory in rotavirus infection. Features of the child's body that contribute to the occurrence of diarrhea:

1) imperfection of physiological barriers, which is manifested by:

- low bactericidal capacity of gastric juice;

- weak mucus-forming function of the child's intestines;

- low production of immunoglobulin A;

2) a smaller supply of nutrients and their rapid consumption in pathology;

3) rapid disruption of the not yet formed intestinal biocenosis in intestinal infections leading to immunological depression;

4) features of water-salt metabolism:

- a large percentage of extracellular fluid, easily lost in intestinal infections;

- high need for water per 1 kg of body weight;

- immaturity of renal and neurohumoral regulatory mechanisms. According to experts from the World Health Organization (WHO), no type of medical institution in any country can claim to be free from the risk of nosocomial infection, which is defined by the modern term - infections associated with the provision of medical care, both during hospitalization and in outpatient settings [3].

Rotavirus and norovirus (infections acquire special significance during the development of AII associated with the provision of medical care. It was previously established that in 2010, 2,518 cases were recorded in children's hospitals, of which 34.8% were AII. At the same time, outbreaks of AII were registered in medical and preventive institutions, in the etiological structure of which 30% were rotavirus and 31.6% is due to norovirus, which dictates the need to establish the importance of AII in the etiological structure associated with the provision of medical care for hospitals with an infectious profile.

Currently, in the clinical picture of AII in children, there is a predominance of gastroenteritis over forms with damage to the large intestine. However, in some patients with rotavirus, there is damage to the colon intestines, manifested by characteristic pains in the abdomen, mainly in the left iliac region, pronounced symptoms of intoxication and a change in the character of the stool (the presence of pathological impurities) and an increase in the number of leukocytes in coprofiltrates more than 10 in the field of vision. At the same time, some authors deny the possibility of developing rotavirus colitis, some attribute these situations to diagnostic errors or insufficient etiological interpretation of combined forms of viral-bacterial AII, which requires clarification of the pathogenetic aspects of colon damage in viral AII of established etiology.

Changing the etiological structure of OKI in children requires rethinking of therapeutic approaches to etiotropic and pathogenetic therapy. It is necessary to determine the location of preparations with antiviral and immunotropic effects. So far, the effectiveness of only umifenovir in the treatment of AII in children older than 3 years has been shown, however, the effectiveness and safety in pediatric practice of release-active preparations and interferons have not been determined to date.

The etiopathogenetic necessity, high efficiency and safety of the use of enterosorbents in acute intestinal diseases have been repeatedly shown earlier. However, the expansion of the currently available range of drugs with sorption action requires a comparative analysis between them to establish their effectiveness and determine the prognosis of the pharmacological expediency of their application in viral striae intestinal infections. Modern

approaches to the therapy of dehydration syndrome imply the use of low-osmolar solutions for oral rehydration - 245 mosmol/l and below. However, evaluation in clinical studies of their effectiveness and safety is presented in the literature by single publications.

Earlier, it was shown that such disorders are noted in Zonne's dysentery in 67.8 - 85.1% of patients, in salmonellosis in 95.1%, and in yersiniosis in 94.9% of patients. However, until now, the place of probiotics in the initial therapy of acute intestinal diseases has not been determined - there is still an opinion that this group of drugs should be used only in the period of convalescence, as a component of rehabilitation therapy. Also, the question of the effectiveness of the application of complex preparations remains open, because international recommendations suggest the use of monocomponent probiotic medicines. The rejection of cultural methods of diagnostics in the world in the last 5-7 years and the lack of universal methods for assessing the microflora of various biotopes of the human body dictate the need to develop new approaches, in particular, the system of integrative assessment of changes in the microflora of the gastrointestinal tract, including acute intestinal diseases, for understanding the pathogenetic mechanisms of the microbiocenosis of the gastrointestinal tract to stress and the direction of correction of these changes. The course of intestinal striae infection in children contributes to the change in the functional state of the kidneys and the formation of pathologies of varying degrees of severity, ranging from mild forms to the development of severe acute kidney damage. Despite numerous studies on the relationship between bacterial infectious diseases and kidney damage, as well as the proven role of viral infections in the development and progression of kidney diseases in children in recent years, an in-depth assessment of the role of infectious diarrhea agents in the formation of acute kidney damage in acute intestinal infections without hemolytic-uremic syndrome in children has not been conducted. The data of the scientific literature is primarily devoted to the problem of typical hemolytic-uremic syndrome in children and in fact does not describe the initial preclinical stages of acute kidney damage. There are practically no studies on the study of impaired kidney function in children who have developed acute cystitis of moderate severity. A number of questions related to the management of children with striae intestinal infections still remain unanswered [4].

Despite modern achievements in the field of laboratory diagnostics and therapy of urgent conditions, the occurrence of fatal outcomes in acute infectious diseases with diarrheal symptoms in children of the first years of life. According to the experts of the World Health Organization, in 2010. acute diarrheal diseases caused 11% of all deaths of children in the first 5 years of life on the planet, giving way to acute pneumonia (18%). In the European region, acute diarrheal infections accounted for 13% of the total number of deaths in children under 5 years of age. American researchers report 150-250 million annually registered cases of infectious diarrhea; about 450 thousand. adults and 160 thousand. Children are hospitalized in hospitals, and more than 300 cases end in death.

A necessary condition for adequate therapy of acute intestinal infections is timely diagnosis of the disease, including preliminary clinical (stage I) and final laboratory diagnostics (stage II). At the first stage of the examination, the doctor's task is to establish the probable causes of the disease (determine the infectious nature of the disease and exclude acute surgical pathology), assess the severity of the disease, risk factors for adverse course and the need to prescribe rehydration therapy. Even before laboratory confirmation, a possible cause of AII (viral or bacterial) can be assumed taking into account the main etiopathogenetic groups of diarrhea: invasive (predominantly bacterial etiology) and watery (predominantly viral etiology). However, in real clinical practice, this separation is conditional, since both

mechanisms of development are possible with the same infections, and the combination of different pathogens (viral-bacterial, bacterial-bacterial) can significantly change the clinical picture of the disease. The assessment of the severity of the infectious process is based on the severity of intoxication, dehydration and/or the degree of damage to the gastrointestinal tract. Obliterated forms of acute intestinal infections have minimal clinical manifestations on the part of the gastrointestinal tract (increased to 3-4 times/day mushy stool) in the absence of symptoms of intoxication and impaired well-being. They usually take place in the foci of infection during targeted inspection of contact persons. The mild form of the disease is characterized by moderate intoxication (body temperature not higher than 38–38.5°C) and moderate diarrheal syndrome (stool up to 6–7 times/day without significant fluid loss). Most often, this form occurs with low virulence of the pathogen, with a contact-household route of infection, or with a small amount of the pathogen. The medium-severe form of the disease - the most common and the most favorable for the development of post-infectious immunity - is characterized by severe intoxication (body temperature up to 39-39.5°C, headache, dizziness, lethargy) and a pronounced local syndrome (abdominal pain, flatulence, stool up to 10–12 times/day, water loss with stool, exicosis I or I–II). A severe form of acute intestinal infection develops with high virulence of the causative agent, in children of the risk group (with reduced immunity), with a massive dose of the causative agent, which is realized during the food route of infection, especially during secondary heat treatment (heating) of food, when a large amount of bacterial toxins enters it. It is characterized by a pronounced local syndrome (stool "without an account" or with a very large loss of water) and the development of a number of severe syndromes that require urgent therapy (infectious toxic shock, infectious toxicosis, exicosis II and III and their complications - the syndrome of disseminated intravascular coagulation, acute renal failure, hemolytic-uremic syndrome). In addition to the severity of intoxication and the degree of damage to the gastrointestinal tract, the severity of OKI in children is largely determined by the volume of fluid loss. At the same time, the correctness of the assessment of the degree of dehydration of the patient acquires special importance [5].

Establishing the etiopathogenetic group of diarrhea is an important component of therapy tactics: watery diarrhea in most cases is caused by viruses and requires the appointment of antiviral drugs as an etiotropic therapy, invasive - refers to bacterial AII, which dictates the need to consider antibacterial therapy.

According to the form of severity, acute intestinal infections are divided into mild, medium and severe. Establishing the severity of the disease is carried out by means of an integral analysis of clinical data in three blocks:

1. prevalence of damage to the gastrointestinal tract and other organs by an infectious process;

2. the intensity of manifestation of the main clinical symptoms of the disease;

3. objectification of the mourning patient [4].

Symptoms from the list presented in blocks are evaluated according to their presence (yes or no - block 1), and also according to the intensity of their manifestations in accordance with the proposed scale (blocks 2 and 3). Not all clinical manifestations of this disease, presented in blocks, may be noted in the patient. In this case, the assessment is based on the existing symptoms, absent manifestations of the disease are not taken into account. This method of integral evaluation of clinical data is applicable both in therapeutic and pediatric practice.

Differential diagnosis of acute intestinal infections is based on the clinical features of the leading syndromes - gastrointestinal tract damage, intoxication syndrome and dehydration development (Table 4) and clinical and laboratory confirmation of the etiology of the disease (Table 5). Clinical and laboratory examination of patients with OCI should be carried out in stages:

• 1st stage – preliminary clinical diagnosis;

• 2nd stage – final diagnosis based on the results of laboratory and instrumental diagnostic methods, assessment of further dynamics of clinical manifestations of the disease;

• 3rd stage – diagnosis in the period of recovery (estimation of recovery from the pathogen, state of the organs of the hepatobiliary system, microflora of the gastrointestinal tract, etc.).

The effectiveness of laboratory diagnostics of infectious diarrhea can be changed quite successfully. Thus, it significantly increases with targeted collection of epidanamnesis and correct clinical examination of the patient. For example, the probability of isolation of the pathogen in hemocolitis of an infectious nature increases from 1.5% to 87%, and among the causes of this pathological condition, according to American researchers, Shigella (49% of isolates), campylobacter (20%), salmonella (19%) and enterohemorrhagic Escherichia coli (ЕГКП) O157:H7 (8%) are most often detected [12]. The cause of this clinical variant of OKI in 17.1% is salmonella, less often campylobacter and klebsiella (8.6% each) [8]. If the hemocolitis clinic is not accompanied by a febrile reaction, then in the overwhelming majority of cases it is associated with ЕГКП O157:H7 [12].

Paraclinic research methods can help in solving the issues of differential diagnosis of viral and bacterial diarrhea: leukocytosis in the general blood analysis is a classic sign of bacterial infection; Detection of leukocytes during coprocytoscopy also indirectly confirms the diagnosis of bacterial/invasive diarrhea (sensitivity of this method 0.73, specificity 0.84) [21]. However, in the early stages of the examination, the registration of moderate leukocytosis, relative neutrophilia is possible even with viral diarrhea, which is often the main reason for the unjustified appointment of antibacterial therapy. In developed countries, the method of determining fecal lactoferrin is widely used (sensitivity of the method is 0.92, specificity is 0.79).

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THE ROLE OF SOCIO – ECONOMIC FACTORS IN SHAPING NUTRITION PATTERNS IN AZERBAIJAN

ABSTRACT

This study explores the impact of socio-economic factors on the dietary behaviors of the Azerbaijani population. It examines the roles of variables such as income level (low, middle, and high-income families), education level, age, and gender through a comparative analysis. The primary objective is to investigate in greater detail how income level influences dietary behaviors and to propose effective healthy eating promotion strategies tailored to each social group.

Findings indicate that socio-economic disparities significantly shape dietary habits, with nutrition-related issues differing across income levels. This article not only addresses a notable gap in research on dietary behaviors in Azerbaijan but also contributes to the formulation of new, targeted nutrition programs.

Keywords: *Dietary behaviors, socio-economic factors, healthy eating, income level, education level, age, gender, health policy.*

Worldwide, non-communicable diseases (NCDs) are considered one of the greatest threats to public health. According to the World Health Organization's (WHO) 2023 report, approximately 41 million people die annually due to NCDs, accounting for about 74% of global deaths (WHO, 2023). One of the main risk factors for these diseases is disrupted dietary behavior. Specifically, excessive consumption of high-calorie, low-nutrient foods, decreased physical activity, and irregular eating patterns accelerate the development of NCDs.

In recent years, the increase in nutrition-related issues and the impact of unhealthy eating on global health and economies have become one of the main causes of current healthcare challenges. This situation is especially pronounced in developing and low-income countries. Socio-economic status is one of the strongest determinants of health behavior across all age groups. Large epidemiological studies have shown that higher socio-economic status is associated with healthier eating habits, including the consumption of more fruits and vegetables, lean meats, dairy products, and limited amounts of carbohydrates, all of which are easily digestible [1, 2]. These associations have been observed to be stronger in high-income countries compared to middle- and low-income countries. Low-income respondents have repeatedly cited economic factors as the main barriers to maintaining a healthy diet [3].

Research conducted in Western countries has shown that low-income individuals tend to consume more grains, potatoes, processed meats, eggs, fats, and sweets, while high-income individuals consume more whole-grain bread, fruits, vegetables, lean meat, fish, dairy products, and seafood [3]. In Japan’s National Health and Nutrition Survey (NHNS), low- and middle-income families reported higher consumption of grains, potatoes, starches, and legumes, and lower consumption of vegetables, fruits, mushrooms, fish and seafood, dairy, and spices compared to high-income families. These findings indicate significant differences in food consumption patterns across families with varying income levels in different countries [4].

In recent years, socioeconomic differences, particularly income levels, have led to variations in dietary habits in Azerbaijan. For instance, middle- and high-income families tend to prefer diets rich in fresh fruits and vegetables, while low-income families gravitate toward cheaper, lower-quality foods. Such disparities ultimately increase the risk of non-communicable diseases (NCDs) such as obesity, diabetes, and cardiovascular diseases. According to a 2020 WHO report, unhealthy eating habits are more prevalent among low-income families, contributing to increased health problems in these populations.

Socioeconomic status directly impacts food security, diet quality, and overall health status. Most studies emphasize the influence of socioeconomic factors on eating behaviors, highlighting their effects on health outcomes and healthcare costs. For example, Mayen AL et al. (2014) observed that individuals with relatively higher social status in low- and middle-income countries exhibit healthier dietary behaviors, while also consuming more calories, cholesterol, and saturated fats per day [1]. In addition to food stereotypes, dietary diversity is influenced by the socioeconomic characteristics of one’s living area, as well as individual education and income levels [5]. The phenomenon of different eating behaviors among populations with varying income levels still requires further explanation and research. However, evidence suggests that an individual’s socioeconomic status may have a stronger influence on their dietary behavior than the socioeconomic characteristics of the area they live in [5].

Thus, the relationship between eating behaviors and socioeconomic factors is of great significance both scientifically and practically. Addressing these issues may present new challenges for the organization and development of healthcare systems. To improve the effectiveness of health policies, reduce unhealthy eating behaviors, and eliminate socioeconomic inequalities, it is necessary to implement a range of new measures. Additionally, raising public awareness through educational campaigns and expanding social support programs would be beneficial for enhancing diet quality across various social groups.

Recent research shows that the economic and social impacts of obesity and other NCDs are expanding. For example, a study published in The Lancet estimates that the economic burden of diet-related diseases will exceed $2.1 trillion globally between 2019 and 2030 (Lancet, 2020). This highlights the importance of properly managing resources, as rising healthcare costs place financial strain on healthcare systems. Vegetables and fruits, recognized as essential components of a healthy diet, account for a significant portion of dietary expenses. Data from the Encuesta Nacional de Salud y Nutrición (ENSANUT 2012) indicate that high-calorie foods, fats, and sweets are less costly per calorie than dairy products, meat, vegetables, and fruits [6]. Many studies have identified that fruits, vegetables, fresh meat, and fish contribute the most to diet costs [7, 8].

In addition to economic constraints, low-income individuals face several additional challenges related to food choices and eating behaviors. It is hypothesized that poverty activates biological and psychological mechanisms — such as endocrine, immune, and neurological responses — that affect food choice and consumption. Living in poverty can directly impact stress levels, sleep quality, and cognitive performance. The body's biological response activates hormones that regulate stress, appetite, and hunger by signaling the hypothalamus, influencing eating behaviors. Combined with reduced purchasing power for healthy foods, this leads to a decline in diet quality [9].

Therefore, the research supports the hypothesis that food prices influence diet quality and that diet should be considered one of the key social determinants of health.

In the Azerbaijani context, this issue is particularly significant. According to the 2021 data from the State Statistical Committee of the Republic of Azerbaijan, 29% of the population is affected by obesity, and 33% suffer from high blood pressure. These figures highlight the growing prevalence of NCDs in the region and emphasize the need to correct dietary behaviors to prevent these diseases. Additionally, cases of unbalanced nutrition and physical inactivity are widespread among schoolchildren and young people (Ministry of Education of the Republic of Azerbaijan, 2022).

The WHO's Global Strategy on Diet, Physical Activity and Health stresses that governments should integrate preventive measures more closely into healthcare systems to curb the spread of NCDs (WHO, 2019). In recent years, Azerbaijan has taken steps in this direction by adopting national strategies on nutrition. However, more effective approaches are needed to promote behavior change and public awareness.

Research Objective:

The research aims to analyze the eating behaviors of the Azerbaijani population across various socioeconomic groups (low, middle, and high-income families) and investigate the relationship between these behaviors and socioeconomic factors. Additionally, the study

seeks to assess the impact of dietary differences on public health, NCDs (obesity, diabetes, cardiovascular diseases), and overall quality of life.

Moreover, by exploring the influence of socioeconomic factors on dietary behaviors, the research aspires to provide recommendations for the Azerbaijani healthcare system to develop more targeted interventions promoting healthy eating and healthy lifestyles.

Materials and Methods:

The study involved 450-600 respondents from low, middle, and high-income families in Azerbaijan, with 150-200 respondents selected from each socioeconomic group. A stratified random sampling method was used to ensure the representation of individuals from different socioeconomic backgrounds.

Selection criteria:

• Respondents aged 18-60 years

• Families categorized into low, middle, and high socioeconomic groups

• Data collected in compliance with ethical standards and with informed consent from respondents

Data collection was conducted through structured questionnaires, covering dietary habits, food choices, health status, socioeconomic conditions, income levels, and other demographic factors. Respondents filled out the questionnaires themselves, though interviews were conducted in some cases to clarify responses.

The questionnaire aimed to identify the relationship between dietary behaviors and socioeconomic factors within each group (low, middle, and high-income families) and to assess health status and the influence of socioeconomic factors. The responses were analyzed to reveal differences and general trends across socioeconomic groups.

The data analysis was carried out using both quantitative and qualitative methods:

• Descriptive statistical analysis: To examine respondents' demographic characteristics (age, gender, education, income level, etc.) and general eating behaviors.

• Correlation analysis: The relationship between dietary behaviors and socioeconomic factors was evaluated using the Spearman correlation test. Below is a structured table summarizing the results of the chi-square test and the Spearman correlation test.

Results and Discussion of the Study:

As a result, the analysis conducted clearly reveals the relationship between nutritional behaviors and socioeconomic status. Statistical analyses distinctly show the differences among low, middle, and high-income families, and based on this data, suggestions can be made regarding healthy nutrition policies and promotion measures.

Additionally, when interpreting the results, it becomes possible to better understand the impact of socioeconomic factors on nutritional behaviors and their connection to health status.

The relationship between income level and eating behavior disorders was found to be $X^2 = 12.28$ ($P < 0.05$).At the same time, it was confirmed that as income level increases, the decrease in eating behavior disorders is strongly associated with a negative correlation ($p = -0.98$).

The overall results of nutrition habits, health status, and income levels based on a total of 600 respondents. The study comparatively examines the impact of socioeconomic factors on dietary behaviors across different socioeconomic groups (low, middle, and high-income families) in Azerbaijan. Additionally, as one of the studies conducted in this field within the Azerbaijani context, it contributes to a more in-depth analysis of socioeconomic differences in eating habits.

Conclusion:
Awareness programs on nutrition should be organized for the low-income population, offering them cheaper but healthier alternatives. Furthermore, campaigns should be conducted to raise awareness of the negative health impacts of fast food consumption, utilizing mass media (TV, social media, radio). Relevant laws could also be introduced to limit trans fats and sugar content in fast food products.

Such findings and recommendations summarize the main results of the research and can contribute to significant steps toward regulating eating behaviors and preventing non-communicable diseases in the future.

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ANALYSIS OF THE IMPACT OF OPTIMIZED TREATMENT ON THE VOLUME OF MYOMATOUS NODES IN UTERINE MYOMA

ABSTRACT

The aim of research was analysis of the ımpact of optimized treatment on the volume of myomatous nodes in uterine myoma. The study material included 200 patients with uterine fibroids of various sizes and shapes admitted to the Research Institute of Obstetrics and Gynecology in the period from 2019 to 2022. The patients were divided into 4 groups: Group I consisted of 50 patients who underwent surgical treatment of uterine fibroids; Group II - 50 women treated with magnetized water; Group III included 50 women treated with a drug containing zeolite; Group IV: 50 women receiving hormonal treatment. According to the results of the study, the use of zeolite and magnesium water can be considered an optimised method for treating uterine fibroids.

Keywords: uterine myoma, zeolite, magnetized water, myomatous nodes, volume

In our study, we aimed to determine the change in the volume of myomatous nodes as the main marker for determining the effectiveness of the treatment methods we used, namely the method of treatment with magnetized water and zeolite. According to the researchers, the type of myomatous nodes, i.e. their location and size, are of great importance in treatment [3].

As the main marker for determining the effectiveness of the proposed treatment methods, we used a change in the size of the nodes. The change in the size of the uterine myoma was determined using two-dimensional ultrasound. The true causes of the increase in uterine myoma remain a subject of debate [4]. The effectiveness of treatment measures is manifested in a reduction in its volume.

Materials and methods of the study. The study material included 200 patients with uterine fibroids of various sizes and shapes admitted to the Research Institute of Obstetrics and Gynecology in the period from 2019 to 2022. The patients were divided into 4 groups: Group I consisted of 50 patients who underwent surgical treatment of uterine fibroids; Group II - 50 women treated with magnetized water; Group III included 50 women treated with a drug containing zeolite; Group IV: 50 women receiving hormonal treatment.

The average age in the surgical treatment group was 36.86 years, in the hormonal treatment group - 37.94 years, in the magnetic water group - 36.24 years and in the zeolite group - 35.28 years. As can be seen, there were no differences in age between the groups. The number of nodes in different groups varied. Patients with the highest number of nodes (11–15 nodes) were in group III, which accounted for 54%. Patients with a small number of nodes (1 to 5 nodes) were included in group IV, accounting for 58%. Subserosal node accounted for 38% in group I, 22% in group II, 24% in group III, and 38% in group IV; submucosal node accounted for 46% in group I, 22% in group II, 18% in group III, and 18% in group IV; intramural node accounted for 16% in group I, 56% in group II, 58% in group III, and 44% in group IV.

The situation in the groups was different depending on the size of the nodes. Thus, patients with a volume of up to 15 cm3 made up 38% in the II group, 42% in the III group, and 44% in the IV group. In group I, that is, in the group of patients who underwent surgical treatment, there were no nodules of small sizes. Patients with a volume of 16-100 cm3 were registered in 24% of the I group, in 38% of the II group, in 52% of the III group and in 44% of the IV group. Patients with large volumes, more than 101 cm3, more often fell into group I, accounting for 48%. Myomatous nodes of this size were recorded in 26% of patients of the II group, in 6% of the III group and in 12% of the IV group.

Thus, in groups I and IV, the traditional tactics of treating uterine fibroids were used. The treatment tactic proposed by us was applied in the II (magnified water) and III (zeolite) groups.

Patients of the II group were treated with magnetized water. Magnetized water is obtained by amplifying the magnetizing effect of water by 50-100 times with the help of a special 3D magnetic matrix in the MAGMATRIX device [1]. The course of treatment was 45 days. The course was repeated in 1 month. The course of treatment lasted 6 months.

The zeolite-containing drug "Tseolimed" was prescribed to patients of group III. We have prescribed a preparation that has antioxidant efficiency and the ability to modulate the

microbiome, with the following dosage and instructions for use: 2 capsules 2 times a day. Course of treatment — 30 days. 1 month break and 1 more course of treatment - 6 months.

Group IV patients underwent hormonal therapy. Patients with small nodules were prescribed Mifepristone [2] at 10–25 mg/day for 3 months. Patients with large nodules were prescribed 25–50 mg/day for 3 months.

Patients with small nodules were prescribed 10–25 mg/day for 3 months. Patients with large nodes were prescribed 25 mg/day [3].

The results. We considered it expedient to use the following classification when determining the volume of the nodule:

- small - lvolume - up to 15 cm^3;
- medium – volume from 15 to 100 cm^3;
- large - volume more than 100 cm^3.

Myomatous nodes with a volume of up to 15 cm^3, as a rule, were not registered before treatment in group I. In group II, a node volume up to 15 cm^3 was detected in 19 (38%) patients, in group II - in 21 (42%), and in group IV in a greater number of cases - in 22 (44%) patients. Myomatous nodes with a volume of 16-100 cm3 were more often detected in group III - in 26 (52%) patients. Nodes with the lower border are found in group I, fixed in 12 (24%) people. Myomatous nodes with a volume of 16 to 100 cm^3 were identified in 19 (38%) people of the II group and in 22 (44%) people of the IV group. The number of myomatous nodes with a volume of more than 101 cm^3 was higher in group I, that is, in the group of patients who underwent surgical treatment, and was detected in 24 (48.0%) patients. In the III group, it occurred less often and was recorded in 3 (6%) patients. Myomatous nodes with a size of more than 101 cm^3 were detected in 13 (26%) patients of group II and in 6 (12%) patients of group IV.

Some statistically significant differences in the average volume of nodules were observed between the groups. A statistically significant difference between groups I (82.85±9.77 cm^3) and II (62.91±26.78 cm^3) was observed in the volume of myomatous nodes 16–100 cm^3 ($p=0,3318$, $p<0,05$). A statistically significant difference in the average volume of nodules with a volume of more than 101 cm^3 was revealed between group I (106,5±3,23 cm^3) and group II (110,66±4,63 cm^3). The average volume of nodes with a volume of more than 101 cm^3 in the II group was statistically significantly higher than in the I group ($p=0,3318$, $p<0,05$).

The studies showed that there were no statistically significant differences between groups II and III in the volume of nodules before treatment ($p<0.05$). There were no statistically significant differences in the volume of nodules between groups II and IV ($p<0.05$). There were no statistically significant differences between groups III and IV in the average volume of nodules ($p<0.05$).

When determining the average volume of dominant nodes before treatment, no statistically significant differences were found between the groups ($p<0.05$).

Certain differences were found in the indicators obtained after treatment. Thus, patients with myomatous nodes after surgery in group I are no longer mentioned. In group II, a greater

number of patients with myomatous nodes up to 15 cm3 after hysterectomy were found in group IV - 25 (50%) patients. After treatment, myomatous nodes with a volume of up to 5 cm3 were detected in 23 (46%) patients of group II and in 24 (48%) patients of group III. The number of patients with a myomatous node volume from 16 to 100 cm^3 was higher in group II and was recorded in 27 (54%) patients. Myomatous nodes with a volume of 16 to 100 cm^3 were detected in 26 (52%) patients of group III and in 22 (44%) patients of group IV. After treatment, myomatous nodes larger than 101 cm3 were not detected in patients of groups II and II. In group IV, only 3 (6%) patients had nodes of this size. Although they decreased in size relative to their initial volume, they remain in the range of nodules exceeding 101 cm^3.

We determined the average volume of nodules in patients by groups after treatment. It was found that statistically significant differences in these parameters were observed after treatment. There were no statistically significant differences in the average volume of myomatous nodes in groups II (9.21±1.04 cm3) and III (9.46±1.54 cm3) either up to 15 cm3 or in the range of 16-100 cm3 ($p=0.31732$, $p<0.05$). There were no statistically significant differences in the average volume of myomatous nodes up to 15 cm3 between group II (9.21±1.04 cm3) and group IV (9.17±2.69 cm3) ($p=0.31732$, $p<0.05$). The average values of nodule volumes in the range of 16–100 cm3 showed statistically significant differences between group II (26.44±6.24 cm3) and group IV (50.26±18.57 cm3) after treatment. In group II, as in group IV, the statistics were significantly lower ($p<0.00001$).

There was also a statistically significant difference between groups III (9.46±1.54 cm^3) and IV (9.17±2.69 cm^3) in the average nodule volume up to 15 cm3 after treatment. In group III, as in group IV, the statistics were significantly higher ($p<0.00001$). Statistically significant differences were found in the average volume of myomatous nodes between groups III (24.94±5.82) and IV (50.26±18.57) in the range of 16–100 cm^3. Group III, no myomatosis, node size IV, statistics were honestly low ($p<0.00001$).

After treatment, a comparative analysis of the volume of dominant nodules in the study groups showed that there were no statistically significant differences between groups II (33.3±2.28 cm^3) and III (30.71±2.86 cm^3) ($p<0.05$). In addition, statistically significant differences were calculated between group II (33.3±2.28 cm3) and group IV (95.8±11.16 cm^3). Thus, the volume of the nodule after treatment with magnetized water was statistically significantly less than the volume of the dominant nodule after hormonal treatment ($p=0.00804$; $p<0.05$). After treatment, a statistically significant difference was also determined between groups III (30.71±2.86 cm^3) and IV (95.8±11.16 cm^3) for this indicator. The nodule volume after zeolite treatment was statistically significantly less than the dominant nodule volume after hormonal treatment ($p=0.00578$; $p<0.05$). Thus, treatment with magnetized water and zeolite showed higher efficiency in reducing the dominant nodule volume.

After treatment, the average nodule volume in Group II was 0.25 cm^3 less than in Group III and 0.04 cm^3 more than in Group IV, up to 15 cm^3. Thus, zeolite was somewhat more efficient, although not significantly, in treating myomatous nodules with a volume of up to 15 cm3.

In Group II, the nodule volume decreased more in the range of 16–100 cm^3, on average by 23.84 cm^3 less than in Group III. The nodule volume in Group II was calculated within the range of 16–100 cm^3, in Group IV it was 23.88 cm^3. It follows that treatment with magnetized water was more effective in treating nodules with a volume of 16–100 cm^3.

Nodules larger than 101 cm3 were registered only in group IV after treatment. Both magnetized water and zeolite showed their effectiveness in treating large nodules. There were significant differences in the reduction in the volume of dominant myomatous nodes between the groups. Thus, in group II of patients treated with magnetized water, the volume of the dominant node was on average 114.5 cm^3 before treatment, and 33.3 cm^3 after treatment. This indicates an average reduction in the volume of the dominant node by 81.2 cm^3. In group III, the average volume of the dominant node was 116.33 cm^3 before treatment and 30.71 cm3 after treatment. Thus, after treatment with zeolite, the volume of the dominant myomatous node decreased by an average of 85.62 cm^3. In Group IV, the volume of the dominant myomatous node before treatment was 116.33 cm^3, and after treatment – 95.8 cm3. After hormonal treatment, the volume of the dominant myomatous node decreased by an average of 20.95 cm^3. This also shows that treatment with magnetized water and zeolite is more intensive in achieving effective results.

According to the results of the study, the use of zeolite and magnesium water can be considered an optimised method for treating uterine fibroids.

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STUDY OF DENTAL STATUS IN PATIENTS WITH PERIMUCOSITIS AND PERIIMLANTITIS

ABSTRACT

The aim of this study was to analyze the clinical and dental status of patients with perimucositis and peri-implantitis. After confirmation of the inclusion and exclusion criteria, some subjects were included in the study and this population included individuals who visited the clinic for regular examination of the condition of installed dental implants between 2019 and 2024. The following factors were considered as inclusion criteria: 1. men and women over 18 years old; 2. patients with partial edentia who have at least one implant; 3. prosthesis with cement, screw or mechanical fixation; 4. single and bridge prosthesis. Exclusion criteria from the study: 1. The presence of severe systemic pathologies in patients (oncological diseases, endocrine diseases, tuberculosis, etc.). 2. Pregnancy. 3. Mental illness. 4. Systemic use of any antibiotics or anti-inflammatory drugs during the studies. 5. implants with bone loss >2-3 mm. The patient examination protocol included: a survey to identify complaints and their nature, examination, use of modern diagnostic methods, and, if necessary, consultation with other specialists. According to the initial clinical studies, in all three groups of orthopedic patients, a statistically significant decrease was observed in the periodontal index BOP indicators in the above-mentioned study periods ($p < 0.0001$), compared with the results recorded before treatment.

When studying the level of significance of intragroup differences in the BOP index, the average intragroup difference in the indicators identified in the control group 1 and 3 months after the start of treatment measures was statistically significant ($p = 0.0102$, $t = 2.71$). The level of significance of differences in the BOP index between the groups before and after

Thus, according to the data obtained, statistically significant intragroup change in the average value of the studied bleeding index both after 1 month and after 3 months is recorded in all three study groups ($p <0.05$). Slightly different assessment criteria were revealed when comparing the digital index values between the groups. Thus, statistically significant differences were not found between some groups in the bleeding index on probing (BOP) both before and 1.3 months after treatment.

Keywords: *implant, perimucositis, treatment, dental indexes*

Prosthetics on dental implants for the purpose of replacing lost teeth and restoring the functional state of the dental system has been a very frequently used method of orthopedic treatment in recent years due to the high rates of implant survival [1]. However, there is an obvious fact of frequent cases of negative attitude on the part of patients and significant negative economic consequences due, apparently, to frequent technical and biological complications [2].

Dental implant therapy has become the prosthetic standard of care in modern comprehensive dental care. With increase in placement of dental implants, increase in prevalence of peri-implant diseases have also been reported. 1 Two entities are described within the concept of peri-implant diseases; peri-implant mucositis and peri-implantitis. Peri-implant mucositis is the reversible inflammation in the soft tissue surrounding implants. Peri-implantitis is an irreversible inflammatory reaction involving the underlying supporting bone. 2 The bacteria from dental biofilms are considered as the major etiological factor for peri-implant disease. The associated risk factors for peri-implant diseases are alteration in the balance of host-parasite interaction, cigarette smoking, oral hygiene and history of periodontitis. 3 The other possible factors such as genetic traits and implant surface are under investigation. Porphyromonas gingivalis, Prevotella intermedia and Aggregatibacter actinomycetemcomitans are some of the bacterial species responsible for peri-implant disease. The prosthetic design is also considered as risk factor when the prosthesis obstructs the patient or the dental professional in daily hygiene measures or gaining access to the implant surface. 4 Peri-implantitis is classified based on severity of the disease as Early, Moderate and Advanced. Different methods have been used to assess peri-implant tissue health and to diagnose these disease entities. 3 The diagnostic methods include evaluation of peri-implant microbiota, peri-implant probing, analyses of peri-implant crevicular fluid or saliva and radiographic evaluation of peri-implant bone loss. The treatment modality includes two types: surgical therapy and non-surgical therapy. Mechanical debridement of the implant surface is the commonest treatment employed for peri-implant diseases.

The dental implant has revolutionized oral rehabilitation and become a part of routine treatment in prosthetic rehabilitation. There has been marked advancement in implant design, materials used, and surgical protocols. A high implant survival rate (94.6%) has been reported over a 13.4-year follow-up. [2] Approximately 90% of patients who received an implant were satisfied with their chewing ability and accessibility for plaque control at the implant sites. Despite high long-term survival rates, complications due to peri-implant diseases are frequent and, in severe cases, result in the loss of the implants and their prostheses [3].

Healthy peri-implant soft tissues (termed peri-implant mucosa) can be achieved when an implant is correctly placed (ie in an appropriate three-dimensional position surrounded by an adequate volume of bone) and restored with a well-designed and fabricated prosthesis in a patient with good plaque control and oral health. Following the completion of oral rehabilitation involving dental implants, the clinician should measure and record circumferential peri-implant probing depths and soft tissue levels (four to six sites) to establish a baseline for future comparisons. It is also recommended to assess and record the width of keratinised peri-implant mucosa surrounding the implant.

Healthy peri-implant mucosa should have a similar appearance as that of healthy gingiva. There should be no visual signs of inflammation such as erythema (redness) or oedema (swelling) and when the peri-implant sulcus is probed circumferentially (at four to six sites)

using a periodontal probe with a light probing force (approximately 0.2 N), there should be no bleeding. Histologic features of healthy peri-implant tissues are described in the paper by Araujo in this themed issue [4].

The most probable cause of peri-implantitis may be the penetration of an oral infection into the area of contact between the implant and the bone. The microbial composition of peri-implantitis is currently known and represents a wide variety of aerobes and anaerobes, the presence of which is characteristic of inflammatory processes of the periodontium - gingivitis and periodontitis (Prevotella Intermedia, Porphyromonas Gingivalis, Treponema Denticola, Veillonella spp, Branhamella Catarrhalis). No specific pathogens of oral diseases have been identified. Most of the identified microorganisms are opportunistic, some are saprophytes. Such a high proportion of anaerobic agents and their diversity makes it difficult to identify the leading pathogenic microorganism, which could be the "leader" of the infectious and inflammatory process. It is obvious that it is the combined effect of the most frequently diagnosed pathogens and the peculiarities of the interaction of anaerobic parasitocenosis agents that can largely determine the nature of the inflammatory process in the peri-implant zone, capable of destroying and resorbing bone tissue in the implant area. According to a number of authors, without adequate treatment, mucositis develops into peri-implantitis in 43% of cases within five years, while the presence of maintenance therapy reduces this frequency to 18%.

A number of authors have already conducted studies on the influence of individual factors on the condition of peri-implant tissues. Thus, smoking is the most common and most frequently identified risk factor for peri-implantitis. According to Clementini, the annual rate of bone loss around the implant in smokers is 0.16 mm. The rate and degree of osseointegration of the implant also decreases in smokers. According to Wallowy, cigarette smoking, as well as a history of periodontitis, increases the risk of peri-implantitis by 4.7 times. Speaking about systemic pathology, first of all, it is necessary to pay attention to the presence of diabetes mellitus. It has become customary to put this disease at the forefront of the list of risk factors and relative contraindications to any surgical and periodontal intervention. However, a number of publications do not provide a categorical conclusion regarding the higher frequency of peri-implantitis in patients with diabetes mellitus. High blood glucose levels can affect tissue repair. However, there is no evidence in the literature of a direct relationship between these diseases.

The aim of this study was to analyze the clinical and dental status of patients with perimucositis and peri-implantitis.

Material and methods. After confirmation of the inclusion and exclusion criteria, some subjects were included in the study and this population included individuals who visited the clinic for regular examination of the condition of installed dental implants between 2019 and 2024. The following factors were considered as inclusion criteria: 1. men and women over 18 years old; 2. patients with partial edentia who have at least one implant; 3. prosthesis with cement, screw or mechanical fixation; 4. single and bridge prosthesis. Exclusion criteria from the study: 1. The presence of severe systemic pathologies in patients (oncological diseases, endocrine diseases, tuberculosis, etc.). 2. Pregnancy. 3. Mental illness. 4. Systemic use of any antibiotics or anti-inflammatory drugs during the studies. 5. implants with bone loss >2-3 mm. The patient examination protocol included: a survey to identify complaints and their nature, examination, use of modern diagnostic methods, and, if necessary, consultation with other specialists.

The patients were divided into 3 groups: the main group, the comparison group, and the control group: the control group - 20, in which treatment was limited to traditional methods with hygienic training and professional oral hygiene using special plastic curettes. The comparison group (20 people) received treatment according to the generally accepted standard scheme and with the help of an ultrasonic device (Master Piezon EMS) - with rinsing with a 0.05% chlorhexidine solution. The main group (20 people) received standard therapy with an ultrasonic device (Master Piezon EMS) and applications of oromucosal gel (HY + AL Gel Oromucosal Gel). To assess intergroup differences in the values of the characteristics, Student's t-test and the nonparametric Wilcoxon-Mann-Whitney U-test were used. The results are presented as the arithmetic mean and its standard error (M±m). The statistical difference between the groups was considered significant at a value of $p<0.05$. Statistical processing of the material was performed using a standard software package for applied statistical analysis (Microsoft Excel, Statistica for Windows v. 7.0).

Results of our research. The condition of the periodontium and peri-implant tissues was assessed using clinical methods using periodontal indices to assess the intensity of inflammation - the bleeding index during probing BOP and the gingival index (GI, Loe and Sillness). A comparative assessment of the effectiveness of the application of the proposed agent and a traditional antiseptic, as well as generally accepted basic therapy, was carried out before treatment, as well as after 1 and 3-month periods.

Clinical studies of patients before treatment showed that the greatest decrease in quality of life indicators was demonstrated by patients with perimucositis in the comparison group. An assessment of the comparatively long-term results of the application of the conducted complex treatment and preventive measures showed obvious advantages of the proposed additional therapy in terms of long-term positive dynamics of clinical and functional indicators, in contrast to the control group and the comparison group, as evidenced by the summary data of the tests conducted in all three groups.

According to the initial clinical studies, in all three groups of orthopedic patients, a statistically significant decrease was observed in the periodontal index BOP indicators in the above-mentioned study periods ($p < 0.0001$), compared with the results recorded before treatment.

When studying the level of significance of intragroup differences in the BOP index, the average intragroup difference in the indicators identified in the control group 1 and 3 months after the start of treatment measures was statistically significant ($p = 0.0102$, $t = 2.71$). The level of significance of differences in the BOP index between the groups before and after

Thus, according to the data obtained, statistically significant intragroup change in the average value of the studied bleeding index both after 1 month and after 3 months is recorded in all three study groups ($p <0.05$). Slightly different assessment criteria were revealed when comparing the digital index values between the groups. Thus, statistically significant differences were not found between some groups in the bleeding index on probing (BOP) both before and 1.3 months after treatment.

At the same time, it is important to note the fact that positive results from the conducted treatment and preventive measures are achieved by the effectiveness of the proposed remedy and, at the same time, optimal professional oral hygiene in combination with the patient's motivation for timely treatment of pathology and compliance with all necessary preventive instructions for individual care of the oral cavity. The periodontal and peri-implant tissue

condition was also assessed to determine the severity of the inflammatory process in the marginal periodontal tissues using the gingival index. The index was calculated before the start of treatment and preventive measures and 1.3 months after their completion, i.e., at relatively long observation periods. In 60 individuals with perimucositis, divided into three groups, the periodontal condition was assessed based on a comparative assessment of the degree of pathological disorders in soft tissues after the use of certain therapeutic agents. The control group consisted of 20 patients with affected tissues, among whom generally accepted traditional methods were used.

Statistical calculations were performed using software packages for applied statistics. As for the gingival index at the initial stage, in the first group it was 2.30±0.015, and in the second it was lower 2.28±0.017, while in the main group in the area of teeth and implants it was comparatively higher and averaged 2.33±0.024. Based on the results of the study conducted at the above-mentioned times, we found no significant intergroup differences in the gingival index values identified before the start of the corresponding treatment ($p>0.05$).

Analysis of the index data recorded after 1 month of observation showed a reliable difference between the main and two other groups of orthopedic patients ($p <0.0001$). The differences between the first and second groups, that is, between the control group and the comparison group, were not significant ($p=0.2874$). Thus, in patients with orthopedic structures on implants in the oral cavity, as a result of the implementation of the proposed new treatment regimen for peri-implant mucositis, a significant reduction and weakening of the clinical manifestations of the inflammatory process was achieved after 1 month, as evidenced by the dynamics of the studied gingival index. At the same time, the effect of this therapeutic course was significantly stable and by 3 months it significantly increases, against the background of a relatively more pronounced, compared to other groups, decrease in the gingival index.

The main pathogens of the disease are considered to be: peptostreptococcus micros, fusobacterium nucleatum, prevotella intermedia, gram-negative anaerobes, as well as s. aureus, etc. All these microorganisms are present in the oral cavity, they are the causative agents of periodontitis. Factors contributing to the development of periimplantitis should be divided into general and local. General factors include, firstly, a history of periodontitis - from a study of 13 patients who underwent implantation, periimplantitis developed: in those with a history of periodontitis in 23%, and in those who did not have this disease only in 7% of cases. Secondly, general diseases - diabetes mellitus, diseases of the blood system, etc. In diseases of the blood system, implantation is not indicated and periimplantitis develops in almost all cases, so attention should be paid to the common disease diabetes mellitus. Diabetes mellitus, depending on its severity, can contribute to the development of peri-implantitis. A statistical study has revealed a direct relationship between the glycosylated hemoglobin index, which reflects the severity of diabetes, and the incidence of peri-implantitis. Studies have concluded that the risk of peri-implantitis in patients with diabetes increases with a glycosylated hemoglobin index of 7% or more. Thirdly, these are environmental factors - smoking, stress, alcohol.

Peri-implantitis in smoking patients after implantation, according to various studies, is on average 3.5 times higher and there is a correlation with the amount of nicotine consumed. This is associated with vascular spasm, decreased blood supply, and deterioration of reparative abilities, which is especially important in the postoperative period. Genetic predisposition is in fourth place among general factors. Among local factors, independent oral hygiene is important, since poor hygiene, poor access leads to rapid accumulation of

bacteria. The degree of roughness of the surface of the subgingival part of the structure also has a great influence, as a result of which the adhesion of microorganisms in this area increases. Quite often, the cause of peri-implantitis is insufficient congruence between the implant and the superstructure, which contributes to the accumulation of microorganisms at their junction. The cause of peri-implantitis is an infectious agent, but its development must be facilitated by one or more specific environmental factors. Several options can be attributed to surgical treatment methods for peri-implantitis, the choice depends on the specific case, skills and preferences of the doctor. The most reliable and simple is the removal of the implant, followed by healing of the bed, restoration of bone tissue and possible re-installation of the implant. The second option is to remove the implant, curettage of the bone walls, removal of granulation tissue and simultaneous insertion of a new implant. Re-implantation is performed at one time only in cases where all 4 bone walls of the bed have been preserved. Other treatment options using bone grafting operations are also possible, but they are performed only in cases where it is possible to eliminate the cause, remove all granulation tissue without damaging the implant and without significant loss of bone tissue.

According to microbiological studies, the effectiveness of the probiotic agent is almost 2 times higher than that of traditional methods of treating mucositis, and in the samples taken in the main group where the probiotic was used, representatives of the normoflora and opportunistic microorganisms were more often dominant. This to a certain extent confirms the specificity of the action of probiotic agents in terms of preventing dysbacteriosis and a positive effect on the normal microflora of the oral cavity. Thus, the use of a probiotic as a means of accompanying basic dental therapy allows for a significant and timely reduction in the severity of perimucositis. The installation of prosthetic structures on dental implants requires constant monitoring of the condition of the surrounding soft and hard tissues with timely diagnosis, prognosis of the situation and the use of effective therapeutic and preventive measures for the complete correction of emerging pathological changes.

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CHANGES IN THE MICROBIOLOGICAL PICTURE OF THE BODY IN WOMEN WITH BREAST CANCER

ABSTRACT

The aim of research was to study changes in the microbiological picture of the body in women with breast cancer. There were 92 women with breast cancer and 10 healthy women took part in the study. Most women with breast cancer live and work in rural areas, but a significant proportion of them are unemployed. The prevalence of Streptococcus pyogenes in respiratory tract smears was 20% in the main group and 14.3% in the control group. Streptococcal pneumonia was 11.1% in the main group and was absent in the control group. Klebsiella pneumoniae was mainly detected in the main group (11.1%) and was not observed in the control group. Enterobacter spp. This indicator was 11.1% in the main group and zero in the control group. The detection rate of Escherichia coli was 11.1% in the main group and 14.3% in the control group. The detection rate of Pseudomonas aeruginosa in the main group was 8.9%, and this microorganism was not detected in the control group. Bifidobacteria spp., Lactobacilli spp. in probiotic maintenance therapy for breast cancer. and Enterococcus spp., beneficial bacteria such as probiotics increased significantly with treatment. This indicates that probiotics enhance the activity of these microorganisms. Candida spp., Proteus spp., and Staphylococcus aureus completely disappeared with probiotic treatment. This indicates that probiotics are effective in suppressing these microorganisms. Escherichia coli completely disappeared from the nasopharyngeal contents with treatment. No Escherichia coli was detected in either treatment group (without or with probiotics). This indicates that probiotics completely eradicated this microorganism.

Keywords: breast cancer, microbioloji, infections

Being characterized by six major hallmarks, carcinogenesis might occur in every cell, tissue, and organ, leading to the pathological alternations that result in a vast number of cancers. The major mechanisms that enable its progression include evasion of apoptosis, limitless capacity to divide, enhanced angiogenesis, resistance to anti-growth signals and induction of own growth signals, as well as the capacity to metastasize [1].

According to the WHO, malignant neoplasms are the greatest worldwide burden for women, estimated at 107.8 million Disability-Adjusted Life Years (DALYs), of which 19.6 million DALYs are due to breast cancer. [2]

Besides being the most common, breast cancer is also the leading cause of cancer death in women worldwide. Although incidence rates were the highest in developed regions, the countries in Asia and Africa shared 63% of total deaths in 2020 [5]. Most women who develop breast cancer in a high-income country will survive; the opposite is true for women in most low-income and many middle-income countries [3].

92 women with breast cancer and 10 healthy women took part in the study.

The criteria for the inclusion of patients in this single-center prospective study were as follows:

1. Morphologically confirmed diagnosis of mammary gland cancer stage I-II.

2. There are no contraindications to the operation.

The criteria for excluding patients from this study are as follows:

1. Morphologically confirmed diagnosis of mammary gland cancer stage III-IV.

2. Presence of severe uncontrolled chronic or acute diseases.

Women with breast cancer, included in the study, were analyzed by place of residence, employment status, marital status, and the presence of harmful habits. It turned out that 60.8% of the population lives in villages, and 39.1% — in cities. A significant part of patients lived in rural areas. 58.6% of women included in the study are working, and 41.3% are unemployed. Patients were divided into two groups by marital status: married and single. Of the women with breast cancer included in the study, 80.3% were married, and 19.6% were single. This number is relatively small, which means that most of the population was married. Among the harmful habits revealed in women, a tendency to alcohol consumption and smoking was revealed. It turned out that 31.5% of 92 women suffered from alcoholism, and 5.4% of women were prone to smoking. The level of smoking was relatively low.

The incidence of complications was studied in two different types of treatment: chemotherapy and maintenance therapy. Pneumonia developed in 23.9% of patients after finishing chemotherapy. Chemotherapy can weaken the immune system, making you more susceptible to infections. For this reason, patients receiving chemotherapy are at an increased risk of developing pneumonia. Pneumonia occurred in 9.8% of patients receiving maintenance therapy. Maintenance therapy aims to keep patients stable and, because it supports the immune system, reduces the risk of pneumonia. Gastrointestinal disorders were observed in 43.5% of patients receiving chemotherapy. Chemotherapy can affect the gastrointestinal tract, causing disorders such as vomiting, nausea, diarrhea, and constipation. This is one of the side effects of chemotherapy that can seriously affect the gastrointestinal

tract of patients. Gastrointestinal disorders were observed in 22.8% of patients receiving maintenance therapy.

Based on the presented data, the frequency of occurrence of microorganism associations in the nasopharyngeal contents of patients and control group individuals was determined, as well as a comparison of these associations between the control and main groups. Statistical inconsistencies were found between the groups. Klebsiella spp. / Enterococcus spp.: control group - 30%, main group - 27.5% of cases. The difference between the groups was statistically insignificant ($p = 0.875$). Klebsiella spp. / Enterococci spp. The association was observed in 30% of cases in the control group and in 27.5% in the main group, statistical significance was not found.

Pseudomonas spp. / Enterococci spp. In the main group, this was observed in 2.5% of cases, but in the control group, this association was also absent.

Escherichia coli / Klebsiella spp. The main group was detected in 5% of cases, but was not present in the control group. Thus, associations of microorganisms were more common in the nasopharyngeal contents of breast cancer patients. This once again indicates that these patients are systematically exposed to infectious agents.

The presence of chronic obstructive pulmonary disease, along with lung cancer, has a strong negative impact on the respiratory tract microbiome, further worsening the condition of patients and leading to an acceleration of the dying process and an increase in mortality. Given this, we conducted a comparative analysis of the results of microbiological studies in breast cancer patients in various aspects. 92 patients with breast cancer were divided into two groups depending on COPD: 22 patients with chronic obstructive pulmonary disease (COPD) in addition to cancer formed the main group, and 20 patients without COPD formed the comparison group. 10 people were included in the practical control group. During the studies, 45 strains of opportunistic microbes were isolated from the main group. When analyzing the proportions of these microorganisms and their distribution by groups, it becomes clear that. Streptococcus pyogenes is 20% in the main group, 25% in the comparison group, 14.3%. The comparison group shows a higher result. Streptococcus pneumoniae was more common in the main group and made up 11.1% of cases.

Enterobacter spp. The highest incidence in the main group was 11.1%, in the comparison group - 3.6%, in the control group it was not recorded. Pseudomonas aeruginosa 8.9% in the main group. In the comparison group it was detected in 7.1% of cases. There was no control group. Candida albicans was 20% in the main group and 21.4% in the comparison group.

Klebsiella pneumonia was registered only in 11% of patients in the main group. In the comparison and control groups it was not detected. The results of the analysis show that. In all three groups, various microorganisms are common. However, Enterobacter spp. are more common in patients with COPD and breast cancer. Such dangerous microorganisms as Pseudomonas aeruginosa prevailed, in the main group only Klebsiella was found.

During the study, the sensitivity and resistance of various strains to antibiotics were determined. 61.9% of the 13 E. coli strains were resistant to ampicillin/sulbactam. This indicates that this antibiotic has some effect in the treatment of E. coli. Ceftazidime against E. coli gives 33.3% of positive results. This indicates that the effect of this drug on E. coli is relatively weak.

It was determined that resistance to the drug ceftriaxone is 95.2±4.65%. The drug is very effective, since 95.2% of E. coli strains react positively to ceftriaxone. Cefepime was resistant in 23.8% of cases. This indicates that E. coli is highly resistant to this drug. Imipenem was selected with a resistance rate of 14.3%, and meropenem with a resistance rate of 23.8%. Only 14.3% of E. coli strains tested positive for imipenem, indicating its very low efficacy against E. coli. Thus, the most effective drugs against E. coli strains are: ceftriaxone and ertapenem, each of which gave 95.2% positive results. Less effective drugs: imipenem, amikacin and cefepime give only 14.3% and 23.8% positive results, respectively, indicating their weak effect on E. coli. Moderate efficacy: ampicillin/sulbactam (61.9%) and ciprofloxacin (47.6%) have moderate efficacy.

These data indicate that some antibiotics (such as ceftriaxone and ertapenem) are more effective against E. coli strains, while others cause bacterial resistance and therefore have a weak therapeutic effect.

Ampicillin/sulbactam was resistant to 91.7% of K. pneumoniae strains. Such high efficacy indicates that this antibiotic is ineffective in the treatment of K. pneumoniae. Piperacillin/tazobactam showed resistance in 83.3%. This also indicates very low efficacy. 79.2% of K. pneumoniae strains tested positive for imipenem. Although this is a bit high, it is still low compared to other drugs. Meropenem also shows an efficacy of 83.3% against K. pneumoniae strains. This is also a good result, but not as high as drugs such as Ceftriaxone and Cefepime. Ertapenem also has 100% activity against K. pneumoniae strains, at the same level as ceftriaxone. It shows high potency and is a very unreliable antibiotic for K. pneumoniae. Only 20.8% of K. pneumoniae strains tested positive for amikacin. This is a very high potency, indicating that this antibiotic has strong activity against K. pneumoniae. Ciprofloxacin showed a positive result of 87.5%, indicating moderate to weak activity against K. pneumoniae. Trimethoprim/sulfamethoxazole is also effective against K. pneumoniae with an efficacy of 83.3%. This is at a high level, similar to other ineffective drugs. The drugs with the lowest potency: ceftriaxone and ertapenem, each of which gave 100% positive results, are the least effective drugs against K. pneumoniae. Low-efficacy drugs: ampicillin/sulbactam (91.7%), piperacillin/tazobactam (83.3%), ceftazidime (83.3%), cefepime (87.5%) and ciprofloxacin (87.5%) show moderate efficacy. High-efficacy drugs: amikacin efficacy is only 20.8%, which is very high.

There were also differences in the dynamics of detection of antibiotic-resistant strains of Enterobacteriaceae. Cephalexin resistance was 66.7%, sensitivity was 26.7%. The rate of resistance of bacteria to cephalexin was very high. In contrast to cefoxitin, the rate of resistance was low, and most bacteria were sensitive to this drug. Cefotaxime showed 40.0% resistance, 26.7% sensitivity. The rate of resistance of bacteria to cefotaxime was moderate. Cefepime differed with 20.0% resistance, 73.3% sensitivity. Resistance to cefepime is very low, and the vast majority of bacteria are sensitive. Resistance to ampicillin was 73.3%, sensitivity was 13.3%. Resistance to ampicillin was very high. This indicates that ampicillin is ineffective against many bacterial strains. Resistance to amoxicillin/clavulanic acid was 60.0%, sensitivity was 33.3%. Resistance to ciprofloxacin was 33.3%, sensitivity was 46.7%. This indicates that ciprofloxacin can treat some bacteria. Resistance to ofloxacin was 13.3%, sensitivity was 66.7%. This indicates that ofloxacin has a good effect. Azithromycin was also distinguished by its somewhat greater effectiveness. Gentamicin was distinguished by its good effectiveness. Imipenem and Meropenem showed high effectiveness.

The dynamics of detection of antibiotic-resistant strains of Staphylococcus aureus was also studied. The resistance and sensitivity thresholds of Staphylococcus aureus to antibiotics were different. Cephalexin showed 52% resistance and 28% sensitivity. This indicates that Cephalexin is effective for some strains, but most are resistant. Resistance to cefoxitin was 52%, sensitivity was 44%. Ciprofloxacin is also considered effective in the treatment of Staphylococcus aureus. Ofloxacin has shown itself to be a highly effective drug.

Thus, the most effective drugs were: Ofloxacin (4.0% resistance, 84.0% sensitivity), Ciprofloxacin (4.0% resistance, 64.0% sensitivity), Imipenem (8.0% resistance, 72.0% sensitivity). The least effective drugs were Cefepime (72.0% resistance, 24.0% sensitivity), Azithromycin (52.0% resistance, 24.0% sensitivity), Cephalexin and Cefoxitin (52.0% resistance and 28.0%-44.0% sensitivity). The moderately effective drugs were Ampicillin (44.0% resistance, 52.0% sensitivity) and Amoxicillin/clavulanic acid (36.0% resistance, 28.0% sensitivity). Ofloxacin and Imipenem were very effective drugs, while Cefepime and Azithromycin were the least effective drugs.

We determined the composition and concentration of intestinal microflora before and after treatment with and without probiotics. It was found that before treatment, bifidumbacterium and lactobacilli were less abundant in the intestinal contents of patients with breast cancer, accounting for 56% and 67%, respectively. After treatment with probiotics, an increase was recorded, reaching 95%, and after treatment without probiotics, 62%.

The species composition and quantitative indices of the nasopharyngeal microflora were determined before and after treatment with and without probiotics. Although the level of Staphylococcus aureus was 27.5% before treatment, it decreased to 10% after treatment with and without probiotics. Candida spp. If the reduction rate was 30% without treatment, then under the influence of probiotics it was 15%. However, in the absence of probiotics, this figure was 20%. After treatment with probiotics, Proteus spp. and Escherichia coli were not detected in patients. However, in patients who did not receive probiotics, Proteus spp. It was detected in 10% of cases. The composition and quantitative indices of the nasopharyngeal microflora were determined before and after treatment with probiotics. Bifidobacteria spp. in a smear before treatment. 67% and Lactobacillus spp. 84% were detected, while under the influence of probiotics, 99% and 98% were recorded, respectively. Escherichia coli was detected in 92.3% before treatment and in 45% after treatment with probiotics. However, the number of dangerous microorganisms, such as Klebsiella, did not decrease. Before treatment, Candida was detected in 15.4% of cases, and after treatment - in 7.7%. Before treatment, Staphylococcus aureus was detected in 7.7% of patients, after treatment it was not detected at all. Simply, probiotics could not affect the composition of most Klebsiella. However, in addition to Bifidobacterium spp., Lactobacillus spp. An increase in the number of beneficial microorganisms is also good.

Spielberg-Hanin scale for reactive anxiety, personal anxiety and asthenia before and after treatment. Personal anxiety is an individual characteristic in which a person perceives events as dangerous and reacts to them with anxiety. Reactive anxiety occurs as a result of a certain situation at a certain time and is characterized by tension, anxiety, and irritability in a certain environment. Asthenia is a state of fatigue and weakness that occurs with aging of the human body. The reactivity index was 51 points, but decreased to 36.1 points after treatment with probiotics and to 35 points after treatment without probiotics. If before the treatment personal anxiety was 50.9 points, then after treatment with probiotics it decreased to 46 points, and without probiotics - to 49 points. The asthenic state before the treatment was 57.3

points, after treatment with probiotics it decreased to 53.7 points. As can be seen, probiotic therapy had a significant positive effect on the psychoemotional state and mood of breast cancer patients.

Thus, as a result of our study, we obtained a number of necessary indicators. Thus, the majority of women with breast cancer live and work in rural areas, but a significant part of them are unemployed. The number of married women exceeded the number of single women by 60.7%. In total, 34 women had a bad habit. Among them, smokers drank alcohol 26.1% less often. Physical activity among them was also very low. There were 67.4% more women who did not engage in any physical activity. Patients with breast cancer had more skin changes over the lesion (28.2%) and less pain (13.1%). Nodal derivation was 90.2%, and diffuse derivation was 9.8%. In the study of smears from the respiratory tract, Streptococcus pyogenes was 20% in the main group and 14.3% in the control group. Streptococcal pneumonia was 11.1% in the main group and was absent in the control group. Klebsiella pneumoniae was mainly detected in the main group (11.1%), and was not observed in the control group. Enterobacter spp. In the main group, this figure was 11.1%, and in the control group - zero. The detection rate of Escherichia coli was 11.1% in the main group and 14.3% in the control group. The detection rate of Pseudomonas aeruginosa in the main group was 8.9%, and this microorganism was not detected in the control group. 3. The most effective drugs against the E. coli strain were: Ceftriaxone and Ertapenem, and less effective were Imipenem, Amikacin and Cefepime. Ceftriaxone and ertapenem demonstrated higher efficacy against K. pneumoniae, with a 100% positive result achieved for each of them. Meropenem and cefepime are the most effective antibiotics against P. aeruginosa, while azithromycin and cefoxitin are the least effective.

4. Bifidobacteria spp., Lactobacilli spp. in probiotic maintenance therapy for breast cancer. and Enterococcus spp. the number of beneficial bacteria such as probiotics increased significantly as a result of treatment. This indicates that probiotics enhance the activity of these microorganisms. Candida spp., Proteus spp. and Staphylococcus aureus microorganisms completely disappeared as a result of probiotic treatment. This indicates that probiotics are effective in suppressing these microorganisms. Escherichia coli microorganism completely disappeared from the nasopharyngeal contents as a result of the treatment. Escherichia coli was not detected in any of the treatment groups (without and with probiotics). This indicates that probiotics completely destroyed this microorganism.

Finally, as a result of the study, we developed practical recommendations. We believe that microbiological examination of the respiratory tract and gastrointestinal tract before the start of treatment in women with breast cancer is appropriate to determine further therapeutic measures. The use of probiotics in maintenance therapy of patients with breast cancer is of great importance.

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ANALYSIS OF THE EFFECT OF IMMUNOFAN ON INFLAMMATION MARKERS IN PATIENTS WITH LIVER ECHINOCOCCOSIS

ABSTRACT

140 healthy people and 100 patients who were diagnosed with echinococcosis at the Teaching and Surgical Clinic of the Azerbaijan Medical University between 2016 and 2020 took part in the study (100 patients of the main group and 40 patients of the comparison group). In patients with a severe course of echinococcosis, biochemical and immune indicators normalized faster and more significantly on the background of treatment with Immunofan.

Cystic echinococcosis is a severe zoonosis caused by the larvae of Echinococcus granulosus sensu lato (E. granulosus s.l.) [3]. The great danger of the disease to the human body has led to its classification as a socially significant disease. Treatment of hepatic echinococcosis is carried out by surgical resection and antiparasitic drugs [4].

Hydatid cysts can be found in any organ, including bone and muscle tissue. However, they develop mainly in the liver (50-85%), less often in the lungs and other organs and tissues (12-53%), causing severe chronic diseases. Echinococcus vesicles can grow to 40-50 mm in 3-5 months, and their rupture leads to clinical exacerbation of the disease and the development of anaphylactic shock. The study of immune parameters, especially inflammatory markers, is of great importance in echinococcosis. During infection, the body's immune system, through immune cells and cytokines, fights E. granulosus s. [5].

Immunofan reduces the resistance of tumor cells to drugs and increases their sensitivity to the effects of cytostatic agents. It is used for the prevention and treatment of immunodeficiency and toxic conditions, chronic processes of various etiologies in children over 2 years of age and adults. [1].

After surgery, an immunomodulator called “Immunofan” was also used as part of general treatment in patients. Immunofan is a transparent, colorless and odorless liquid intended for injection. Its composition in a 1 ml ampoule contains 50 mcg of hexapeptide (arginyl-α-aspartyl-lysyl-tyrosyl-arginine) as the main active ingredient and glycine-5 mg, sodium chloride-9 mg, distilled water-1 ml as excipients. Immunofan is an immunomodulatory drug. The pharmacological effect of the drug is based on the correction of the immune system and the restoration of the body's acid-base balance.

In toxic and infectious liver lesions, the drug prevents cytolysis, reduces transaminase activity and the amount of bilirubin in the blood serum.

In the middle phase (starts on the 2nd-3rd day from the start of drug administration and continues until the 7th-10th day), phagocytosis reactions are enhanced, which leads to increased destruction of bacteria and viruses. During the slow phase (starts 7-10 days after

the start of drug administration and continues up to 4 months), the immunocorrective effect of Immunofan is manifested, and impaired indices of cellular and humoral immunity are restored. At this stage, normalization of the immune system regulation indices and an increase in the production of specific antibodies are observed [2].

Materials and methods of the study. The study involved 140 healthy individuals and 100 patients diagnosed with echinococcosis at the Educational and Surgical Clinic of the Azerbaijan Medical University between 2016 and 2020 (100 patients in the main group and 40 patients in the comparison group). We performed liver echinococcectomy in patients diagnosed with echinococcosis. Of the patients meeting the criteria, 102 (72.8%) underwent open laparoscopic surgery and 38 (27.2%) underwent closed laparoscopic surgery.

Biochemical parameters (C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), amylase, albumin, creatinine, cholesterol) were determined before and after surgery in blood samples taken before surgery from 140 patients with liver echinococcosis included in the study.

Of the 140 patients who underwent echinococcectomy, 98 had uncomplicated forms and 42 had complicated forms, which amounted to 70.0% and 30.0%, respectively.

In our study, patients who underwent echinococcectomy were prescribed an immunomodulator (Imunofan) for 7 days, including the day of surgery.

Other studies have examined the dynamics of changes in interleukins, and these markers have been identified for echinococcosis and have shown their importance for monitoring the response to treatment.

Results. During the study, one echinococcal cyst was detected in 52 (37.1%) of 140 patients, and 88 (62.9%) had 2 or more echinococcal cysts. Of these, 32 (22.8%) had small (up to 5 cm), 72 (51.4%) had medium (5–10 cm), and 36 (25.8%) had large (more than 10 cm) cysts.

Before surgery, biochemical markers such as ALT, AST, ALP, GGT, and amylase were determined in the main group, comparison group, and healthy individuals.

Patients included in the study were divided into two subgroups depending on severe and non-severe forms. The comparison group was conditionally assigned to C1 with a severe form (n=14), and the subgroup of patients with an uncomplicated form (n=26) was assigned to C2; In the main group, the subgroup of patients with severe forms (n=28) was designated as M1, and the subgroup of patients with mild forms (n=72) was designated as M2.

Based on these data, we analyzed the differences between various biochemical parameters of groups C1 and M1 before surgery.

It was found that the ALT level in group C1 was statistically significantly lower than in group M1 ($t=1.65$, $p>0.05$). The AST level was statistically significantly lower in group C1 than in group M1 ($t=2.18$, $p<0.05$). The ALP level was statistically significantly lower in group C1 compared to group M1 (240.0 ± 4.8) ($t=1.39$, $p>0.05$). The GGT level was statistically significantly lower in group C1 compared to group M1 ($t=1.09$, $p>0.05$). The amylase level was statistically significantly lower in group C1 than in group M1 ($t=1.05$, $p>0.05$).

Thus, in patients with preoperatively exacerbated echinococcosis, only the AST indicator was statistically significantly higher in group M1 than in group C1.

We analyzed the biochemical parameters between the groups of patients with uncomplicated echinococcosis before surgery. Among these groups, only the ALP level was statistically significantly lower in group C2 compared to group M2. The levels of ALT ($t=0.80$, $p>0.05$), AST ($t=0.51$, $p>0.05$), GGT ($t=0.38$, $p>0.05$) and amylase ($t=0.58$, $p>0.05$) were statistically significantly lower in group C2 compared to group M2.

The average values of the immune parameters we studied in patients with complicated echinococcosis and uncomplicated echinococcosis are presented. As can be seen, the IL-1 level was 21.0±0.8 pg/mL in the comparison group with complicated echinococcosis, 24.0±0.5 pg/mL in the main group with complicated echinococcosis, 15.5±0.5 pg/mL in the comparison group with uncomplicated echinococcosis, and 15.0±0.3 pg/mL in the main group with uncomplicated echinococcosis. The preoperative IL-4 level was 11.0±0.4 pg/mL in the comparison group with complicated echinococcosis, 12.0±0.2 pg/mL in the main group with complicated echinococcosis, 10.5±0.4 pg/mL in the comparison group with uncomplicated echinococcosis, and 10.0±0.2 pg/mL in the main group with uncomplicated echinococcosis. The level of IL-6 was determined as 31.0±1.1pg/mL in patients with aggravated echinococcosis in the comparison group, 32.0±0.6pg/mL in patients with aggravated echinococcosis in the main group, 16.0±0.6pg/mL in patients with uncomplicated echinococcosis in the comparison group, and 16.5±0.3 pg/mL in patients with uncomplicated echinococcosis in the main group.

The level of IL-10 before surgery was recorded as 26.0±0.9pg/mL in patients with aggravated echinococcosis in the comparison group, 28.0±0.6pg/mL in patients with aggravated echinococcosis in the main group, 15.0±0.5pg/mL in patients with uncomplicated echinococcosis in the comparison group, and 15.5±0.3 pg/mL in patients with uncomplicated echinococcosis in the main group.

The level of TNF-α was also different in patients with aggravated and uncomplicated echinococcosis. The level of IgA in patients with severe echinococcosis in the comparison group was 22.0±0.8pg/mL, in patients with severe echinococcosis in the main group was 24.0±0.5pg/mL, in patients with uncomplicated echinococcosis in the comparison group was 16.0±0.6pg/mL, and in patients with uncomplicated echinococcosis in the main group was 19.0±0.3pg/mL.

We conducted comparative analyses between patients with severe and uncomplicated echinococcosis on immunoglobulin A, G, and M before surgery. As can be seen, the level of IgA was 7.0±0.3 g/L in patients with severe echinococcosis in the comparison group, 8.0±0.2 g/L in patients with severe echinococcosis in the main group, 6.4±0.2 g/L in patients with uncomplicated echinococcosis in the comparison group, and 6.5±0.1 g/L in patients with uncomplicated echinococcosis in the main group.

The level of IgG was recorded as 18.0±0.7 g/L in patients with severe echinococcosis in the comparison group, 20.0±0.4 g/L in patients with severe echinococcosis in the main group, 14.0±0.5 g/L in patients with uncomplicated echinococcosis in the comparison group, and 14.5±0.3 g/L in patients with uncomplicated echinococcosis in the main group.

The level of IgM was recorded as 4.0±0.1 g/L in patients with severe echinococcosis in the comparison group, 4.2±0.1 g/L in patients with severe echinococcosis in the main group,

4.2±0.1 g/L in patients with uncomplicated echinococcosis in the comparison group, and 4.0±0.1 g/L in patients with uncomplicated echinococcosis in the main group.

Analysis: IgM levels were similar in groups C1 and M1 (4.0 and 4.2), and similar levels were also found in groups C2 and M2 (4.2 and 4.0). The IgM level is similar in each group, which may indicate a similar degree of initial immune response. The similar immunoglobulin M level indicates a similar initial immune response in both groups. The results obtained show that severe echinococcosis had a more profound effect on the immune system in patients and activated the immune response more.

Preoperatively, IL-1 ($t=3.09$, $p<0.01$), IL-4 ($t=2.22$, $p<0.05$), TNF-α ($t=2.13$, $p<0.05$), IgA ($t=2.78$, $p<0.05$), IgG ($t=2.44$, $p<0.05$) parameters were statistically significantly lower in the C1 group than in the M1 group. No statistically significant differences were found between the C1 and M1 groups in the parameters IL-6 ($t=0.80$, $p>0.05$), IL-10 ($t=1.82$, $p>0.05$) and IgM ($t=1.43$, $p>0.05$) (Table 3). In the C2 group with uncomplicated echinococcosis, the concentration parameters of IL-1 ($t=1.02$, $p>0.05$), IL-4 ($t=0.98$, $p>0.05$), IL-6 ($t=1.02$, $p>0.05$), IL-10 ($t=1.02$, $p>0.05$) were statistically significantly different from the M2 group in terms of cytokine concentrations.Functional markers of the liver, pancreas and biliary tract were compared between the groups 1, 5 and 10 days after surgery in patients with complicated (M1, C1 groups) and uncomplicated (M2, C2) echinococcosis.

In the comparison groups (n=26) and the main group (n=72), the average values of biochemical parameters such as ALT, AST, GGT, CRZ, as well as cytokines such as IL-1, IL-6, TNF-α, and the level of IgA were compared with the norm in patients with uncomplicated liver echinococcosis (groups M2, C2) (table).

Cədvəl

Ağırlaşmamış exinokokkoz olan xəstələrdə biokimyəvi və immun parametrlərin orta göstəriciləri və həmin parametrlərin norma göstəriciləri

İndexes	C2 group (n=26)		Ə2 group (n=72)		Normal indexes
	Before treament	After treatment	Before treament	After treatment	
ALT, U/l	60	29	64,2	28,2	10-40
AST, U/l	60	29	64,2	27,4	15-45
GGT, IU/l	44	27	46	26,5	10-40
CRP, mg/dL	14	8	15	6	1-5
IL-1, pq/mL	15,5	6,9	15	5,2	1-6
IL-6, pg/mL	16	7,8	16,5	5	1-6
TNF, pg/mL	16	6,8	19	4,6	1-6
IgA, q/L	6,4	4,3	6,5	3,2	0,5-2,5

In patients with uncomplicated echinococcosis, biochemical and immune parameters returned to normal levels against the background of Imunofan treatment. In groups C2 and M2, the ALT, AT, and GGT indicators were also very different before the operation.

In group C2, before the operation, ALT was 60 U/l, AST was 60 U/l, GGT was 44 IU/l, CRP was 14 mg/dL, IL-1 level was 15.5 pg/mL, IL-6 was 16 pg/mL, TNF was 16 pg/mL, IgA was 6.4 g/L, and 10 days after the operation, ALT was 29 U/l, AST was 29 U/l, GGT was 27 IU/l, CRZ was 8 mg/dL, IL-1 was 6.9 pg/mL, IL-6 was 7.8 pg/mL, TNF was 6.8 pg/mL, IgA was 4.3 g/L. 10 days after the operation, the values returned to normal in group M2, which was administered Imunofan. In this group, ALT 64.2 U/l, AST 64.2 U/l, GQT 46 IU/l, CRZ 15 mg/dL, IL-1 level 15 pg/mL, IL-6 level 16.5 pg/mL, TNF 19 pg/mL, IgA 6.5 g/L were determined before the operation. 19 days after the operation, ALT 28.2 U/l, AST 27.4 U/l, GQT 26.5 IU/l, CRZ 6 mg/dL, IL-1 level 5.2 pg/mL, IL-6 level 5 pg/mL, TNF 4.6 pg/mL, IgA 3.2 g/L were determined.

In the C2 group, CRZ decreased by 42.9% compared to the value 10 days before the operation, and by 60% in the M2 group. The level of CRZ completely returned to normal in the M2 group 10 days after the operation. IL-1 in the C2 group decreased by 55.5% after the operation, and by 69.7% in the M2 group. The average value of IL-6 decreased by 51.5% in the C2 group, by 69.7% in the M1 group, and decreased to the normal range in the M2 group. The average value of TNF-α decreased by 57.5% in the C2 group, and by 75.8% in the M2 group. In both groups, this parameter was within the normal range 10 days after the operation. The level of IgA decreased by 32.9% in the C2 group, and by 50.8% in the M2 group. Unlike the C2 group, it completely returned to normal in the M2 group.

During echinococcal cyst of the liver, the biochemical indicators CRZ and cytokines such as IL-1, IL-4, IL-6, IL-10 and TNF-α, immunoglobulin fractions such as IgA, IgG and IgM in the blood change, and in the correction of these changes, it is more appropriate to combine the drug "Imunofan" with traditional postoperative medical treatment measures. In addition to the above-mentioned cytokine profile and immunoglobulin fraction indicators, the drug Imunofan has similar effects on the quantitative indicators of enzymes such as ALT, AST, GGT in the blood.

According to the results of the analysis we obtained before the operation, in the comparison group, the biochemical indicators increased by 10-35%, CRZ 65%, Cytokines 60-65%, IgA 61% in the uncomplicated patients, and in the main group, the biochemical indicators increased by 15-40%, CRZ 67%, Cytokines 60-70%, IgA 62%. In the complicated patients of the comparison group, the biochemical indicators increased by 35-60%, CRZ 84%, Cytokines (IL1, IL6, TNF) 70-85%, IgA 65%, and in the main group, the biochemical indicators increased by 37-60%, CRZ 85.3%, mcytokines 75-85%, mIg A 68.8%.

10 days after the operation, biochemical indicators in uncomplicated patients of the comparison group decreased by 35-60%, CRZ by 43%, biochemical indicators in uncomplicated patients of the main group decreased by 40-60%, CRZ by 60%. In the comparison group, the biochemical indicators in the aggravated patients decreased by 30-55%, CRZ by 62%, and in the main group, the biochemical indicators in the aggravated patients decreased by 60-85%, CRZ by 86%. As a result, in the main group, the biochemical indicators in the uncomplicated patients decreased by 3-5%, CRZ by 17% compared to the comparison group. In the main group, the biochemical indicators in the aggravated patients decreased by 25-30%, CRZ by 24% compared to the comparison group.

10 days after surgery, cytokine levels in uncomplicated patients in the comparison group decreased by 50-60%, and in the main group by 65-80%. In patients in the comparison group with aggravated echinococcosis, cytokine levels decreased by 55-60%, and in the main group by 80-90%. As a result, a 15-20% improvement was recorded in cytokine levels in uncomplicated patients in the main group compared to the comparison group. In the aggravated patients in the main group, a 25-30% improvement in dynamics was recorded compared to the comparison group.

10 days after surgery, IgA decreased by 32.9% in patients in the comparison group with uncomplicated echinococcosis, and by 50.8% in the main group. IgA decreased by 12.9% in aggravated patients in the comparison group, and by 72.5% in aggravated patients in the main group. As a result, an 18% improvement was recorded in the uncomplicated patients of the main group compared to the IgA comparison group. A 60% improvement was recorded in the aggravated patients of the main group compared to the IgA comparison group.

Thus, in patients with severe echinococcosis, biochemical and immune parameters returned to normal more quickly and significantly against the background of Imunofan treatment.

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THE EFFECTIVENESS OF SIMULATION SUPPORTED PEDIATRIC NURSING EDUCATION ON NURSING STUDENTS: A SYSTEMATIC REVIEW

ABSTRACT

Objectives: This literature review was conducted to review the effectiveness of simulation use in pediatric nursing education of nursing students.

Materialand Metod: Six electronic databases including Google Scholar, Web of Science, Pubmed, Scopus, Science Direct and Cochrane Library were searched between 2000 and 2025. The databases were systematically searched with the keywords “nursing students”, “child”, ‘education’ and “simulation” in Turkish and English. The articles that were applied for simulation applications in pediatric health and diseases nursing education, where the effectiveness of the application was evaluated, systematic review and meta-analysis reports were created, and the full text of which could be accessed were included in the review.

Results: As a result of the analysis, 18 articles whose full text could be accessed constituted the sample of the study. Published reports showed that simulation-supported trainings improved knowledge and basic practice skills for child care, facilitated the application of theoretical knowledge, provided critical thinking skills, increased the perception of family-centered care, and reduced anxiety about planning, implementing and evaluating child care in pediatric nursing students. It was found to improve knowledge, skills, self-confidence and self-efficacy for the diagnosis of neglect and abuse in children, care of premature newborn, cardiopulmonary resuscitation, management of chronic disease process and team collaboration.

Conclusıon: Simulation-assisted training method is an important training method for nursing students to evaluate and identify sick children, to acquire basic skills related to the care of the child, to increase the efficiency of climatic practice, to gain disease management skills, and to support cooperation and communication within the team. Supporting nursing students with simulation applications for the management of children, one of the specific groups, will be useful in developing clinical practice and patient management skills after graduation.

Key words: Pediatric nursing, educatıon, nursing students, simulation applications

SİMÜLASYON DESTEKLİ ÇOCUK SAĞLIĞI VE HASTALIKLARI HEMŞİRELİĞİ EĞİTİMİNİN HEMŞİRELİK ÖĞRENCİLERİ ÜZERİNDEKİ ETKİNLİĞİ: SİSTEMATİK İNCELEME

ÖZET

Amaç: Bu literatür incelemesi hemşirelik öğrencilerinin çocuk sağlığı ve hastalıkları hemşireliği eğitimlerinde simülasyon kullanımının etkinliğini derlemek amacıyla yapılmıştır.

Materyal ve Metot: 2000-2025 yılları arasında Google Akademik, Web of Science, Pubmed, Scopus, Science Direct ve Cochrane kütüphanesi olarak altı elektronik veri tabanı taranmıştır. Veri tabanları Türkçe ve İngilizce dillerde "hemşirelik öğrencileri", "çocuk", "eğitim" ve "simülasyon" anahtar kelimeleri ile sistematik olarak taranmıştır. Çocuk sağlığı ve hastalıkları hemşireliği eğitiminde simülasyon uygulamalarına yönelik uygulanan, uygulamanın etkinliğinin değerlendirildiği, sistematik inceleme ve metaanaliz raporlarının oluşturulduğu, tam metnine ulaşılabilen makaleler incelemeye dahil edilmiştir.

Bulgular: Yapılan analizler sonucunda tam metnine ulaşılabilen 18 makale araştırmanın örneklemini oluşturmuştur. Yayınlanan raporlar simülasyon destekli eğitimlerin çocuk hastalıkları hemşireliği eğitimi alan öğrencilerde çocuğun bakımına yönelik bilgi ve temel uygulama becerilerini geliştirdiği, teorik bilginin uygulamaya geçirilmesini kolaylaştırdığı, eleştirel düşünme becerisi kazandırdığı, aile merkezli bakım algısını arttırdığı ve çocuğun bakımının planlanması, uygulanamsı ve değerlendirilimesine yönelik kaygıları azalttığı belirlenmiştir. Çocuklarda ihmal ve istismarın tanılanması, prematüre yenidoğanın bakımı, kardiyopulmoner resüsitasyon, kronik hastalık sürecinin yönetimi ve ekip işbirliğine yönelik bilgi, beceri, özgüven ve özyeterliliklerini geliştirdiği bulunmuştur.

Sonuç: Simülasyon destekli eğitim metodu hemşirelik öğrencilerinin hasta çocukların değerlendirilmesi, tanımlanması, çocuğun bakımına ilişkin temel beceriler edinmesi, klimik uygulama verimliliğinin arttırılması, hastalık yönetimi becerisi kazandırılması ve ekip içi işbirliği ve iletişimin desteklenmesinde önemli bir eğitim metodudur. Hemşirelik öğrencilerinin spesifik gruplardan biri olan çocukların yönetimine yönelik simülasyon uygulamaları ile desteklenmesi mezuniyet sonrası klinik uygulama ve hastağın yönetimi becerilerinin geliştirilmesinde yararlı olacaktır.

Anahtar Kelimeler: Çocuk hemşireliği, eğitim, hemşirelik öğrencileri, simülasyon uygulamaları

Giriş

Hemşirelik eğitiminde simülasyon tabanlı öğrenme, öğrencilerin teorik bilgilerini pratik becerilere dönüştürmelerine olanak tanıyan etkili bir öğretim yöntemidir. Senaryo temelli simülasyonlar, hemşirelik öğrencilerinin mesleki bilgi düzeyini, klinik uygulama becerilerini ve öğrenme özgüvenini anlamlı düzeyde artırmaktadır(Wang et al., 2022). Bu tür simülasyonlar, öğrencilerin gerçek klinik ortamlarda karşılaşamayacakları durumları deneyimlemelerine olanak tanıyarak, klinik karar verme becerilerini geliştirmelerine katkı sağlar . Ayrıca, sanal gerçeklik ve artırılmış gerçeklik gibi teknolojilere dayalı simülasyonlar, öğrencilerin bilgi düzeyi, özgüven ve öz-yeterlik düzeylerinde geleneksel yöntemlere kıyasla daha etkili sonuçlar elde etmelerini sağlamaktadır. Simülasyon tabanlı eğitim, aynı zamanda hemşirelik öğrencilerinin empati düzeylerini artırmakta ve hasta bakımında daha duyarlı yaklaşımlar geliştirmelerine yardımcı olmaktadır . Bu bulgular, simülasyonun hemşirelik eğitiminde teorik bilgilerin pekiştirilmesi, klinik uygulamaların güvenli bir ortamda deneyimlenmesi ve öğrencilerin mesleki becerilerinin geliştirilmesi açısından önemli olduğunu göstermektedir(Wang et al., 2022).

Hemşirelik eğitiminde simülasyon temelli öğrenme, teorik bilginin klinik uygulamaya aktarımını kolaylaştıran ve öğrencilerin mesleki yeterliliklerini geliştiren bir yaklaşımdır(Cleaver et al., 2021). Simülasyonlar, öğrencilerin hasta güvenliği riskine maruz kalmadan klinik senaryoları deneyimlemelerine olanak tanırken; aynı zamanda kritik düşünme, klinik karar verme, problem çözme ve etkili iletişim becerilerinin gelişimini desteklemektedir (Shin et al., 2023). Bu yöntem, özellikle yoğun bakım, acil servis gibi yüksek riskli alanlarda gerçek yaşam durumlarının modellenmesiyle öğrencilerin stresle başa çıkma ve kriz yönetimi kapasitelerini artırmakta; böylece mezuniyet öncesi dönemde profesyonel kimlik gelişimini hızlandırmaktadır (Kim & Park, 2024). Ayrıca yapılandırılmış geribildirim ve tekrar imkânı sayesinde öğrenme kalıcılığı artmakta, öğrenci merkezli bir öğrenme ortamı sağlanmaktadır (Cant & Cooper, 2020). Yapılan güncel araştırmalar, simülasyon temelli eğitimin hem bilgi düzeyinde hem de psikomotor becerilerde anlamlı artış sağladığını ve öğrencilerin klinik uygulamalara daha yüksek özgüvenle katıldığını ortaya koymaktadır (Ahn & Song, 2024). Tüm bu yönleriyle simülasyon, hemşirelikte yalnızca teknik becerilerin kazandırılması değil; aynı zamanda etik duyarlılık, empati ve multidisipliner iş birliği gibi profesyonel değerlerin pekiştirilmesinde de kritik bir rol oynamaktadır(Broussard et al., 2009; Dnp, 2023).

Pediatri hemşireliği eğitimi, çocukların benzersiz fizyolojik, psikolojik ve gelişimsel özelliklerine uygun bakım sunabilme becerilerinin kazandırılmasını hedeflemektedir(Darcy Mahoney et al., 2013; Weston & Zauche, 2021). Bu süreçte, simülasyon temelli eğitim yöntemleri, hemşirelik öğrencilerinin klinik uygulama becerilerini güvenli, kontrollü ve tekrarlanabilir ortamlarda geliştirmeleri için kritik bir rol oynamaktadır(Appiah-Kusi & Christianson, 2024; Beauchesne & Douglas, 2011; Cheng et al., 2014). Simülasyon, öğrencilere teorik bilgi ile pratik uygulamaları bütünleştirme imkânı sağlayarak, klinik karar verme ve problem çözme yetkinliklerinin artırılmasına yardımcı olmaktadır(Jeffries, 2005).

Pediatrik hasta bakımında, özellikle çocukların yaş, gelişim düzeyi ve aile dinamiklerinin göz önünde bulundurulması gerekliliği, hemşirelik uygulamalarının karmaşıklığını artırmaktadır. Simülasyon yoluyla gerçekleştirilen uygulamalar, öğrencilerin yaşa uygun bakım planlama, etkili iletişim stratejileri geliştirme, kriz yönetimi ve acil müdahale becerilerini edinmelerini desteklemektedir (Cant & Cooper, 2010). Bu bağlamda, simülasyon temelli eğitimler, hemşirelik öğrencilerinin mesleki özgüvenini artırmakta ve

gerçek klinik ortamlarında karşılaşabilecekleri zorluklara karşı hazırlıklı olmalarını sağlamaktadır(Bani Salameh et al., 2024). Literatürde, simülasyonun pediatri hemşireliği eğitiminde öğrenme çıktılarını iyileştirdiği ve hasta güvenliği açısından risklerin minimize edilmesine katkıda bulunduğu belirtilmektedir (Rosen et al., 2012; Mohammed et al., 2017). Ayrıca, simülasyon sonrası yapılan yapılandırılmış geri bildirimler ve yansıtıcı uygulamalar, öğrenme sürecinin derinleşmesini ve öğrencilerin öz-yansıtma becerilerinin gelişmesini sağlamaktadır (Tosterud et al., 2016; Bowling,2015). Bu literatür incelemesi hemşirelik öğrencilerinin çocuk sağlığı ve hastalıkları hemşireliği eğitimlerinde simülasyon kullanımının etkinliğini derlemek amacıyla yapılmıştır.

Gelişme

2000-2025 yılları arasında Google Akademik, Web of Science, Pubmed, Scopus, Science Direct ve Cochrane kütüphanesi olarak altı elektronik veri tabanı taranmıştır. Veri tabanları Türkçe ve İngilizce dillerde "hemşirelik öğrencileri", "çocuk", "eğitim" ve "simülasyon" anahtar kelimeleri ile sistematik olarak taranmıştır. Çocuk sağlığı ve hastalıkları hemşireliği eğitiminde simülasyon uygulamalarına yönelik uygulanan, uygulamanın etkinliğinin değerlendirildiği, sistematik inceleme ve metaanaliz raporlarının oluşturulduğu, tam metnine ulaşılabilen makaleler incelemeye dahil edilmiştir. Yapılan analizler sonucunda tam metnine ulaşılabilen 18 makale araştırmanın örneklemini oluşturmuştur. Yayınlanan raporlar simülasyon destekli eğitimlerin çocuk hastalıkları hemşireliği eğitimi alan öğrencilerde çocuğun bakımına yönelik bilgi ve temel uygulama becerilerini geliştirdiği, teorik bilginin uygulamaya geçirilmesini kolaylaştırdığı, eleştirel düşünme becerisi kazandırdığı, aile merkezli bakım algısını arttırdığı ve çocuğun bakımının planlanması, uygulanaması ve değerlendirilimesine yönelik kaygıları azalttığı belirlenmiştir. Çocuklarda ihmal ve istismarın tanılanması, prematüre yenidoğanın bakımı, kardiyopulmoner resüsitasyon, kronik hastalık sürecinin yönetimi ve ekip işbirliğine yönelik bilgi, beceri, özgüven ve özyeterliliklerini geliştirdiği bulunmuştur(Arslan et al., 2018; Bowling, 2015; Joshi et al., 2022; McIntosh, 2022; Shorey & Ng, 2021; Yıldırım Sarı et al., 2018).

Simülasyon temelli müdahaleler öğrencilerin bilgi düzeyini arttırmakta, öz yeterliliklerini geliştirmekte, öz güven kazanmalarını sağlamakta ve memnuniyet düzeylerini arttırmaktadır(Appiah-Kusi & Christianson, 2024; Bani Salameh et al., 2024; Lubbers & Rossman, 2016; Saied, 2017). Arslan vev arkadaşları pediatrik değerlendirme, antropometrik ölçümler ve yaşamsal bulguların alınması, bazı ilaç uygulamaları ve bakım aktivitelerine katılımda simülasyon destekli eğitim alan öğrencilerin anlamlı olarak daha özgüvenli olduklarını bulmuşlardır (Arslan et al., 2018) Aynı zamanda çocuk kliniklerindeki uygulama sürecine yönelik kaygı ve stresin de simülasyon uygulaması ile azaltılabileceği belirlenmiştir(Megel et al., 2012). Toqan ve arkadaşları yüksek sadakat simülasyonunun hemşirelik öğrencileri arasında öz memnuniyet ve öz güven düzeylerini anlamlı olarak arttırdığını belirlemiştir(Toqan et al., 2023). Valizadeh ve arkadaşları hemşirelik öğrencilerinin çocuklarda uygulanacak çeşitli invaziv girişimlere yönelik yeterlilik düzeylerinin simülasyon uygulamaları ile geliştirilebileceğini belirtmektedir(Valizadeh et al., 2021). Aynı zamanda çocuklarda bakım sürecinin temelini oluşturan aile merkezli bakım uygulamalarına yönelik bakış açısı kazandırmaktadır(Ayed et al., 2021; Khalil et al., 2023). Özellikle Covid 19 pandemisi sürecinde aksayan hemşirelik klinik eğitimi simülasyon uygulamaları ile desteklenmiş ve öğrencielrin çocukların bakımına ilişkin bilgi ve uygulama becerileri geliştirilmeye çalışılmıştır(Cook & Camp-Spivey, 2022; Shin & Kim, 2015). Mohamed ve arkadaşlarının çocuklarda kardiyopulmoner resüsitasyonun yönetimine yönelik pediatri hemşireliği eğitimi alan 100 öğrenci ile

yaptıkları araştırmada çocuklarda kardiyopulmoner resüsitasyon yönetim bilgi düzeyleri, tutum ve uygulama beceri puan ortalamalarında anlamlı farklılık saptamışlardır(Mohamed et al., 2017). Çocuklarda ihmal ve istismarın tanılama düzeyini arttırmak için simülasyon destekli araştırmalar yürütülmüştür. Çocuklarda ihmal ve istismara yönelik verilen eğitimin hemşirelik öğrencilerde tanılama ve değerlendirme becerilerini anlamlı olarak geliştirdiği saptanmıştır(Han et al., 2025; Lee & Lee, 2022).

Sonuç

Simülasyon destekli eğitim metodu hemşirelik öğrencilerinin hasta çocukların değerlendirilmesi, tanımlanması, çocuğun bakımına ilişkin temel beceriler edinmesi, klimik uygulama verimliliğinin arttırılması, hastalık yönetimi becerisi kazandırılması ve ekip içi işbirliği ve iletişimin desteklenmesinde önemli bir eğitim metodudur. Hemşirelik öğrencilerinin spesifik gruplardan biri olan çocukların yönetimine yönelik simülasyon uygulamaları ile desteklenmesi mezuniyet sonrası klinik uygulama ve hastağın yönetimi becerilerinin geliştirilmesinde yararlı olacaktır.

Pediatri hemşireliği alanında simülasyonun eğitim programlarına entegrasyonu, öğrenci hemşirelerin teorik bilgi ve klinik becerilerinin eşzamanlı gelişimini destekleyerek, hasta bakım kalitesinin yükseltilmesine ve hasta güvenliğinin sağlanmasına önemli katkılar sağlayacağı öngörülmektedir.

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SIMULATION APPLICATIONS IN THE DEVELOPMENT OF PROFESSIONAL COMPETENCIES OF NURSES WORKING IN PEDIATRIC CLINICS

ABSTRACT

Objectives: This study was conducted to examine the results of simulation applications used in the development of professional knowledge, skills, satisfaction and self-efficacy of nurses working in pediatric clinics.

Materials and Methods: Six electronic databases including Google Scholar, Web of Science, Pubmed, Scopus, Science Direct and Cochrane library were searched in the last 20 years. The databases were systematically searched in Turkish and English with the keywords 'pediatric nurses', 'education' and 'simulation applications'. The full-text articles were analyzed

Results: As a result of the analysis, 15 articles whose full text could be accessed constituted the sample of the study. Published reports showed that simulation-supported trainings improved pediatric nurses' knowledge and basic practice skills for child care, increased critical thinking skills in emergency and intensive care, and improved professional competence in the management of children with special care needs. It was found to improve knowledge, skills, self-confidence and self-efficacy in the diagnosis of neglect and abuse in children, pediatric intensive care and emergency management, multidisciplinary management of pediatric trauma, cardiac critical intensive care management, sedation and analgesia drug management in emergency services, management of chronic disease process, management of parents in emergency situations, ensuring pediatric patient safety, management of specific infections such as Covid-19, and team collaboration. Cardiopulmonary resuscitation, Pediatric Extracorporeal Cardiopulmonary Resuscitation (ECPR), tracheal intubation, tracheostomy, care processes. In addition, it is stated that it has an important effectiveness in the symptom management of the child with oncologic diagnosis, which is one of the special groups, and in the management of the physical and psychosocial process of the child and parents in the palliative period.

Conclusion: It was determined that simulation applications used in the training of pediatric nurses have an important effect on the identification of the child, planning, implementation and evaluation of the effectiveness of appropriate nursing interventions, and management of critical processes. Utilizing simulation applications in in-service training programs of pediatric nurses will be effective in increasing the number of qualified and competent nurses.

Keywords: Pediatric nurses, education, child care, simulation applications

ÇOCUK HASTALIKLARI KLİNİKLERİNDE GÖREV ALAN HEMŞİRELERİN MESLEKİ YETERLİLİKLERİNİN GELİŞTİRİLMESİNDE SİMÜLASYON UYGULAMALARI

ÖZET

Amaç: Bu araştırma çocuk kliniklerinde çalışan hemşirelerin mesleki bilgi, beceri, memnuniyet ve öz yeterliliklerinin geliştirilmesinde kullanılan simülasyon uygulamalarının sonuçlarının incelenmesi amacıyla yapılmıştır.

Materyal ve Metot: Son 20 yıl içinde Google Akademik, Web of Science, Pubmed, Scopus, Science Direct ve Cochrane kütüphanesi olarak altı elektronik veri tabanı taranmıştır. Veri tabanları Türkçe ve İngilizce dillerde 'çocuk hemşireleri', "eğitim" ve "simülasyon uygulamaları" anahtar kelimeleri ile sistematik olarak taranmıştır. Tam metnine ulaşılan makaleler incelenmiştir.

Bulgular: Yapılan analizler sonucunda tam metnine ulaşılabilen 15 makale araştırmanın örneklemini oluşturmuştur. Yayınlanan raporlar simülasyon destekli eğitimlerin çocuk hemşirelerinin çocuğun bakımına yönelik bilgi ve temel uygulama becerilerini geliştirdiği, acil ve yoğun bakımlarda eleştirel düşünme becerilerini arttırdığı, özellikli bakım ihtiyacı olan çocukların yönetiminde mesleki yeterliliği geliştirdiği bulunmuştur. Çocuklarda ihmal ve istismarın tanılanması, çocuk yoğun bakım ve acil yönetimi, pediatrik travmaların multidisipliner yönetimi, kardiyak kritik yoğun bakım yönetimi, acil servislerde sedasyon ve analjezi ilaç yönetimi, kronik hastalık sürecinin yönetimi, acil durumlarda ebeveynlerin yönetimi, pediatrik hasta güvenliği sağlama, Covid-19 gibi spesifik enfeksiyonların yönetimi, ve ekip işbirliğine yönelik bilgi, beceri, özgüven ve özyeterliliklerini geliştirdiği bulunmuştur. Kardiyopulmoner resüsitasyon, Pediatrik Ekstrakorporeal Kardiyopulmoner Resüsitasyon (ECPR), trakeal entübasyon, , trakeostomi, bakımı süreçlerinde temel beceri kazanmalarını sağladığı saptanmıştır. Ayrıca özellikli gruplardan olan onkolojik tanılı çocuğun semptom yönetiminde, palyatif dönemde olan çocuğun ve ebeveynlerinin fiziksel ve psikososyal sürecin yönetiminde de önemli bir etkinliğinin olduğu belirtilmektedir

Sonuç: Pediatri hemşirelerinin eğitimlerinde kullanılan simülasyon uygulamaları hemşirelerin çocuğun tanımlanması, uygun hemşirelik girişimlerinin planlanması, uygulanması ve etkinliğinin değerlendirilmesi, kritik süreçlerin yönetiminde önemli bir etkinliğinin olduğu belirlenmiştir. Pediatri hemşirelerinin hizmet içi eğitim programlarında simülasyon uygulamalarından yararlanılması nitelikli ve yetkin hemşire sayısının artmasında etkili olacaktır.

Anahtar Kelimeler: Pediatri hemşireleri, eğitim, çocuk bakımı, simülasyon uygulamaları

Giriş

Simülasyon, hemşirelik eğitiminde öğrencilerin klinik becerilerini geliştirmek, hasta güvenliğini artırmak ve mesleki yeterliliklerini pekiştirmek amacıyla kullanılan yapılandırılmış, kontrollü ve gerçek yaşamı taklit eden öğretim yöntemidir(Dnp, 2023). Simülasyon uygulamaları, öğrencilerin gerçek hasta ile karşılaşmadan önce teorik bilgilerini pratikle birleştirmelerine, hata yaparak öğrenmelerine ve profesyonel rol gelişimlerine katkı sağlamaktadır.

Günümüzde hemşirelik eğitimi, yalnızca teorik bilgi aktarımını değil, aynı zamanda öğrencilerin ve hemşirelerin klinik karar verme, eleştirel düşünme, iletişim, iş birliği ve teknik beceri geliştirme süreçlerini de kapsayan bütüncül bir yaklaşıma dönüşmektedir(Wang et al., 2022). Bu bağlamda, simülasyon temelli eğitim yöntemleri, klinik deneyimlerin yapılandırılmış, güvenli ve tekrarlanabilir biçimde sunulmasını sağlayarak hemşirelik eğitim programlarında önemli rol oynamaktadır(Dnp, 2023; Shorey & Ng, 2021). Simülasyon, gerçek klinik ortamları yansıtan senaryolar aracılığıyla öğrencilerin hasta bakımına dair bilişsel, psikomotor ve duyuşsal becerilerini geliştirmeye yönelik uygulamalı bir öğrenme stratejisidir. Yüksek teknolojili hasta simülatörleri, standardize hasta kullanımı ve sanal gerçeklik gibi farklı düzey ve biçimlerde uygulanabilen simülasyonlar, öğrencilerin hem teknik hem de etik boyutlarıyla mesleki yeterlilik kazanmalarını desteklemektedir (Jeffries, 2012). Simülasyonun en önemli katkılarından biri, hasta güvenliğini riske atmadan öğrenme sürecinin gerçekleştirilmesini sağlamasıdır. Gerçek hasta ortamında nadiren karşılaşılabilecek, karmaşık ya da acil durum senaryoları simülasyon yoluyla tekrar edilebilir hale getirilmekte; bu da öğrencilerin kriz yönetimi ve hızlı karar verme becerilerini artırmaktadır (Rosen et al., 2012). Ayrıca, yapılandırılmış geri bildirim ve yansıtıcı düşünme süreçleri, öğrencilerin öz farkındalık geliştirmelerine ve profesyonel rol davranışlarını içselleştirmelerine olanak tanımaktadır (Fey & Jenkins, 2015). Literatürdeki bulgular, simülasyon temelli öğrenmenin geleneksel öğretim yöntemlerine kıyasla bilgi düzeyi, klinik uygulama yeterliliği ve öz güven üzerinde daha yüksek etkisini vurgulamaktadır(Cant & Cooper, 2017). Bu durum, özellikle klinik alanlarda öğrenci sayısının fazla, vaka çeşitliliğinin ise sınırlı olduğu koşullarda, simülasyonun alternatif ve tamamlayıcı bir öğrenme ortamı oluşturmaktadır(Shorey & Ng, 2021; Yaeger et al., 2004).

Pediatri hemşireliği hasta olan çocukların bakım ve tedavilerini yürütülmesini sağlayan, aile üyelerinin bakıma katılımını destekleyen, tedavi sonrası sağlığın devamlılığın sürdürülmesinde kanıta dayalı bakım yaklaşımları ile çocupa ve ebeveynlere rehberlik ve danışmanlık sağlayan önemli sağlık profesyonelleri arasında bulunmaktadır. Sağlık hizmetlerinin gelişen ve karmaşıklaşan yapısı, pediatri hemşirelerinin yalnızca temel klinik becerilere değil, aynı zamanda hızlı karar verme, etkili iletişim, kriz yönetimi ve multidisipliner iş birliği gibi ileri düzey mesleki yeterliliklere de sahip olmalarını gerektirmektedir(Wang et al., 2022). Bu çerçevede, simülasyon temelli eğitimler, yalnızca hemşirelik öğrencileri için değil, klinikte aktif olarak görev yapan çocuk hemşirelerinin sürekli mesleki gelişimi açısından da önemli bir eğitim stratejisi haline gelmiştir(Gamble et al., 2016). Pediatri klinik hemşirelerinin mesleki yetkinliklerinin artırılması, çocuk hastaların karmaşık bakım ihtiyaçlarını karşılamada kritik bir rol oynamaktadır. Bu bağlamda, simülasyon uygulamalı eğitim programları hemşirelik eğitiminde giderek daha yaygın şekilde kullanılmakta ve etkili bir öğrenme yöntemi olarak öne çıkmaktadır. Literatürde yer alan çeşitli çalışmalar, pediatri klinik hemşirelerine yönelik yapılandırılmış simülasyon eğitimlerinin, hemşirelerin klinik karar verme becerilerini, iletişim yetkinliklerini ve kriz yönetimi kabiliyetlerini anlamlı düzeyde artırdığını ortaya

koymaktadır. Çocuk hastaların fizyolojik ve psikososyal özellikleri, gelişimsel düzeyleri ve iletişim biçimleri, erişkin hastalardan önemli ölçüde farklılık göstermektedir. Bu durum, çocuk hemşirelerinin hata toleransının düşük olduğu, hızlı ve doğru müdahale gerektiren klinik durumlara hazırlıklı olmasını zorunlu kılmaktadır(Yaeger et al., 2004). Simülasyon uygulamaları, özellikle pediatrik acil müdahaleler, nadir görülen klinik tablolar, ileri yaşam desteği ve aile merkezli bakım gibi karmaşık durumların tekrarlanabilir ve güvenli biçimde çalışılmasına olanak sağlar (Hunt et al., 2008). Simülasyon, klinik hemşirelerin hasta güvenliğini tehdit eden durumlara müdahalede bilgi, beceri ve öz güvenlerini artırmakta; aynı zamanda ekip içi iletişim, görev paylaşımı ve liderlik gibi mesleki yetkinlikleri güçlendirmektedir (Weinstock et al., 2009). Ayrıca, gerçeğe uygun senaryolar üzerinden yapılan uygulamalar ve yapılandırılmış geri bildirim süreçleri, hatalardan öğrenme ve öz değerlendirme fırsatı sunarak, sürekli mesleki gelişimi desteklemektedir(Shorey & Ng, 2021; Wang et al., 2022). Araştırmalar, klinik hemşireler için düzenlenen simülasyon temelli eğitimlerin, özellikle pediatri alanında hasta sonuçları üzerinde doğrudan olumlu etkileri olduğunu göstermektedir (Andreatta et al., 2011). Bu kapsamda, simülasyon yalnızca bilgi ve beceri kazandırma aracı değil, aynı zamanda hasta bakım kalitesinin sürdürülebilirliği için temel bir öğrenme yönetmidir(Gamble et al., 2016). Bu araştırma çocuk kliniklerinde çalışan hemşirelerin mesleki bilgi, beceri, memnuniyet ve öz yeterliliklerinin geliştirilmesinde kullanılan simülasyon uygulamalarının sonuçlarının incelenmesi amacıyla yapılmıştır

Gelişme

Son 20 yıl içinde Google Akademik, Web of Science, Pubmed, Scopus, Science Direct ve Cochrane kütüphanesi olarak altı elektronik veri tabanı taranmıştır. Veri tabanları Türkçe ve İngilizce dillerde ‘çocuk hemşireleri’, “eğitim” ve “simülasyon uygulamaları” anahtar kelimeleri ile sistematik olarak taranmıştır. Tam metnine ulaşılan makaleler incelenmiştir. Yapılan analizler sonucunda tam metnine ulaşılabilen 15 makale araştırmanın örneklemini oluşturmuştur.

Yayınlanan raporlar simülasyon destekli eğitimlerin;

- ✓ çocuk hemşirelerinin çocuğun bakımına yönelik bilgi ve temel uygulama becerilerini geliştirdiği(Butler et al., 2009; Hassanein et al., 2021; Karageorge et al., 2020; Straka et al., 2012),
- ✓ özellikli bakım ihtiyacı olan çocukların yönetiminde mesleki yeterlilik sağladığı(Brown et al., 2020)
- ✓ çocuklarda ihmal ve istismarın tanımlama becerilerini geliştirdiği(Anderst et al., 2016; Shih et al., 2024),
- ✓ pediatrik hasta güvenliği sağlamaya yönelik bakış açısı kazandırdığı(Lee et al., 2021; Sapyta & Eiger, 2017),
- ✓ pediatrik travmaların multidisipliner yönetim becerisi kazandırdığı(Falcone et al., 2008; Messmer, 2008),
- ✓ acil servislerde güvenli sedasyon ve analjezik ilaç yönetim becerisini kazandırdığı(Nucci et al., 2022),

- ✓ yoğun bakımda ekip içi etkili iletişim becerilerini geliştirdiği(Colman et al., 2019; Messmer, 2008; Ulmer et al., 2022),
- ✓ çocuk acil ve çocuk yoğun bakımlarda kritik hasta yönetim ve eleştirel düşünme becerilerini arttırdığı(Brown et al., 2020; Colman et al., 2019; Mohammed et al., n.d.),
- ✓ kardiyak kritik yoğun bakım yönetimi(Pye et al., 2010; Ralston et al., 2021),
- ✓ çocuklarda kardiyopulmoner resüsitasyon ve yenidoğanın yeniden canlandırma becerisini geliştirdiği(Mills et al., 2013; Mohammed et al., n.d.; Pye et al., 2010; van den Bos-Boon et al., 2021; Yaeger et al., 2004),
- ✓ Pediatrik Ekstrakorporeal Kardiyopulmoner Resüsitasyon yönetim becerisini geliştirdiği (ECPR)(Sawyer et al., 2019),
- ✓ trakeal entübasyon uygulama ve takip etme becerisini geliştirdiği(Balikai et al., 2021; Nishisaki et al., 2010)
- ✓ trakeostomi bakım becerisini arttırdığı(Wooldridge & Carter, 2021)
- ✓ onkolojik tanılı çocuklarda kemoterapi sonrası semptomların(oral mukozit, bulantı-kusma, konstipasyon, ağrı, yorgunluk, psikolojik sorunlar, ebeveyn yönetimi) yönetimlerinin sağlanmasında etkili olduğu(Helt et al., 2020),
- ✓ palyatif dönemde olan çocuğun ve ebeveynlerinin fiziksel ve psikososyal sürecin yönetimini desteklediği(Brock et al., 2017)
- ✓ Covid-19 gibi spesifik enfeksiyonların yönetimi ve ekip işbirliğine yönelik bilgi, beceri, özgüven ve özyeterlilik geliştirmesinde (Balikai et al., 2021)önemli bir etkinliğinin olduğu belirlenmiştir.

Çeşitli araştırma raporlarının çocuk kliniklerinde görev alan hemşirelerin simülasyon uygulamalı eğitimler ile desteklenemsinin olumlu sonuçlarına yer verdiği görülmektedir. Simülasyon temelli eğitim programları, hemşirelerin gerçek klinik ortamlarda karşılaşabilecekleri durumları risksiz bir ortamda deneyimlemelerine olanak tanımakta ve bu sayede hemşirelik bakımında hata yapma olasılığını azaltmaktadır. Özellikle pediatrik hastaların fizyolojik ve psikososyal gereksinimlerinin hassasiyeti göz önünde bulundurulduğunda, bu tür eğitimlerin hemşirelerin özgüven düzeylerini artırdığı ve stres yönetimi becerilerini geliştirdiği görülmektedir. Ayrıca, simülasyon destekli eğitimlerin, ekip içi iş birliğini güçlendirdiği ve hasta güvenliğini önceleyen bir bakım yaklaşımının yerleşmesine katkı sağladığı belirtilmektedir. Hemşirelerin mesleki bilgi ve becerilerinin pekiştirilmesiyle birlikte, klinik uygulamalarda daha hızlı, doğru ve etkili müdahalelerde bulunabildikleri gözlemlenmiştir. Bu durumun, hem hasta sonuçlarının iyileştirilmesine hem de sağlık hizmetlerinde bakım kalitesinin gelişmesine katkı sağlayacağı öngörülmektedir.

Sonuç

Sonuç olarak, hemşirelik eğitiminde simülasyon uygulamaları, öğrenci merkezli, aktif ve deneyimsel öğrenmeyi teşvik eden pedagojik bir yaklaşım olarak, mesleki bilgi, beceri ve tutumun bütüncül gelişimini desteklemekte; aynı zamanda hasta bakım kalitesinin ve güvenliğinin sürdürülebilir biçimde artırılmasını sağlamaktadır.

Pediatri hemşirelerinin eğitimlerinde kullanılan simülasyon uygulamaları hemşirelerin çocuğun tanımlanması, uygun hemşirelik girişimlerinin planlanması, uygulanması ve etkinliğinin değerlendirilmesi, kritik süreçlerin yönetiminde önemli bir etkinliğinin olduğu belirlenmiştir. Pediatri hemşirelerinin hizmet içi eğitim programlarında simülasyon uygulamalarından yararlanılması nitelikli ve yetkin hemşire sayısının artmasında etkili olacaktır.

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NEUROINFLAMMATION AS A KEY MECHANISM IN NEUROLOGICAL DISEASES

ABSTRACT

Neuroinflammation has emerged as a critical pathophysiological mechanism in the development and progression of numerous neurological diseases, including neurodegenerative disorders such as Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS), as well as acute conditions like stroke and traumatic brain injury (TBI). It involves the activation of the brain's resident immune cells, particularly microglia and astrocytes, which release pro-inflammatory cytokines, chemokines, reactive oxygen species (ROS), and other inflammatory mediators in response to injury, infection, or disease. While this inflammatory response is initially protective, chronic or excessive neuroinflammation leads to neuronal dysfunction, synaptic loss, and neuronal death, driving disease progression. Key signaling pathways, including the activation of cytokines such as TNF-α, IL-1β, and IL-6, play a central role in sustaining the inflammatory environment and exacerbating neuronal damage. This article reviews the current understanding of neuroinflammation's role in neurological diseases and highlights emerging therapeutic strategies aimed at modulating the inflammatory response. Targeting neuroinflammation presents a promising approach to slowing disease progression and improving outcomes for patients with these debilitating conditions. However, balancing the beneficial and harmful effects of inflammation remains a significant challenge, requiring precise modulation of immune responses within the brain.

Keywords: neuroinflammation, neurodegenerative diseases, microglia, cytokines, neuronal dysfunction.

Exploring the Basic Mechanisms of Neuroinflammation and Its Role in the Central Nervous System

Neuroinflammation is a term used to describe the inflammatory response within the central nervous system (CNS). While inflammation is a crucial part of the body's defense mechanisms, neuroinflammation, when chronic or misdirected, can have profound detrimental effects on brain health. It plays an essential role in the pathogenesis of various neurological diseases such as Alzheimer’s disease, Parkinson’s disease, multiple sclerosis (MS), and traumatic brain injury (TBI). The underlying mechanisms of neuroinflammation are complex, involving a variety of cellular and molecular processes, which help to mediate the brain's immune response. To understand neuroinflammation's significance in neurological disorders, it is essential to explore its basic mechanisms and its dual role as both a protective and potentially harmful process.

Neuroinflammation: The Immune Response in the Brain:The immune system of the brain is distinct from the peripheral immune system, as the brain is shielded by the blood-brain barrier (BBB), a selective semipermeable membrane that protects the brain from potentially harmful pathogens and toxins. However, the brain is not entirely isolated from the immune system. Instead, it has its own set of resident immune cells, primarily microglia, along with astrocytes and other glial cells, which play vital roles in detecting and responding to harmful stimuli. These cells are responsible for maintaining homeostasis, protecting against infection, and mediating recovery following injury or disease.Microglia are the primary immune cells in the CNS and act as the first line of defense. Under normal conditions, microglia are in a resting or surveillant state, constantly monitoring their environment for signs of damage or infection. Upon detecting pathological events, microglia become activated and initiate inflammatory responses. They can release pro-inflammatory cytokines, chemokines, reactive oxygen species (ROS), and other molecules that promote inflammation. While acute inflammation is beneficial in defending the brain against infections or injuries, chronic or excessive activation of microglia can lead to sustained neuroinflammation, which is implicated in the development and progression of various neurological diseases.Astrocytes, another type of glial cell, also play a significant role in neuroinflammation. In addition to providing metabolic support to neurons, astrocytes can become reactive in response to injury or disease. Reactive astrocytes may release pro-inflammatory molecules and cytokines, contributing to the inflammatory environment. In some instances, this astrocytic reactivity may further exacerbate neuroinflammation, making it a self-perpetuating process. Therefore, while microglia and astrocytes are essential in protecting the brain, their prolonged activation can have harmful effects, leading to neurodegeneration and neuronal death.

Molecular Mechanisms of Neuroinflammation:At the molecular level, the activation of microglia and astrocytes triggers a cascade of events that leads to the release of various inflammatory mediators. One of the key pathways involved in neuroinflammation is the nuclear factor-kappa B (NF-κB) pathway. The activation of NF-κB in microglia and astrocytes is a central event that governs the production of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukins (e.g., IL-1β, IL-6), and chemokines like CCL2 (MCP-1). These cytokines recruit additional immune cells into the brain and amplify the inflammatory response.Additionally, the inflammasome plays a crucial role in neuroinflammation. The inflammasome is a multi-protein complex that activates caspase-1, an enzyme responsible for processing pro-inflammatory cytokines, including IL-1β and IL-18. Once activated, these cytokines are released into the extracellular space, where they

propagate the inflammatory process by acting on neighboring cells and tissue. In certain neurological diseases, such as Alzheimer's and Parkinson's disease, abnormal activation of the inflammasome is thought to contribute to chronic inflammation, leading to neuronal damage.Another critical component of neuroinflammation involves reactive oxygen species (ROS) and nitric oxide (NO). Microglia, astrocytes, and other immune cells in the brain produce ROS and NO during inflammation. These molecules play important roles in pathogen defense and tissue repair. However, when produced in excess, they can lead to oxidative stress, damaging cellular components such as lipids, proteins, and DNA. This oxidative damage can exacerbate neuroinflammation and contribute to neuronal dysfunction and death, making it a key factor in neurodegenerative diseases.The blood-brain barrier (BBB), which normally protects the brain from harmful substances, can also become disrupted during neuroinflammation. Inflammatory mediators, such as cytokines, can compromise the integrity of the BBB by altering the expression of tight junction proteins. This disruption allows peripheral immune cells and inflammatory mediators to infiltrate the CNS, further amplifying the inflammatory response and worsening neuronal injury.

Neuroinflammation in Neurological Diseases:Chronic neuroinflammation has been implicated in a variety of neurological diseases, where it acts as both a consequence of the disease and a contributor to its progression.

In Alzheimer's disease, neuroinflammation is considered a key pathological feature. The accumulation of beta-amyloid plaques and tau tangles in the brain triggers the activation of microglia and astrocytes. These activated glial cells release pro-inflammatory cytokines and ROS, which contribute to neuronal damage and cognitive decline. Although neuroinflammation in Alzheimer's may initially serve as a protective response to clear amyloid plaques, over time, it becomes chronic and exacerbates the disease process. The sustained activation of the immune cells can further promote tau hyperphosphorylation and neuronal death, accelerating the progression of Alzheimer's disease.

Parkinson's disease is characterized by the progressive loss of dopaminergic neurons in the substantia nigra, a brain region involved in motor control. Neuroinflammation in Parkinson's disease is primarily driven by the activation of microglia in response to the accumulation of alpha-synuclein aggregates, which are a hallmark of the disease. Activated microglia release inflammatory cytokines and ROS, which contribute to neuronal degeneration. The role of neuroinflammation in Parkinson's disease has prompted research into targeting microglial activation as a potential therapeutic strategy to slow disease progression.

In multiple sclerosis, the immune system attacks the myelin sheath that insulates neurons, leading to demyelination and neurological dysfunction. Neuroinflammation in MS is primarily driven by the infiltration of peripheral immune cells, such as T cells and macrophages, into the CNS. These immune cells release cytokines and promote the activation of microglia, leading to further damage to the myelin and underlying axons. The inflammatory response in MS is a central mechanism that drives the formation of lesions and exacerbates disease symptoms.

Traumatic brain injury triggers a cascade of events, including the activation of microglia and the release of pro-inflammatory cytokines. This acute neuroinflammatory response can lead to secondary injury, exacerbating the damage caused by the initial trauma. In TBI, neuroinflammation is a double-edged sword: it may initially help clear damaged tissue and promote repair, but if the inflammation persists, it can contribute to long-term neurodegeneration and cognitive deficits.

Following a stroke, ischemic damage to brain tissue leads to the activation of microglia and astrocytes, as well as the infiltration of peripheral immune cells. These immune responses aim to contain the damage and promote tissue repair. However, persistent neuroinflammation can lead to further neuronal injury and exacerbate the effects of the stroke. The inflammatory response also impairs neurogenesis and tissue recovery in the affected brain regions.

Therapeutic Implications and Strategies:Given the central role of neuroinflammation in neurological diseases, targeting the inflammatory response has become an area of intense research. Several therapeutic strategies aim to modulate neuroinflammation to reduce neuronal damage and improve outcomes in diseases like Alzheimer's, Parkinson's, and multiple sclerosis.

Anti-inflammatory drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids have shown some promise in reducing neuroinflammation, but their use is limited by side effects and concerns about efficacy in chronic neuroinflammatory conditions. Immunomodulatory therapies that target specific immune pathways, such as TNF-α inhibitors or cytokine-blocking agents, are being investigated in clinical trials for diseases like Alzheimer's and multiple sclerosis.

Another promising avenue is the development of small molecules or biologics that specifically target microglial activation or the inflammasome. Inhibiting microglial activation could help prevent or reduce the damaging effects of chronic neuroinflammation without compromising the brain’s ability to respond to acute injury or infection.Additionally, neuroprotective agents that reduce oxidative stress or improve mitochondrial function are being explored as potential therapies to mitigate the effects of neuroinflammation. These agents could work in tandem with anti-inflammatory strategies to slow the progression of neurodegenerative diseases.

Neuroinflammation is a complex and multifaceted process that plays a crucial role in maintaining the health and function of the brain. While it serves as a protective mechanism against infection and injury, prolonged or excessive inflammation can be harmful and contribute to the progression of many neurological diseases. Understanding the cellular and molecular mechanisms of neuroinflammation is critical for developing therapeutic strategies aimed at modulating this response. As research continues to uncover the intricate roles of glial cells, cytokines, and other immune mediators in the brain, new and more effective treatments for neuroinflammatory diseases may emerge, offering hope for patients suffering from conditions like Alzheimer’s, Parkinson’s, multiple sclerosis, and stroke.

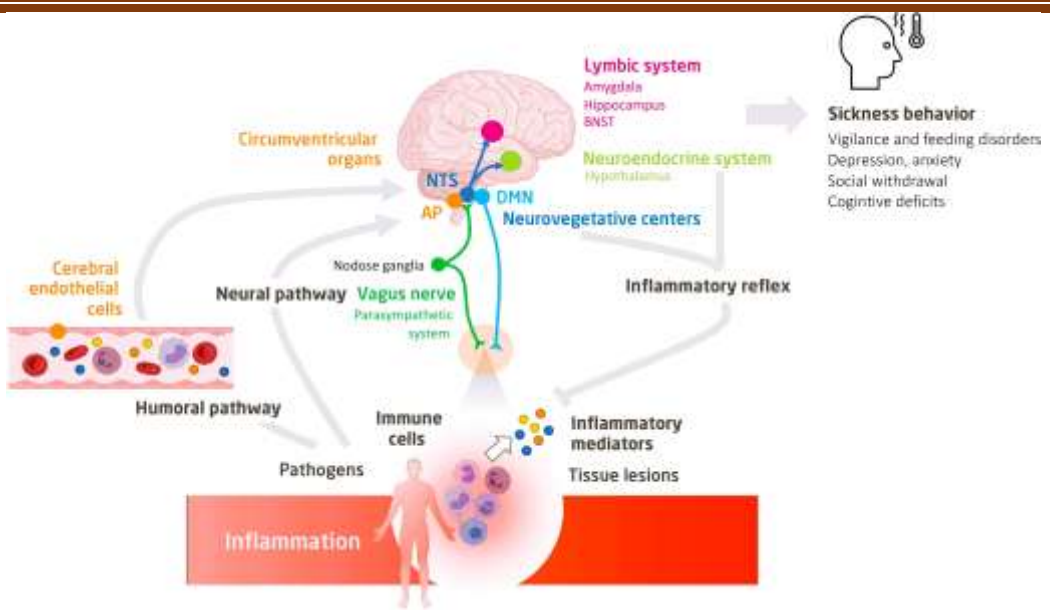


Figure:1 This image illustrates how inflammation can lead to sickness behavior by triggering immune responses that affect the brain. Inflammation activates immune cells that release mediators, which can influence the brain through the bloodstream and neural pathways, particularly the vagus nerve. Key brain regions like the neurovegetative centers, hypothalamus, and limbic system respond to these signals. This process results in symptoms such as vigilance and feeding disorders, depression, anxiety, social withdrawal, and cognitive deficits. It highlights the complex interactions between the immune system, nervous system, and brain in response to inflammation.

Examining How Neuroinflammation Contributes to the Progression of Alzheimer's Disease and Emerging Strategies to Target This Process

Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, memory loss, and behavioral changes. It is the most common form of dementia, affecting millions of individuals worldwide. While the hallmark features of Alzheimer's include the accumulation of amyloid-beta plaques and tau tangles, increasing evidence suggests that neuroinflammation plays a critical role in the disease's progression. Neuroinflammation, once considered a secondary or reactive process in Alzheimer's, is now recognized as a central mechanism that contributes significantly to the initiation, development, and exacerbation of the disease. This inflammation is primarily mediated by the activation of microglia and astrocytes, which are the brain's resident immune cells. Understanding how neuroinflammation interacts with other pathophysiological processes in Alzheimer's is crucial for developing effective therapeutic strategies. This article explores the mechanisms through which neuroinflammation contributes to Alzheimer's disease and highlights emerging strategies aimed at targeting this process.

The Role of Neuroinflammation in Alzheimer's Disease:Neuroinflammation in Alzheimer's disease is a complex, multifaceted process that involves both the innate and adaptive immune systems of the brain. Microglia, the brain's resident immune cells, are primarily responsible for initiating the inflammatory response in AD. Under normal conditions, microglia are in a resting or surveillant state, constantly monitoring the brain for signs of damage or infection. However, when amyloid-beta plaques accumulate in the brain, microglia become activated, leading to the release of pro-inflammatory cytokines, reactive oxygen species (ROS), and

other neurotoxic molecules.While the initial activation of microglia is thought to be a protective response aimed at clearing amyloid-beta plaques, prolonged or excessive microglial activation can become harmful. This chronic activation results in sustained neuroinflammation, which exacerbates neuronal damage and accelerates the progression of Alzheimer's. Activated microglia release pro-inflammatory cytokines such as interleukins (IL-1β, IL-6), tumor necrosis factor-alpha (TNF-α), and other inflammatory mediators that induce neuronal injury, synaptic dysfunction, and neuronal loss. Additionally, the overproduction of ROS and nitrogen species during chronic inflammation leads to oxidative stress, which further contributes to cellular damage and death.Astrocytes, another type of glial cell, also play a crucial role in neuroinflammation. While astrocytes are involved in maintaining homeostasis and supporting neuronal function under normal conditions, they become reactive in response to neuroinflammation. Reactive astrocytes release pro-inflammatory cytokines, chemokines, and ROS, contributing to the inflammatory environment and further aggravating neurodegeneration. The combined effects of activated microglia and reactive astrocytes in Alzheimer's create a self-perpetuating cycle of inflammation that drives the disease's progression.

The Link Between Amyloid-Beta and Neuroinflammation:Amyloid-beta (Aβ) plaques are one of the defining pathological features of Alzheimer's disease. The aggregation of Aβ peptides into plaques in the brain is thought to trigger an inflammatory response that contributes to neuronal damage. When amyloid-beta accumulates, it binds to receptors on the surface of microglia, such as the complement receptor 3 (CR3) and the scavenger receptor CD36. This binding activates microglia and initiates the release of inflammatory cytokines and ROS. In response, microglia attempt to clear the amyloid plaques by phagocytosis. However, this process is inefficient, and the continuous activation of microglia leads to the chronic inflammation seen in Alzheimer's.The role of neuroinflammation in amyloid-beta pathology is bidirectional. On one hand, amyloid-beta deposits trigger microglial activation and the inflammatory cascade, while, on the other hand, sustained inflammation may promote the accumulation of more amyloid-beta, thus creating a vicious cycle. Inflammatory mediators released by microglia can enhance amyloid-beta aggregation, as cytokines such as IL-1β and TNF-α have been shown to increase the production and deposition of amyloid-beta in the brain. This cycle of amyloid-beta accumulation and microglial activation further accelerates the progression of Alzheimer's, leading to more extensive neuronal damage.

Tau Pathology and Neuroinflammation:In addition to amyloid-beta plaques, the accumulation of tau protein into neurofibrillary tangles is another hallmark feature of Alzheimer's disease. The relationship between tau pathology and neuroinflammation is less well understood, but growing evidence suggests that neuroinflammation may play a significant role in tau propagation. Microglial activation and the release of pro-inflammatory cytokines have been shown to promote tau phosphorylation, which is a key step in the formation of neurofibrillary tangles.Tau pathology itself can also activate microglia and astrocytes. Studies have demonstrated that tau aggregates can bind to specific receptors on glial cells, triggering an inflammatory response. The activation of microglia and astrocytes in response to tau deposition exacerbates tau hyperphosphorylation and neuronal dysfunction, which leads to further neurodegeneration. Thus, tau pathology and neuroinflammation are intricately linked, with each amplifying the other in a vicious cycle that drives Alzheimer's progression.

The Role of the Blood-Brain Barrier in Neuroinflammation:The blood-brain barrier (BBB) plays a critical role in maintaining the homeostasis of the central nervous system by preventing the entry of harmful substances and immune cells into the brain. However, during neuroinflammation, the BBB becomes compromised, allowing peripheral immune cells, including T cells and monocytes, to infiltrate the brain. This infiltration exacerbates the inflammatory response and contributes to neuronal damage.In Alzheimer's disease, the BBB is often disrupted as a result of the chronic neuroinflammation. Pro-inflammatory cytokines and ROS released by microglia and astrocytes can increase the permeability of the BBB, making it easier for peripheral immune cells to cross into the CNS. Once in the brain, these immune cells can further activate microglia and astrocytes, creating a feedback loop of inflammation. This breakdown of the BBB is an important factor in the progression of Alzheimer's, as it facilitates the infiltration of immune cells that perpetuate the inflammatory environment.

Emerging Strategies to Target Neuroinflammation in Alzheimer's Disease:Given the critical role of neuroinflammation in Alzheimer's disease, targeting inflammation has become a promising therapeutic strategy. Although several drugs have been investigated to modulate neuroinflammation, none have been successful in fully halting or reversing Alzheimer's disease. However, emerging therapies are focusing on novel approaches to modulate the brain's immune response, with the goal of reducing neuroinflammation and slowing disease progression.

Anti-inflammatory Drugs:Nonsteroidal anti-inflammatory drugs (NSAIDs) have been studied extensively for their potential to reduce neuroinflammation in Alzheimer's disease. Early studies suggested that NSAIDs could decrease the risk of Alzheimer's by inhibiting the cyclooxygenase (COX) enzymes, which are involved in the production of pro-inflammatory prostaglandins. However, clinical trials with NSAIDs have largely been disappointing, with no significant benefit observed in terms of cognitive improvement. Additionally, the use of NSAIDs carries risks, including gastrointestinal and cardiovascular side effects, which limit their use in Alzheimer's patients.

Microglial Modulation:Microglial activation is central to the neuroinflammatory process in Alzheimer's. As a result, several strategies aim to modulate microglial activation to reduce chronic inflammation. One promising approach is the use of P2Y12 receptor antagonists. P2Y12 receptors are involved in microglial activation and the release of inflammatory mediators. In animal models, P2Y12 receptor antagonists have shown potential in reducing neuroinflammation and amyloid-beta pathology. Clinical trials are ongoing to evaluate the efficacy of these compounds in Alzheimer's disease.Another promising target is TREM2 (Triggering Receptor Expressed on Myeloid Cells 2), a receptor expressed on microglia. TREM2 plays a crucial role in microglial activation and the phagocytosis of amyloid-beta. Loss-of-function mutations in TREM2 have been associated with an increased risk of Alzheimer's disease. Researchers are exploring strategies to enhance TREM2 function to improve microglial-mediated clearance of amyloid-beta and reduce neuroinflammation.

Cytokine Inhibition:Pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α are key mediators of neuroinflammation in Alzheimer's disease. Inhibiting these cytokines has the potential to reduce inflammation and slow disease progression. Several cytokine inhibitors, including IL-1β and TNF-α inhibitors, are being investigated in clinical trials. For instance, canakinumab, a monoclonal antibody that targets IL-1β, has shown promise in reducing inflammation and improving cognitive function in Alzheimer's patients in early-stage trials.

Modulating the Blood-Brain Barrier:Protecting the integrity of the blood-brain barrier (BBB) is another therapeutic strategy for targeting neuroinflammation. Researchers are investigating compounds that can strengthen the BBB and prevent the infiltration of peripheral immune cells into the brain. Some studies suggest that protective compounds, such as certain flavonoids or hormones, may help restore BBB integrity and reduce neuroinflammation in Alzheimer's disease.

Microbiome Modulation:The gut-brain axis, which links the gut microbiota to brain health, is an emerging area of interest in Alzheimer's research. Changes in the gut microbiome have been associated with neuroinflammation and cognitive decline. Modulating the gut microbiome through diet, probiotics, or prebiotics may offer a novel approach to reducing neuroinflammation in Alzheimer's patients. Although this area of research is still in its early stages, preliminary studies have shown that manipulating the microbiome can influence brain inflammation and amyloid-beta deposition.

Neuroinflammation plays a central role in the pathogenesis and progression of Alzheimer's disease. The activation of microglia and astrocytes, along with the release of pro-inflammatory cytokines and ROS, exacerbates neuronal damage and accelerates cognitive decline. The link between amyloid-beta deposition, tau pathology, and neuroinflammation creates a vicious cycle that drives the disease forward. Targeting neuroinflammation holds significant promise as a therapeutic approach to slow or halt the progression of Alzheimer's disease. Emerging strategies, including microglial modulation, cytokine inhibition, and BBB protection, offer hope for developing more effective treatments for this debilitating condition. However, more research is needed to better understand the intricate relationship between neuroinflammation and Alzheimer's, and to translate these promising strategies into clinical practice.

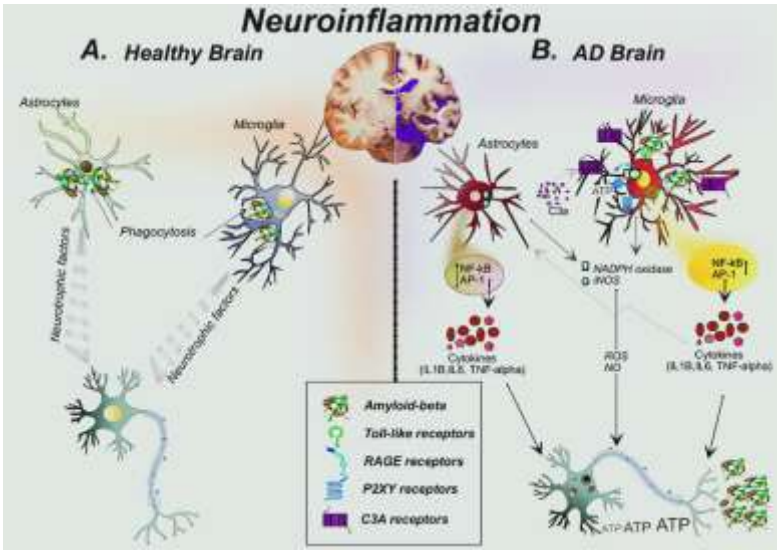


Figure:2 The image highlights the differences in neuroinflammation between a healthy brain and an Alzheimer's Disease (AD) brain. In a healthy brain, astrocytes and microglia play supportive roles. However, in an AD brain, these cells contribute to inflammation by releasing cytokines and activating pathways that increase oxidative stress. The AD brain shows a higher presence of amyloid-beta and various receptors, leading to further inflammation and neuronal damage. This underscores the pathological mechanisms behind neuroinflammation in Alzheimer's Disease.

Investigating the Role of Immune Cells and Inflammatory Cytokines in the Neurodegenerative Process of Multiple Sclerosis

Multiple sclerosis (MS) is a chronic autoimmune disorder of the central nervous system (CNS) characterized by the progressive destruction of myelin, the protective covering around nerve fibers. This destruction leads to demyelination, axonal injury, and, eventually, neuronal death, resulting in neurological dysfunction that can range from mild to severely debilitating. Although the exact etiology of MS remains unclear, it is widely accepted that the disease is driven by an abnormal immune response that targets the myelin sheath, leading to inflammation and neurodegeneration. Immune cells, particularly T cells, B cells, and macrophages, play crucial roles in initiating and perpetuating the inflammatory processes in MS. Furthermore, inflammatory cytokines, which are signaling molecules produced by immune cells, mediate the communication between cells and promote the inflammatory cascade. Understanding how immune cells and cytokines contribute to the neurodegenerative process in MS is essential for developing more targeted and effective therapies. This article explores the involvement of immune cells and inflammatory cytokines in the pathophysiology of multiple sclerosis, their roles in the demyelination process, and how they contribute to the long-term neurodegeneration observed in this disease.

Overview of Multiple Sclerosis and Its Immunological Basis:Multiple sclerosis is considered an autoimmune disorder in which the body's immune system mistakenly attacks the myelin sheath, leading to a range of neurological symptoms such as muscle weakness, vision problems, cognitive dysfunction, and sensory disturbances. The disease manifests in various forms, including relapsing-remitting MS (RRMS), primary progressive MS (PPMS), and secondary progressive MS (SPMS). The majority of MS patients initially present with the relapsing-remitting form, which is characterized by periodic episodes of neurological dysfunction followed by partial or complete recovery. However, over time, many patients transition into a progressive phase marked by a gradual decline in function and the accumulation of irreversible disability.The central pathological feature of MS is the presence of demyelinated lesions in the CNS, often in the white matter of the brain and spinal cord. The myelin destruction in MS leads to the disruption of normal nerve signaling, which results in a range of motor, sensory, and cognitive impairments. The disease is believed to arise from a combination of genetic predisposition and environmental factors, with immune system dysregulation playing a central role in its development and progression.

Role of T Cells in the Pathogenesis of Multiple Sclerosis:T cells, a subset of white blood cells, are central to the pathogenesis of MS. In MS, the immune system incorrectly recognizes components of the myelin sheath as foreign, triggering an autoimmune response. The activation of autoreactive T cells is one of the earliest events in the disease process. These T cells, specifically CD4+ helper T cells, play a crucial role in orchestrating the inflammatory response in the CNS.

The initiation of MS typically begins with the activation of naïve CD4+ T cells in peripheral lymphoid organs (such as lymph nodes) in response to myelin-specific antigens. Once activated, these T cells differentiate into distinct subsets, including Th1 and Th17 cells, both of which are implicated in the pathogenesis of MS.Th1 cells produce pro-inflammatory cytokines such as interferon-gamma (IFN-γ), which activate macrophages and microglia (the resident immune cells of the CNS), leading to the release of further inflammatory mediators. Th1 cells are known to promote myelin destruction by facilitating the recruitment of other immune cells, including T cells and B cells, into the CNS.Th17 cells are another important

subset of T cells involved in MS. These cells produce IL-17, a potent pro-inflammatory cytokine that can drive the activation of astrocytes, endothelial cells, and microglia. IL-17 promotes the breakdown of the blood-brain barrier (BBB), allowing peripheral immune cells to infiltrate the CNS. Th17 cells are thought to be particularly important in the relapsing-remitting phase of MS, as they mediate the acute inflammatory attacks that lead to the formation of demyelinating lesions.The activation and migration of autoreactive T cells across the BBB into the CNS is a critical step in the development of MS. Once inside the brain and spinal cord, T cells recognize myelin as a target and initiate an inflammatory response, leading to the recruitment of additional immune cells and the release of inflammatory cytokines. This cascade of immune activity causes damage to the myelin sheath and results in the clinical manifestations of the disease.

B Cells and Their Contribution to MS Pathogenesis:B cells, another type of immune cell, also play an important role in the pathogenesis of MS. Although T cells are considered the primary drivers of the immune response in MS, B cells contribute to the disease by producing autoantibodies, presenting antigens to T cells, and secreting cytokines that promote inflammation.In MS, B cells are found in high numbers in areas of active demyelination, and evidence suggests that they are involved in the formation of ectopic lymphoid follicles in the CNS. These follicles resemble the structures of lymph nodes and are thought to facilitate the local production of autoantibodies. These autoantibodies may target myelin components, contributing to myelin destruction. However, the exact role of B cells in the pathology of MS remains an area of ongoing research.B cells also contribute to the inflammatory milieu in MS by producing pro-inflammatory cytokines such as IL-6 and TNF-α. These cytokines enhance the activation of T cells and the recruitment of other immune cells into the CNS. Moreover, B cells can directly interact with T cells and promote their activation by acting as antigen-presenting cells. The close interaction between B cells and T cells in MS has led to the development of therapeutic strategies targeting B cell activity, such as the use of monoclonal antibodies (e.g., rituximab and ocrelizumab) that deplete B cells and reduce disease activity in MS patients.

Macrophages and Microglia: The Resident Immune Cells of the CNS:Macrophages and microglia are the innate immune cells of the CNS and play critical roles in the inflammatory response in MS. Microglia are the resident macrophages of the brain and spinal cord and are activated in response to injury or disease. In MS, microglia are activated by the influx of peripheral immune cells, including T cells and B cells, and contribute to the chronic inflammatory environment.Activated microglia release a range of pro-inflammatory cytokines, including TNF-α, IL-1β, and IL-6, which further promote the inflammatory response and exacerbate myelin damage. Microglia also produce reactive oxygen species (ROS) and nitrogen intermediates, which contribute to oxidative stress and neuronal injury. Furthermore, microglia can phagocytose myelin debris, a process that is necessary for tissue repair. However, chronic activation of microglia can lead to prolonged myelin destruction and contribute to neurodegeneration.Macrophages, which are recruited from peripheral tissues to the CNS, also play an important role in the inflammatory process in MS. Like microglia, activated macrophages release pro-inflammatory cytokines and ROS, which perpetuate the inflammatory response and damage myelin. Macrophages also contribute to the clearance of myelin debris and damaged tissue, but their prolonged activation can further contribute to tissue damage and neurodegeneration.

Inflammatory Cytokines and Their Role in MS:Inflammatory cytokines are central mediators of the immune response in MS. These molecules, which are produced by activated

immune cells, serve as signaling factors that regulate the activity of other cells in the immune system. In MS, pro-inflammatory cytokines promote the recruitment of immune cells to sites of inflammation and facilitate the destruction of myelin.TNF-α is one of the most important cytokines involved in MS. Produced by microglia, macrophages, and T cells, TNF-α is a potent pro-inflammatory molecule that contributes to BBB disruption, immune cell infiltration, and myelin degradation. TNF-α has been shown to enhance the activation of microglia and astrocytes, further exacerbating the inflammatory process. Targeting TNF-α with biologic therapies has shown limited success in MS treatment, although its involvement in the disease underscores its importance in disease pathogenesis.IL-1β is another critical cytokine in MS. This cytokine promotes the activation of microglia and astrocytes and contributes to the production of other pro-inflammatory mediators. IL-1β also disrupts the BBB, allowing the infiltration of peripheral immune cells into the CNS. Elevated levels of IL-1β are found in the cerebrospinal fluid (CSF) of MS patients, and blocking IL-1β signaling has been proposed as a potential therapeutic strategy.IL-6 is produced by activated T cells, B cells, and microglia and is involved in the differentiation of T cells into Th17 cells, a subset of T cells that play a critical role in the pathogenesis of MS. IL-6 also promotes the production of acute-phase proteins, which are markers of systemic inflammation. Inhibition of IL-6 signaling has shown promise in reducing disease activity in animal models of MS and is being explored as a potential therapeutic strategy.IL-17, produced by Th17 cells, is another key cytokine implicated in MS. IL-17 promotes the breakdown of the BBB and enhances the recruitment of immune cells to the CNS. IL-17 also induces the production of other pro-inflammatory cytokines and chemokines, which further contribute to the inflammatory process and myelin destruction.

Therapeutic Implications: Targeting Immune Cells and Cytokines in MS

Given the central role of immune cells and inflammatory cytokines in the pathogenesis of MS, several therapeutic strategies have been developed to modulate the immune response. Disease-modifying therapies (DMTs) are designed to reduce the activity of the immune system and slow the progression of MS.Immunomodulatory drugs such as interferon-beta and glatiramer acetate are commonly used in the treatment of relapsing-remitting MS. These therapies aim to reduce the activation and proliferation of T cells and modulate the immune response. However, while these treatments are effective in reducing relapse rates, they do not prevent long-term neurodegeneration.Monoclonal antibodies targeting specific immune cells have emerged as a promising treatment approach. Rituximab and ocrelizumab, which target CD20+ B cells, have shown significant efficacy in reducing disease activity and preventing disability progression in MS patients. Other monoclonal antibodies targeting T cells, such as natalizumab (which inhibits T cell migration into the CNS), also provide substantial benefits in treating MS.The inhibition of pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-17, has been explored as a therapeutic strategy. Biologic agents that block these cytokines are being evaluated in clinical trials, although their use in MS has shown mixed results.

The pathogenesis of multiple sclerosis is driven by complex interactions between immune cells, inflammatory cytokines, and the myelin sheath. T cells, B cells, macrophages, and microglia all contribute to the inflammatory process that leads to myelin destruction and neurodegeneration. Pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-17 play pivotal roles in mediating immune cell activation, blood-brain barrier disruption, and myelin damage. Understanding the intricate relationship between immune cells and cytokines in MS is critical for the development of more targeted and effective therapies. Although current

disease-modifying therapies have improved patient outcomes, there is still a need for more precise treatments that can prevent neurodegeneration and promote repair in the CNS. Advances in our understanding of the immune mechanisms driving MS offer hope for the development of new therapeutic approaches that can better address the underlying causes of the disease.

How Inflammation in the Brain Disrupts Synaptic Plasticity and Contributes to Memory and Cognitive Dysfunction in Various Neurological Disorders

Inflammation in the brain is now recognized as a significant contributor to the pathophysiology of several neurological disorders, including Alzheimer's disease, Parkinson's disease, stroke, multiple sclerosis, and traumatic brain injury. The role of neuroinflammation in these diseases is multifaceted, but one of its most important consequences is its impact on synaptic plasticity. Synaptic plasticity, the ability of synapses to strengthen or weaken in response to activity, is fundamental for learning, memory formation, and cognitive function. Inflammation in the brain disrupts the delicate balance of synaptic plasticity, leading to memory and cognitive dysfunction. This article explores the mechanisms by which neuroinflammation interferes with synaptic plasticity, examines its effects on memory and cognition, and discusses how it contributes to the progression of various neurological disorders.

The Role of Synaptic Plasticity in Memory and Cognition:Synaptic plasticity is the process by which synaptic connections between neurons are modified in response to experience, environmental stimuli, or learning. This mechanism is essential for encoding memories and facilitating cognitive processes such as learning, problem-solving, and adaptation to new information. Synaptic plasticity can occur in several forms, including long-term potentiation (LTP), long-term depression (LTD), and homeostatic plasticity. LTP is a process in which the synaptic strength between two neurons increases after repeated or sustained stimulation, which is thought to be the cellular basis of memory formation. Conversely, LTD involves a decrease in synaptic strength, which is crucial for memory retrieval, synaptic pruning, and maintaining the balance between excitation and inhibition in neural circuits.The hippocampus, a brain structure involved in learning and memory, and the prefrontal cortex, which governs higher cognitive functions, are particularly dependent on synaptic plasticity. Disruption of synaptic plasticity in these regions is strongly associated with impairments in memory formation, cognitive flexibility, and overall cognitive function. The ability to generate new synaptic connections and strengthen existing ones is essential for maintaining these cognitive functions throughout life.

Neuroinflammation and the Immune Response in the Brain:Neuroinflammation refers to the activation of the brain's immune system in response to injury, infection, or disease. Unlike inflammation in other parts of the body, which is typically beneficial and aimed at healing, neuroinflammation can become maladaptive and chronic, leading to neuronal damage and dysfunction. The brain's immune cells, including microglia (resident macrophages) and astrocytes, are key players in neuroinflammation.Under normal conditions, microglia are in a "resting" or surveillant state, constantly monitoring the brain for signs of damage. When the brain is injured or experiences pathological changes, microglia become activated and release pro-inflammatory cytokines, chemokines, and reactive oxygen species (ROS). While this response is initially protective, prolonged activation of microglia leads to chronic inflammation, which can have detrimental effects on neuronal function.Astrocytes, another type of glial cell, also play a role in neuroinflammation. In response to injury or disease,

astrocytes undergo "reactive astrogliosis," a process in which they increase the production of inflammatory mediators and alter their structural properties. This can further exacerbate the inflammatory environment and disrupt neuronal communication.

Inflammation Disrupting Synaptic Plasticity:Synaptic plasticity is highly sensitive to changes in the brain's inflammatory environment. Chronic neuroinflammation alters the normal signaling pathways that regulate synaptic strength and plasticity, leading to impairments in learning and memory. Several mechanisms by which inflammation disrupts synaptic plasticity have been identified, particularly through the effects of pro-inflammatory cytokines and microglial activation.

Cytokine-Mediated Disruption of Synaptic Function:Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6) play a critical role in the inflammatory response in the brain. These cytokines are produced by activated microglia and astrocytes in response to injury or disease and can directly interfere with the molecular processes underlying synaptic plasticity.

TNF-α: This cytokine has been shown to disrupt LTP in the hippocampus, impairing memory formation. TNF-α acts by downregulating the function of glutamate receptors, particularly NMDA receptors, which are essential for synaptic plasticity. By reducing the efficiency of NMDA receptor-mediated signaling, TNF-α impairs the induction of LTP and weakens synaptic connections, thereby compromising memory consolidation.

IL-1β: IL-1β is another cytokine that has been implicated in impairing synaptic plasticity. It interferes with the signaling pathways that promote synaptic strengthening and increases the activity of enzymes such as matrix metalloproteinases (MMPs), which degrade the extracellular matrix and disrupt the structural integrity of synapses. IL-1β also inhibits the expression of brain-derived neurotrophic factor (BDNF), a molecule essential for synaptic plasticity and memory formation.

IL-6: IL-6 is known to affect synaptic plasticity by altering neurotransmitter release and synaptic transmission. It has been shown to inhibit LTP and promote LTD, contributing to cognitive dysfunction in conditions where inflammation is present. Elevated IL-6 levels have been associated with impaired memory and attention in both animal models and humans.

Microglia-Mediated Synaptic Pruning:Microglia play a crucial role in the development and maintenance of synaptic plasticity by actively participating in the process of synaptic pruning, which helps to refine neural circuits during development and learning. However, chronic activation of microglia in neuroinflammatory conditions can lead to excessive synaptic pruning, removing healthy synapses and further impairing cognitive function.In diseases such as Alzheimer's and Parkinson's disease, microglia become hyperactive and begin to indiscriminately prune synapses, even those that are necessary for normal cognitive function. This excessive pruning disrupts the balance of synaptic connections, leading to cognitive decline. The overactivation of microglia can also lead to the release of pro-inflammatory cytokines, creating a feedback loop that exacerbates neuronal damage and impairs synaptic plasticity.

Neuroinflammation and Cognitive Dysfunction in Neurological Disorders:Neuroinflammation and its effects on synaptic plasticity are central to the cognitive dysfunction observed in a wide range of neurological disorders. These disorders share common features of inflammation, synaptic loss, and impaired cognitive function.

Below, we examine how neuroinflammation contributes to cognitive decline in several major neurological disorders.

Alzheimer's disease (AD) is characterized by the accumulation of amyloid-beta plaques and tau tangles, which cause neuronal damage and neuroinflammation. In AD, microglia become activated in response to amyloid-beta deposition, and the release of pro-inflammatory cytokines disrupts synaptic plasticity in the hippocampus and cortex, leading to memory loss and cognitive decline. Chronic neuroinflammation accelerates the progression of the disease by impairing synaptic function and inhibiting synaptic plasticity, preventing effective memory formation and retrieval.The activation of TNF-α and IL-1β in AD has been shown to directly interfere with LTP in the hippocampus, impairing the brain's ability to encode and retrieve memories. The loss of synapses, exacerbated by microglial-mediated pruning and cytokine release, is a key factor in the cognitive deficits seen in AD patients.

Parkinson's disease (PD) is primarily a motor disorder, but it also involves significant cognitive impairment, particularly in the later stages of the disease. Inflammation in PD is driven by the loss of dopaminergic neurons in the substantia nigra and the subsequent activation of microglia in response to neuronal injury. This activation leads to the release of pro-inflammatory cytokines that disrupt synaptic plasticity in the striatum and other brain regions involved in motor and cognitive function.In PD, neuroinflammation impairs synaptic transmission and reduces the plasticity of the dopaminergic system, contributing to both motor deficits and cognitive dysfunction. The release of IL-1β and TNF-α, along with the loss of dopamine, disrupts the signaling pathways necessary for learning and memory. As the disease progresses, these inflammatory processes lead to widespread synaptic loss, further impairing cognitive function.

Multiple sclerosis (MS) is an autoimmune disorder that causes demyelination of nerve fibers in the CNS, leading to neuroinflammation, axonal damage, and cognitive dysfunction. The immune response in MS targets myelin and the oligodendrocytes that produce it, leading to the activation of microglia, macrophages, and other immune cells. These activated cells release pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which disrupt synaptic plasticity and contribute to memory and cognitive impairments.

Chronic neuroinflammation in MS leads to the formation of lesions in the white matter of the brain and spinal cord, impairing communication between brain regions. The disruption of synaptic plasticity in areas such as the hippocampus and prefrontal cortex contributes to the cognitive deficits observed in MS, including difficulties with attention, memory, and executive function.

Traumatic brain injury (TBI) leads to an immediate and localized inflammatory response in the brain, which can disrupt synaptic plasticity and lead to long-term cognitive impairments. Following a traumatic event, microglia and astrocytes become activated and release inflammatory cytokines that promote synaptic dysfunction. In the acute phase after injury, there is an initial disruption of synaptic connections, followed by a prolonged phase of neuroinflammation that leads to chronic cognitive dysfunction.In TBI, the loss of synapses and the inhibition of synaptic plasticity in the hippocampus and other regions involved in memory and learning contributes to cognitive decline. Chronic inflammation after TBI, particularly the continued activation of microglia and the release of TNF-α, IL-1β, and IL-6, further exacerbates these effects.

Therapeutic Strategies to Target Neuroinflammation and Improve Synaptic Plasticity:Given the central role of neuroinflammation in disrupting synaptic plasticity and contributing to cognitive dysfunction, several therapeutic strategies have been proposed to reduce inflammation and enhance synaptic function. These include:

Anti-inflammatory drugs: Nonsteroidal anti-inflammatory drugs (NSAIDs) and other immunomodulatory drugs, such as corticosteroids, have been explored for their potential to reduce neuroinflammation. However, their efficacy in improving cognitive function remains limited, and side effects may limit their long-term use.

Cytokine inhibitors: Targeting specific pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, may help reduce neuroinflammation and improve synaptic plasticity. Several biologic agents targeting these cytokines are in clinical development for various neurological disorders.

Microglial modulation: Drugs that modulate microglial activation, such as P2Y12 receptor antagonists, hold promise for reducing neuroinflammation and protecting synaptic function. These therapies aim to normalize microglial activity and prevent excessive synaptic pruning.

Neurotrophic factors: Boosting the levels of brain-derived neurotrophic factor (BDNF) or other neurotrophic factors may help enhance synaptic plasticity and promote neuronal survival in the context of chronic inflammation.

Neuroinflammation plays a pivotal role in disrupting synaptic plasticity and contributing to memory and cognitive dysfunction across a range of neurological disorders. Inflammation-induced changes in cytokine release, microglial activation, and synaptic remodeling impair the brain's ability to form and retrieve memories, leading to cognitive decline. Understanding the mechanisms by which neuroinflammation disrupts synaptic plasticity is crucial for developing effective therapeutic strategies aimed at restoring cognitive function and preventing further neuronal damage. Through the development of targeted therapies that modulate inflammation and promote synaptic health, it may be possible to mitigate the cognitive impairments associated with these debilitating diseases.

The Role of Microglial Cells in Neuroinflammation and Their Involvement in the Pathogenesis of Parkinson’s Disease

Parkinson’s disease (PD) is a neurodegenerative disorder that primarily affects motor function but is increasingly recognized for its broader impacts on cognition, mood, and other neurological processes. The hallmark of Parkinson’s disease is the progressive loss of dopaminergic neurons in the substantia nigra, a region of the brain responsible for controlling movement. While the cause of PD is not fully understood, it is clear that the underlying pathogenesis involves a complex interplay between genetic and environmental factors. One of the most critical contributors to the progression of PD is neuroinflammation, particularly the role of microglial cells, the resident immune cells of the central nervous system (CNS). Microglia are crucial for maintaining homeostasis in the brain, but under pathological conditions, they can become over-activated and contribute to neuronal damage and disease progression. This article explores the role of microglial cells in neuroinflammation, their involvement in the pathogenesis of Parkinson’s disease, and the potential therapeutic implications of targeting microglial activity.

Understanding Microglial Cells and Their Functions:Microglial cells are the resident immune cells of the CNS and are considered the first line of defense against injury, infection, or disease. Unlike other immune cells in the body, microglia do not originate from the bone marrow but rather arise from yolk sac progenitors during early development. Once in the brain, microglia settle into specific regions and take on a variety of functions, including surveillance of the extracellular environment, response to neuronal damage, and modulation of synaptic activity. In their resting state, microglia constantly monitor the brain for signs of injury or infection through highly branched, motile processes.When the brain is exposed to injury or disease, microglia become activated, transforming into an amoeboid shape and releasing various signaling molecules, including pro-inflammatory cytokines, chemokines, and reactive oxygen species (ROS). This activation is essential for the inflammatory response, as it helps to clear damaged neurons and cellular debris. However, chronic or sustained activation of microglia can become detrimental, leading to the overproduction of inflammatory molecules that contribute to neurodegeneration.Microglia are known to engage in two distinct activation states: a pro-inflammatory “M1” phenotype and an anti-inflammatory “M2” phenotype. The M1 phenotype is typically associated with neuroinflammation and neuronal damage, while the M2 phenotype is more reparative and involved in tissue repair and resolution of inflammation. In Parkinson’s disease, there is a shift toward the M1 phenotype, contributing to chronic neuroinflammation and exacerbating neuronal loss.

The Role of Neuroinflammation in Parkinson’s Disease:Parkinson’s disease is characterized by the progressive loss of dopaminergic neurons in the substantia nigra, leading to motor symptoms such as tremors, rigidity, bradykinesia, and postural instability. However, non-motor symptoms, including cognitive impairment, mood disorders, and sleep disturbances, are also prevalent and contribute significantly to the burden of the disease. The neurodegeneration observed in PD is not limited to the loss of dopaminergic neurons but also involves complex interactions between glial cells, neurotransmitter systems, and genetic factors.Neuroinflammation, particularly the activation of microglial cells, has emerged as a central feature in the pathogenesis of PD. The inflammatory response in PD is believed to be triggered by multiple factors, including the accumulation of misfolded alpha-synuclein proteins, mitochondrial dysfunction, oxidative stress, and genetic susceptibility. Microglial activation in PD is thought to exacerbate neurodegeneration by releasing a variety of pro-inflammatory mediators, which contribute to the progressive loss of dopaminergic neurons.One of the key findings in PD is the presence of increased microglial activation in the substantia nigra, the region most affected by dopaminergic degeneration. Post-mortem studies of PD patients have shown an elevated presence of microglial cells in the substantia nigra, often in close proximity to areas of neuronal damage. This suggests that microglia play an active role in the progression of the disease. The activation of microglia in PD is not a mere bystander phenomenon but rather a critical driver of neuroinflammation that worsens the disease pathology.

Microglial Activation and its Consequences in Parkinson’s Disease:The activation of microglial cells in Parkinson’s disease is associated with several harmful processes that contribute to neuronal injury and the progression of neurodegeneration. These processes include the release of pro-inflammatory cytokines, chemokines, and ROS, as well as alterations in neuroprotective mechanisms. Together, these factors create a toxic environment in the brain, which accelerates neuronal damage and impairs neuronal survival.

Cytokine and Chemokine Release:One of the primary ways in which activated microglia contribute to neuroinflammation in PD is through the release of pro-inflammatory cytokines and chemokines. These signaling molecules can create a positive feedback loop that exacerbates the inflammatory response. Some of the most important pro-inflammatory cytokines involved in PD include:

Tumor necrosis factor-alpha (TNF-α): TNF-α is a potent pro-inflammatory cytokine that plays a crucial role in the activation of microglia and the progression of neuroinflammation. Elevated levels of TNF-α have been detected in the brains of PD patients and animal models, and TNF-α has been shown to contribute to the degeneration of dopaminergic neurons. It does so by disrupting the blood-brain barrier, enhancing the infiltration of peripheral immune cells, and increasing the production of other inflammatory mediators.

Interleukin-1 beta (IL-1β): IL-1β is another key cytokine produced by activated microglia. It has been shown to impair synaptic plasticity, contribute to oxidative stress, and reduce the ability of neurons to repair themselves. IL-1β also induces the release of additional inflammatory cytokines and promotes neurodegeneration. In animal models of PD, blocking IL-1β has been shown to reduce microglial activation and protect dopaminergic neurons.

Interleukin-6 (IL-6): IL-6 is a pleiotropic cytokine that has been implicated in the pathogenesis of PD. It can induce both pro-inflammatory and anti-inflammatory responses, depending on the context. In PD, however, chronic elevations in IL-6 contribute to neuroinflammation and the degeneration of dopaminergic neurons.

In addition to cytokines, microglia also release chemokines that recruit additional immune cells to the site of injury. These immune cells can further exacerbate inflammation and contribute to the neurodegenerative process. In PD, the recruitment of T cells and other peripheral immune cells into the brain may worsen the local inflammatory response and further damage neurons.

Reactive Oxygen Species (ROS) and Oxidative Stress:Activated microglia release reactive oxygen species (ROS) and nitrogen intermediates, which are highly reactive molecules that can cause cellular damage. ROS are known to attack cellular components such as lipids, proteins, and DNA, leading to oxidative stress. In PD, oxidative stress is a critical factor in dopaminergic neurodegeneration, and microglial activation plays a significant role in exacerbating this process.Microglial ROS production is tightly linked to mitochondrial dysfunction, a hallmark of Parkinson’s disease. Mitochondria in dopaminergic neurons are particularly vulnerable to oxidative stress, and the accumulation of ROS can lead to mitochondrial damage, further impairing cellular function. This creates a vicious cycle in which mitochondrial dysfunction and oxidative stress contribute to microglial activation, which in turn exacerbates neuronal damage and accelerates disease progression.

Synaptic Dysfunction and Neurodegeneration:Microglial activation in Parkinson’s disease also affects synaptic function and plasticity. Microglia are known to play a role in synaptic pruning, a process by which unnecessary or damaged synapses are removed. While this is a normal part of brain development and maintenance, in the context of neuroinflammation, microglia may over-prune healthy synapses, contributing to neuronal dysfunction and cognitive decline.In PD, excessive microglial activation leads to the release of pro-inflammatory molecules that interfere with synaptic transmission and impair long-term potentiation (LTP), the cellular mechanism underlying learning and memory. The disruption of synaptic plasticity contributes to both motor and cognitive deficits in Parkinson’s disease,

and this process may be further exacerbated by the loss of dopaminergic signaling in key brain regions involved in cognition and memory.

The Impact of Alpha-Synuclein Aggregation on Microglia Activation:Alpha-synuclein, a protein that forms toxic aggregates in the brains of PD patients, is another key player in the interaction between neuroinflammation and neuronal damage. Aggregated alpha-synuclein has been shown to activate microglia, contributing to the inflammatory response in Parkinson's disease. The presence of alpha-synuclein aggregates triggers the release of pro-inflammatory cytokines and ROS from microglia, which in turn exacerbate neuronal damage and promote the spread of alpha-synuclein aggregates to neighboring neurons.The interplay between alpha-synuclein and microglia in PD is a central mechanism that drives the progressive nature of the disease. Alpha-synuclein aggregates not only contribute to the neurodegenerative process but also promote a chronic inflammatory environment that accelerates neuronal loss and cognitive decline.

Therapeutic Implications: Targeting Microglial Activation in Parkinson's Disease given the central role of microglial activation in the pathogenesis of Parkinson's disease, strategies that target microglial activity and neuroinflammation are being explored as potential therapeutic options. These approaches aim to modulate microglial function to reduce inflammation and protect dopaminergic neurons.

Anti-inflammatory drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), have been investigated for their potential to reduce neuroinflammation in PD. While some studies have shown that NSAIDs can reduce the levels of pro-inflammatory cytokines, their clinical efficacy in PD remains inconclusive, and long-term use of these drugs may be limited due to side effects.

Microglial Modulation:More targeted therapies aimed at modulating microglial activity are currently under investigation. For example, drugs that inhibit the activation of microglial cells, such as P2Y12 receptor antagonists, may help to reduce the release of pro-inflammatory cytokines and ROS. By inhibiting microglial activation, these therapies could help protect dopaminergic neurons and slow disease progression.

Alpha-Synuclein Targeting:Targeting alpha-synuclein aggregates directly is another promising therapeutic approach. Several strategies, including the use of antibodies and small molecules, aim to prevent the formation of alpha-synuclein aggregates or promote their clearance from the brain. By reducing the toxic effects of alpha-synuclein on microglia, these therapies may help to reduce neuroinflammation and protect neurons from further damage.

Microglial cells play a crucial role in the pathogenesis of Parkinson's disease through their involvement in neuroinflammation. While microglia are essential for maintaining brain homeostasis and responding to injury, their chronic activation in response to various factors, including alpha-synuclein aggregation and oxidative stress, contributes significantly to the progression of the disease. Through the release of pro-inflammatory cytokines, ROS, and the disruption of synaptic plasticity, activated microglia exacerbate neuronal damage and accelerate neurodegeneration in PD. Understanding the complex role of microglial cells in Parkinson's disease offers new insights into potential therapeutic strategies aimed at modulating microglial activity and reducing neuroinflammation. Targeting microglial activation, along with other approaches aimed at restoring neuronal function and protecting dopaminergic neurons, holds promise for slowing the progression of Parkinson's disease and improving outcomes for patients.

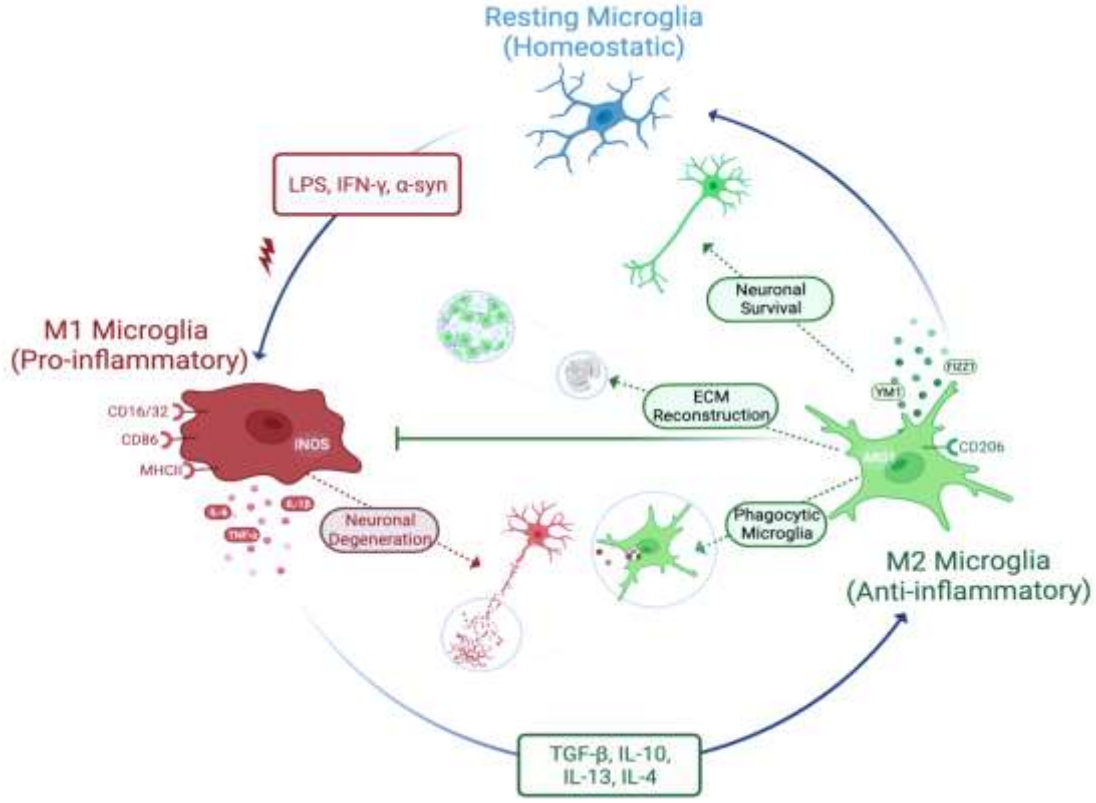


Figure:3 The image demonstrates the states and functions of microglia, the brain's immune cells. It shows how resting microglia can become either M1 microglia (pro-inflammatory) or M2 microglia (anti-inflammatory) based on different stimuli. M1 microglia are involved in neuronal degeneration, while M2 microglia support neuronal survival and tissue repair. The image highlights the dual roles of microglia in neuroinflammation and neuroprotection, illustrating their importance in brain health.

The Inflammatory Response Following a Stroke and How Modulating Neuroinflammation Can Reduce Brain Damage and Improve Recovery

A stroke is a sudden disruption in the blood supply to the brain, leading to the rapid death of neurons and significant neurological deficits. The aftermath of a stroke is characterized not only by neuronal injury but also by an intense inflammatory response. This inflammation, which begins almost immediately after the onset of the stroke, plays a crucial role in both the acute damage and the subsequent recovery process. While inflammation is a necessary component of tissue repair, when dysregulated, it can exacerbate neuronal injury and impair functional recovery. This article explores the mechanisms of neuroinflammation that occur following a stroke, its contribution to brain damage, and the potential for modulating this inflammatory response to reduce neuronal injury and improve post-stroke recovery.

The Pathophysiology of Stroke and Neuroinflammation:Stroke can occur in two primary forms: ischemic stroke and hemorrhagic stroke. Ischemic stroke, which accounts for approximately 85% of all strokes, is caused by a blockage in a blood vessel supplying the brain, resulting in the deprivation of oxygen and glucose to brain tissue. Hemorrhagic stroke, on the other hand, is caused by the rupture of a blood vessel, leading to bleeding in the brain. Regardless of the type of stroke, the inflammatory response that follows plays a key role in secondary brain injury and influences the potential for recovery.After a stroke, the loss of

blood flow triggers a cascade of biochemical events, including the release of excitotoxic neurotransmitters like glutamate, an increase in intracellular calcium levels, and the activation of inflammatory pathways. This cascade results in a toxic environment that can exacerbate neuronal damage. The inflammation that follows is a complex process that involves both the innate and adaptive immune systems and can be broken down into several stages, each of which contributes to the progression of brain injury and the potential for recovery.

Stages of Neuroinflammation After Stroke:The inflammatory response following a stroke can be broadly divided into two phases: the acute phase and the chronic or subacute phase.

Acute Inflammatory Response (First Few Hours to Days):The acute inflammatory response begins immediately after the stroke event and is triggered by cellular injury and the disruption of the blood-brain barrier (BBB). In the first hours following ischemic stroke, there is an influx of immune cells, such as neutrophils and macrophages, into the affected brain region. Microglia, the resident immune cells of the brain, also become activated in response to the ischemic injury.

Microglial Activation: Microglia are the first cells to respond to brain injury, and their activation is a hallmark of neuroinflammation. Under normal conditions, microglia survey the brain for damage or infection, but after a stroke, they rapidly change their morphology, become amoeboid, and release pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. These cytokines can amplify the inflammatory response, recruit additional immune cells, and contribute to the expansion of the infarct region.

Neutrophil Recruitment: Neutrophils are the first peripheral immune cells to infiltrate the ischemic area, and their accumulation is associated with increased tissue damage. Neutrophils release proteases, ROS, and inflammatory mediators that further damage the blood-brain barrier and exacerbate edema and neuronal injury.

Platelet Activation: Platelets also play a role in the inflammatory response to stroke. In ischemic stroke, platelets aggregate at the site of injury and release pro-inflammatory cytokines, growth factors, and thrombin, contributing to both the acute ischemic injury and the subsequent inflammatory process.

Blood-Brain Barrier Disruption: One of the early consequences of stroke-induced neuroinflammation is the breakdown of the blood-brain barrier. This disruption allows immune cells, such as neutrophils, monocytes, and T cells, to infiltrate the brain. It also permits the leakage of toxic substances, such as ROS and proteolytic enzymes, which exacerbate the inflammatory process and worsen neuronal damage.

Chronic Inflammatory Response (Days to Weeks Following Stroke):After the initial acute phase, inflammation transitions into the chronic phase, during which the immune response remains active in the affected brain region. Chronic inflammation can continue for weeks and is associated with prolonged neurodegeneration and impaired recovery.

Macrophage and T Cell Activation: Following the acute response, macrophages and T cells become more prominent in the inflamed brain tissue. These cells release additional cytokines and growth factors that influence tissue repair. However, excessive activation of these cells can lead to further neuronal injury and glial scarring. Prolonged T cell activation is associated with worsening outcomes in stroke patients.

Astrocyte Activation and Gliosis: Astrocytes, the support cells of the brain, become activated in response to injury and contribute to the formation of a glial scar. While glial scarring serves as a protective response to isolate the damaged tissue, it can also impede the regeneration of neurons and axonal growth, ultimately hindering functional recovery.

Ongoing Blood-Brain Barrier Impairment: Persistent inflammation in the chronic phase continues to disrupt the blood-brain barrier, leading to prolonged immune cell infiltration and sustained neuronal injury. The permeability of the blood-brain barrier may remain elevated for weeks after the stroke, making the brain more vulnerable to further damage from circulating immune cells and toxins.

The Role of Inflammatory Mediators in Stroke Pathogenesis:Several key inflammatory mediators are involved in the neuroinflammatory response after a stroke, and their dysregulated production contributes to both the acute and chronic phases of brain injury. These mediators include cytokines, chemokines, ROS, and prostaglandins, all of which can either promote or attenuate the inflammatory response depending on the context and timing of their release.

Cytokines: Pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, are released by activated microglia, astrocytes, and infiltrating immune cells. These cytokines play a dual role in stroke pathogenesis: they promote the initial inflammatory response necessary for tissue repair but, when produced in excess, contribute to neuronal damage, BBB disruption, and prolonged inflammation.

Chemokines: Chemokines are small signaling proteins that attract immune cells to the site of injury. Following a stroke, chemokines such as MCP-1 (monocyte chemoattractant protein-1) and IL-8 are released and facilitate the recruitment of monocytes, macrophages, and other immune cells to the ischemic brain tissue. While this helps clear damaged tissue, excessive chemokine signaling can lead to chronic inflammation and worsen brain injury.

Reactive Oxygen Species (ROS): ROS are generated by both activated microglia and infiltrating neutrophils during the inflammatory response. While ROS are involved in pathogen defense and tissue repair, excessive ROS production can damage cellular structures, including lipids, proteins, and DNA, leading to neuronal death and exacerbating ischemic injury.

Prostaglandins: Prostaglandins, particularly prostaglandin E2 (PGE2), are lipid mediators produced by activated microglia and astrocytes. PGE2 plays a role in promoting neuroinflammation and modulating neuronal excitability. Inhibiting prostaglandin production may reduce inflammation and improve outcomes after a stroke.

Modulating Neuroinflammation to Improve Stroke Outcomes:Given the detrimental role of sustained neuroinflammation in stroke pathogenesis, therapeutic strategies aimed at modulating the inflammatory response offer the potential to improve outcomes and accelerate recovery. However, it is essential to strike a balance between promoting tissue repair and preventing excessive inflammation that can further damage the brain.

One of the most straightforward approaches to modulating neuroinflammation is the use of anti-inflammatory drugs. Nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids have been explored for their ability to reduce pro-inflammatory cytokine production and attenuate neuroinflammation. However, their clinical efficacy in stroke has

been limited by side effects and the complexity of the inflammatory response. Long-term use of NSAIDs, for example, can impair wound healing and increase the risk of bleeding, which is particularly problematic in patients with hemorrhagic stroke.

More targeted therapies, such as monoclonal antibodies or small molecules that specifically inhibit pro-inflammatory cytokines like TNF-α or IL-1β, are under investigation. These therapies aim to dampen the excessive inflammation without suppressing the immune response required for tissue repair.

Toll-Like Receptor (TLR) Inhibition:Toll-like receptors (TLRs) are pattern recognition receptors that play a key role in initiating the inflammatory response after stroke. TLRs, particularly TLR4, are activated by damage-associated molecular patterns (DAMPs) released during brain injury. Inhibiting TLR signaling has been shown to reduce neuroinflammation, decrease neuronal death, and improve functional recovery after stroke. TLR4 antagonists are being tested in preclinical models, with promising results.

As microglia are the primary mediators of neuroinflammation, targeting their activation represents another promising therapeutic strategy. Drugs that inhibit microglial activation, such as P2Y12 receptor antagonists, have been shown to reduce the production of pro-inflammatory cytokines and protect neurons from ischemic damage. Inhibiting microglial activation at the appropriate time point may promote tissue repair and enhance recovery.

In addition to modulating inflammation, therapies that promote neuroprotection and tissue repair are crucial for improving outcomes after stroke. For instance, drugs that enhance neurogenesis, such as brain-derived neurotrophic factor (BDNF) or other growth factors, may help repair damaged brain tissue and facilitate functional recovery. Promoting the resolution of inflammation, through the use of anti-inflammatory cytokines or modulators of the inflammatory response, may also support tissue repair and improve recovery.

Stem Cell Therapy:Stem cell therapy has shown promise in stroke recovery by promoting neurogenesis and tissue repair. Stem cells, particularly mesenchymal stem cells (MSCs), can modulate the immune response, reduce neuroinflammation, and enhance tissue regeneration. Clinical trials are ongoing to evaluate the safety and efficacy of stem cell-based therapies in stroke patients.

Neuroinflammation plays a central role in the pathophysiology of stroke, contributing to both the acute damage and the chronic neurodegeneration that follow the injury. While inflammation is necessary for tissue repair, its dysregulated response can exacerbate neuronal injury and impede recovery. The inflammatory process involves various immune cells, including microglia, neutrophils, and macrophages, as well as inflammatory mediators such as cytokines, chemokines, and ROS. By understanding the complex dynamics of post-stroke inflammation, it is possible to develop therapeutic strategies that modulate the inflammatory response to reduce brain damage, promote tissue repair, and improve functional recovery. Targeting neuroinflammation at the right time, while preserving the immune mechanisms essential for repair, holds great promise for improving outcomes in stroke patients and accelerating the recovery process.

Aspect	Inflammatory Response	Acute Phase	Subacute Phase	Chronic phase	Role of Modulation	Impact on Recovery
Initial Inflammatory Response	Activation of microglia and astrocytes	Inflammatory molecules (cytokines, chemokines) released	Activation peaks and begins to subside	Chronic low-level inflammation persists	Modulation reduces excessive inflammation	Reduces cell death, promotes healing
Microglial Activation	Microglia activated by ischemic injury	Microglia clear debris but also release toxic substances	Persistent activation leads to neurotoxicity	Chronic microglial activation can worsen outcomes	Targeting microglial activation limits damage	Promotes neuroprotection and regeneration
Cytokine Release	Increase in pro-inflammatory cytokines (e.g., TNF-α, IL-1β)	Cytokines exacerbate injury, contributing to neuronal death	Cytokine levels gradually decrease but remain elevated	Chronic elevation leads to long-term damage	Anti-inflammatory treatments can reduce cytokine levels	Improves tissue repair and reduces neurodegeneration
Neurogenesis and Plasticity	BBB permeability increases after stroke	Immediate BBB disruption allows immune cells into the brain	BBB disruption can persist in the subacute phase	Chronic BBB damage allows continued inflammation	Restoring BBB integrity limits inflammation and secondary damage	Enhances recovery by reducing further injury
Neuroprotective Strategies	Inflammation can impair neurogenesis	Acute inflammation impedes neural repair and plasticity	Recovery of plasticity may occur but is impaired by chronic inflammation	Persistent inflammation hinders full recovery of brain function	Reducing inflammation supports neurogenesis and plasticity	Accelerates functional recovery and cognitive restoration

Table:1 This table outlines how neuroinflammation following a stroke can cause ongoing damage and how modulating this response can help improve outcomes by reducing further neuronal injury and enhancing recovery.

The Role of Inflammation in the Aftermath of Traumatic Brain Injury (TBI) and How It Impacts Long-Term Outcomes

Traumatic brain injury (TBI) is a significant public health concern worldwide, affecting millions of people each year. It results from an external force impacting the head, causing damage to the brain. The severity of TBI can vary from mild concussions to severe cases that lead to permanent disability or death. Regardless of the initial injury's severity, the aftermath of TBI often involves complex cellular and molecular responses, one of the most critical being inflammation. While inflammation is an essential protective response that helps to repair tissue and combat infection, excessive or chronic inflammation after TBI can

exacerbate injury, impede recovery, and contribute to long-term neurological deficits. This article explores the role of inflammation in the aftermath of TBI, the mechanisms through which it impacts the brain, and its influence on long-term outcomes, including cognitive, emotional, and physical recovery.

Understanding Traumatic Brain Injury (TBI):Traumatic brain injury is classified into three categories based on its severity: mild, moderate, and severe. Mild TBI (commonly referred to as concussion) may involve a brief loss of consciousness or no loss at all, and typically leads to temporary symptoms such as headaches, dizziness, and confusion. Moderate to severe TBI is associated with prolonged loss of consciousness, physical trauma to the brain, and significant disruption of brain function, which can result in permanent cognitive, emotional, and physical impairments.TBI can result from various causes, including motor vehicle accidents, falls, sports injuries, violence, and combat situations. The injury itself can cause both primary damage, resulting from the initial mechanical impact (e.g., contusions, axonal shearing, and hemorrhage), and secondary damage, which unfolds in the hours, days, and even months after the injury. Secondary brain injury is often caused by biochemical and cellular processes, one of the most significant being inflammation.

The Inflammatory Response Following TBI:The inflammatory response after TBI begins almost immediately and is triggered by several factors, including cellular injury, neuronal damage, and the release of damage-associated molecular patterns (DAMPs). Inflammation in the brain, while essential for tissue repair, can be harmful if it becomes excessive or chronic. The inflammatory process following TBI can be divided into several stages: the acute phase, subacute phase, and chronic phase. Each phase is marked by the activation of various immune cells and the release of inflammatory mediators that collectively contribute to the progression of brain injury.

Acute Phase (Minutes to Hours Post-Injury):The initial inflammatory response after TBI begins within minutes of the injury and is typically marked by the activation of microglial cells, the resident immune cells of the brain. Microglia constantly survey the brain for signs of damage and injury. Upon sensing the damage caused by TBI, microglia become activated, transitioning from their resting state to a more amoeboid shape. Activated microglia release pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), which promote inflammation and recruit additional immune cells to the injury site.In the acute phase, the blood-brain barrier (BBB) also becomes compromised due to mechanical injury and the inflammatory process. This disruption allows immune cells, such as neutrophils and monocytes, to enter the brain from the periphery. These cells contribute to the inflammatory cascade, releasing additional pro-inflammatory molecules, including ROS (reactive oxygen species), matrix metalloproteinases (MMPs), and cytokines. The influx of immune cells and the release of these inflammatory mediators increase neuronal injury and exacerbate the initial damage caused by TBI.

Subacute Phase (Days to Weeks Post-Injury):As the acute inflammatory response subsides, the brain enters the subacute phase, typically lasting several days to weeks following the injury. In this phase, activated microglia and infiltrating macrophages continue to release inflammatory cytokines and ROS, but they also play a role in clearing damaged tissue and promoting repair. However, prolonged activation of microglia and macrophages can lead to chronic inflammation, which contributes to further neuronal injury and tissue death.Astrocytes, another type of glial cell, also become activated during this phase.

Astrocytes contribute to the formation of a glial scar, which helps isolate damaged tissue and prevent further injury. While glial scarring is beneficial in some ways, it can also impair neural regeneration and limit recovery, particularly in terms of axonal regrowth and synaptic plasticity.

Chronic Phase (Months to Years Post-Injury):In some individuals, the inflammatory response persists long after the initial injury. This prolonged inflammation is a hallmark of chronic neuroinflammation and is thought to contribute to the long-term neurological deficits often seen in TBI patients. In this phase, the continued activation of microglia and astrocytes, along with the ongoing release of pro-inflammatory cytokines, ROS, and other mediators, can lead to neurodegeneration. Chronic inflammation is believed to play a significant role in the development of post-TBI cognitive deficits, mood disorders, and neurodegenerative diseases, such as chronic traumatic encephalopathy (CTE).Furthermore, the chronic inflammatory state can also contribute to the development of secondary pathologies, including the formation of tau protein aggregates, which are associated with cognitive decline and dementia. The persistence of neuroinflammation in the chronic phase also affects neurogenesis, the process through which new neurons are generated, particularly in the hippocampus, an area of the brain crucial for learning and memory.

The Mechanisms of Inflammation-Driven Damage in TBI:While inflammation is necessary for tissue repair, its dysregulated response following TBI can have several detrimental effects on the brain. The inflammatory process can exacerbate neuronal death, contribute to tissue edema, and hinder neuroplasticity, all of which negatively affect long-term outcomes. Several mechanisms contribute to the damaging effects of neuroinflammation in TBI:

Excitotoxicity and Glutamate Toxicity:Following TBI, there is an excessive release of the neurotransmitter glutamate, which can lead to excitotoxicity. Glutamate binds to its receptors on neurons, leading to excessive calcium influx and triggering a cascade of events that results in neuronal damage and cell death. Inflammatory mediators released during the inflammatory response, including pro-inflammatory cytokines and ROS, can further enhance glutamate release and impair the clearance of excess glutamate from the synaptic cleft, exacerbating excitotoxic damage.

Oxidative Stress and Reactive Oxygen Species (ROS):ROS are highly reactive molecules that are produced as a byproduct of the inflammatory response. In normal amounts, ROS can play a role in immune defense and cellular signaling, but excessive ROS production can lead to oxidative stress, damaging cellular components such as lipids, proteins, and DNA. In TBI, ROS are generated by activated microglia, neutrophils, and astrocytes, and their overproduction contributes to neuronal death, blood-brain barrier disruption, and edema. The accumulation of ROS can also impair mitochondrial function, further exacerbating neuronal injury and preventing recovery.

Neurodegeneration and Cell Death:Inflammation after TBI accelerates neurodegeneration by promoting the release of proteases, including matrix metalloproteinases (MMPs), which degrade extracellular matrix components and disrupt neuronal structures. Additionally, chronic neuroinflammation is associated with the activation of apoptotic and necrotic pathways in neurons. As a result, the brain’s ability to repair itself is compromised, and neurons are lost over time, contributing to cognitive decline and behavioral changes.

Impaired Neurogenesis:Neurogenesis, the process of generating new neurons, is essential for recovery following brain injury. The hippocampus, a region involved in learning and

memory, is particularly involved in neurogenesis. However, neuroinflammation inhibits neurogenesis by impairing the function of neural stem cells and disrupting the signaling pathways necessary for neuronal regeneration. Chronic inflammation also affects the growth and differentiation of new neurons, limiting the brain's ability to recover functional capacity and contributing to long-term cognitive deficits.

Inflammation and Long-Term Outcomes After TBI:The inflammatory response that follows TBI plays a pivotal role in determining long-term outcomes, which can vary widely from full recovery to permanent disability. Several factors influence the extent to which neuroinflammation impacts recovery, including the severity of the injury, the presence of pre-existing medical conditions, and the individual's genetic predisposition to inflammatory responses.

Cognitive Deficits:One of the most significant long-term consequences of TBI is cognitive impairment. Many individuals with TBI experience memory loss, difficulty concentrating, slowed processing speed, and impaired executive function. Neuroinflammation is believed to contribute to these cognitive deficits by impairing synaptic plasticity, disrupting communication between neurons, and inhibiting neurogenesis. The chronic activation of microglia and astrocytes, along with the sustained release of pro-inflammatory cytokines, is thought to contribute to the progressive neurodegeneration that leads to cognitive decline after TBI.

Mood and Behavioral Disorders:In addition to cognitive deficits, individuals with TBI often experience emotional and behavioral changes, including depression, anxiety, irritability, and impulsivity. Neuroinflammation has been implicated in the development of these mood and behavioral disorders, as pro-inflammatory cytokines and other inflammatory mediators can affect the brain's regions involved in emotional regulation, such as the prefrontal cortex and limbic system. Chronic inflammation can also alter neurotransmitter systems, such as serotonin and dopamine, which are crucial for mood regulation.

Neurodegenerative Diseases and Chronic Traumatic Encephalopathy (CTE):In some individuals, particularly those with repetitive mild TBI (such as athletes involved in contact sports), chronic neuroinflammation can lead to the development of chronic traumatic encephalopathy (CTE). CTE is a progressive neurodegenerative disease that is characterized by the accumulation of tau protein in the brain, leading to cognitive decline, motor dysfunction, and behavioral changes. Inflammation plays a critical role in the development of CTE by exacerbating tau deposition, promoting neurodegeneration, and contributing to the progression of the disease.

Targeting Inflammation for Better Outcomes:Given the detrimental role of inflammation in TBI outcomes, targeting neuroinflammation has become an area of great interest in research aimed at improving recovery and preventing long-term disabilities. Several therapeutic approaches are being explored

Anti-inflammatory Drugs: Nonsteroidal anti-inflammatory drugs (NSAIDs) and other anti-inflammatory agents have been investigated for their ability to reduce neuroinflammation after TBI. While NSAIDs have shown some promise in preclinical models, their clinical application is limited due to potential side effects, particularly in the context of bleeding in TBI patients. More targeted therapies, such as cytokine inhibitors or microglial modulators, are under investigation.

Neuroprotective Agents: Drugs that protect neurons from the damaging effects of inflammation, such as antioxidants or agents that block excitotoxicity, may help mitigate the effects of neuroinflammation. For example, compounds that scavenge ROS or reduce glutamate release may prevent the secondary injury that follows TBI.

Stem Cell Therapy: Stem cells have shown potential for promoting neurogenesis and tissue repair after TBI. Stem cell-based therapies could not only promote recovery by replenishing lost neurons but also modulate the inflammatory response to create a more favorable environment for healing.

Gene Therapy: Gene therapy aimed at regulating the expression of pro-inflammatory cytokines or promoting the resolution of inflammation offers another promising approach for treating TBI. By modulating the brain's inflammatory response at the molecular level, gene therapy may help reduce long-term neuronal damage and improve functional recovery.

Inflammation is a crucial response to traumatic brain injury that is necessary for tissue repair, but its dysregulated persistence contributes significantly to the secondary injury, neurodegeneration, and long-term neurological deficits observed in many TBI patients. The acute phase of inflammation, while initially protective, can progress into chronic neuroinflammation, impairing cognitive function, emotional well-being, and overall recovery. Understanding the complex relationship between inflammation and long-term outcomes is essential for developing effective therapeutic strategies to improve recovery after TBI. By targeting the inflammatory response through pharmacological interventions, stem cell therapies, or gene editing technologies, it may be possible to reduce neuronal damage, promote recovery, and improve the quality of life for individuals living with the aftermath of traumatic brain injury.

Aspect	Inflammatory Response	Acute Phase	Chronic Phase	Cellular Involvement	Impact on Recovery	Long-Term Outcomes
Initial Inflammatory Response	Activation of microglia and astrocytes	Immediate release of cytokines and chemokines	Persistent activation of immune cells	Microglia, macrophages, T-cells	Helps in clearing debris but can cause secondary damage	Contributes to neurodegeneration and cognitive decline
Neuroinflammation	Activation of the blood-brain barrier	Leakage of pro-inflammatory molecules	Chronic low-grade inflammation	Immune cells infiltrate the brain	Increases neuronal damage and impairs healing	Linked to dementia and cognitive deficits
Cytokine Release	Elevation of TNF-α, IL-1β, and IL-6	Pro-inflammatory cytokines promote further injury	Cytokines continue to affect brain function	Cytokines activate both neural and immune cells	Heightens neuronal stress and disrupts recovery	Cognitive impairments, mood disorders, and neurodegenerative diseases
Microglial Activation	Microglial cells become activated post-TBI	Microglia clear debris, but excessive activation leads to neurotoxicity	Chronic activation leads to damage to neurons and synapses	Microglia contribute to cell death and synapse pruning	Delayed or poor recovery due to continued inflammatory signaling	Long-term neurological dysfunction and possible neurodegeneration
Blood-Brain Barrier Disruption	BBB permeability increases post-injury	Initial breach allows immune cells and molecules to enter the brain	Persistent BBB dysfunction contributes to ongoing inflammation	Immune cells, cytokines, and toxins can enter the brain	Causes secondary injury and impedes healing	Increases susceptibility to further brain damage and cognitive issues
Impact on Neuronal Plasticity	Inflammation can hinder neurogenesis	Acute inflammation may initially disrupt plasticity but can promote recovery	Chronic inflammation inhibits neuronal regeneration	Cytokines and immune factors impair synaptic plasticity	Limits functional recovery and plasticity, hindering rehabilitation	Long-term deficits in motor and cognitive functions

Table:2 This table presents a comprehensive overview of how inflammation interacts with the brain following a traumatic injury and how it affects recovery and long-term outcomes.

The Contribution of Systemic and Central Immune System Dysregulation to Diseases like Huntington's and ALS

Huntington’s disease (HD) and amyotrophic lateral sclerosis (ALS) are two of the most well-known neurodegenerative diseases, both characterized by the progressive loss of motor function, cognitive decline, and a devastating impact on the lives of affected individuals. While these diseases have distinct pathophysiological mechanisms—Huntington's disease primarily driven by genetic mutations in the huntingtin gene, and ALS associated with motor neuron degeneration—they share common features of systemic and central immune system dysregulation. Immune system dysfunction, both at the level of the central nervous system (CNS) and throughout the peripheral circulation, contributes significantly to the pathogenesis of these diseases, exacerbating neuronal damage, inflammation, and tissue degeneration. Understanding how immune system dysregulation plays a role in the progression of Huntington’s disease and ALS is critical for developing therapeutic strategies that might mitigate disease progression and enhance quality of life for patients.

Huntington’s disease (HD) is a rare, inherited neurodegenerative disorder caused by an expansion of CAG repeats in the HTT gene. This mutation leads to the production of a mutated form of the huntingtin protein, which aggregates in neurons and leads to progressive neuronal death, particularly in the striatum and other areas of the brain involved in motor control, cognition, and mood regulation. Symptoms typically include uncontrolled movements (chorea), cognitive decline, psychiatric disturbances, and eventual loss of independent functioning. There is currently no cure for HD, and treatments mainly focus on managing symptoms.Amyotrophic lateral sclerosis (ALS), on the other hand, is a progressive motor neuron disease characterized by the degeneration of upper and lower motor neurons, leading to muscle weakness, paralysis, and respiratory failure. In most cases, ALS is sporadic, though about 10% of cases are familial and are associated with genetic mutations in specific genes like SOD1, C9orf72, and TDP-43. As motor neurons die, patients experience progressive loss of muscle control, eventually leading to complete paralysis. ALS has a complex pathophysiology that involves not only motor neuron degeneration but also dysfunction in other cellular systems, including glial cells, synaptic communication, and immune regulation.Both diseases share several common features, including the presence of abnormal protein aggregates, oxidative stress, excitotoxicity, and inflammation. The involvement of immune dysregulation is emerging as a critical aspect of disease progression in both HD and ALS.

The Immune System in the Central Nervous System (CNS):The immune system plays a vital role in the defense against pathogens and the maintenance of tissue homeostasis. In the peripheral circulation, immune cells such as neutrophils, monocytes, and lymphocytes constantly monitor and respond to external insults. However, the CNS, once thought to be an immune-privileged site, also houses a complex immune network that includes resident glial cells—microglia, astrocytes, and oligodendrocytes—that actively contribute to immune responses. These cells maintain the homeostasis of the brain, clear debris, and regulate synaptic function.

Microglia, the brain’s resident immune cells, are comparable to macrophages in peripheral tissues and play a key role in the brain’s immune response. In a healthy brain, microglia continuously monitor the environment, maintaining synaptic homeostasis and responding to injuries or insults by activating inflammatory pathways. Astrocytes, another type of glial cell, are involved in maintaining the blood-brain barrier (BBB), supporting neuronal

function, and responding to neuroinflammatory signals. Both microglia and astrocytes can become activated in response to brain injury, neurodegeneration, and other pathological stimuli.

In the context of neurodegenerative diseases such as Huntington's disease and ALS, dysregulated activation of microglia and astrocytes, as well as disruption of the blood-brain barrier, contributes to the exacerbation of neuronal injury and progression of disease.

Systemic Immune Dysregulation in Neurodegeneration:While immune dysregulation within the brain itself is critical to the pathology of diseases like HD and ALS, peripheral immune responses also play a significant role in the progression of these diseases. In both conditions, systemic inflammation has been observed, which may amplify the inflammatory response in the brain and contribute to neuronal degeneration.One of the hallmarks of neurodegenerative diseases is the disruption of the blood-brain barrier (BBB). The BBB serves as a protective barrier that restricts the entry of immune cells, pathogens, and toxic molecules from the periphery into the brain. However, in diseases like HD and ALS, the BBB becomes compromised, allowing peripheral immune cells (such as macrophages, T cells, and neutrophils) to infiltrate the CNS. This infiltration exacerbates neuroinflammation, leading to further neuronal damage and contributing to the progression of these diseases.Peripheral immune responses may also involve the activation of systemic cytokine signaling. Cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) are often elevated in both the serum and cerebrospinal fluid (CSF) of patients with neurodegenerative diseases. These cytokines can activate both systemic and CNS immune cells, further perpetuating the cycle of neuroinflammation. For example, in ALS, systemic inflammation and elevated levels of IL-6 have been correlated with disease progression, while in HD, cytokines such as TNF-α contribute to neuronal apoptosis and synaptic dysfunction.

Microglial Activation in Huntington's Disease:In Huntington's disease, the mutation in the HTT gene leads to the production of an abnormal huntingtin protein, which aggregates in neurons, leading to neurodegeneration. The accumulation of mutant huntingtin protein triggers an inflammatory response in the brain, primarily through the activation of microglia. In the early stages of HD, microglia become activated in response to neuronal injury and aggregation of toxic proteins, resulting in the release of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. While the activation of microglia is intended to clear damaged cells and debris, prolonged activation of these immune cells results in chronic neuroinflammation, which exacerbates neuronal injury and accelerates disease progression.The inflammatory cytokines released by microglia in HD can further contribute to neuronal death by enhancing oxidative stress, promoting excitotoxicity, and activating apoptotic signaling pathways. In particular, microglial activation leads to the release of reactive oxygen species (ROS) and nitric oxide (NO), both of which are potent neurotoxins that damage cellular components and impair mitochondrial function. Additionally, the activation of the NLRP3 inflammasome in microglia has been implicated in the chronic inflammation observed in HD, further promoting the release of inflammatory cytokines and the perpetuation of neuronal injury.Importantly, microglial activation in HD is not confined to the brain regions directly involved in motor function but also affects regions involved in cognition and mood regulation, such as the striatum and cortex. This widespread activation contributes to the cognitive decline and psychiatric symptoms commonly seen in HD patients, further complicating the clinical presentation of the disease.

Astrocytic Contribution to Neuroinflammation in ALS:In ALS, the dysfunction of motor neurons is accompanied by the activation of both microglia and astrocytes. While microglia are involved in the early stages of inflammation, astrocytes play a critical role in sustaining the inflammatory response and perpetuating motor neuron degeneration. Astrocytes are normally responsible for maintaining homeostasis in the brain, including the regulation of neurotransmitter levels and the support of blood-brain barrier integrity. However, in ALS, activated astrocytes release pro-inflammatory cytokines and chemokines, which exacerbate neuroinflammation and contribute to motor neuron toxicity.Astrocytes in ALS have been shown to promote the release of glutamate, the primary excitatory neurotransmitter, in excessive amounts, contributing to excitotoxicity in motor neurons. Additionally, inflammatory cytokines released by activated astrocytes, such as IL-1β and TNF-α, can impair the function of neighboring neurons and glial cells, promoting neuronal death. The disruption of the blood-brain barrier by activated astrocytes also allows peripheral immune cells to infiltrate the CNS, compounding the inflammatory response and driving further damage.A growing body of evidence suggests that astrocytic dysfunction in ALS is not limited to the local inflammatory response. Rather, it also involves systemic inflammation. The release of pro-inflammatory cytokines by astrocytes can alter the function of the peripheral immune system, influencing the systemic inflammatory response and amplifying neuroinflammation within the brain. Moreover, a recent study showed that in ALS, astrocytes can express elevated levels of C9orf72, a gene associated with familial ALS, further linking astrocytic dysfunction to the pathophysiology of the disease.

Peripheral Immune System Dysregulation in ALS:In ALS, peripheral immune system dysregulation has been linked to disease progression. Chronic activation of the peripheral immune system, particularly the activation of T lymphocytes and macrophages, contributes to systemic inflammation that can worsen neuroinflammation within the CNS. The infiltration of immune cells such as macrophages and T cells into the spinal cord and brain of ALS patients has been observed in postmortem studies, and these cells release pro-inflammatory cytokines that exacerbate motor neuron degeneration.Recent research has focused on the role of the complement system in ALS, which is part of the innate immune system and plays a critical role in neuroinflammation. In ALS, the complement system is often upregulated, leading to the deposition of complement proteins in motor neurons and glial cells. This activation of the complement cascade contributes to neuronal death and synaptic dysfunction, promoting disease progression. The chronic activation of the complement system in ALS further exemplifies the contribution of peripheral immune dysfunction to central neuroinflammation.

Therapeutic Implications: Targeting Immune System Dysregulation:Given the critical role of immune system dysregulation in diseases like Huntington’s and ALS, therapeutic strategies that target neuroinflammation offer potential for slowing disease progression. Several approaches are currently being explored

Microglial Modulation: Strategies aimed at regulating microglial activation could help mitigate the harmful effects of neuroinflammation. For example, drugs that target the P2X7 receptor, a key mediator of microglial activation, may help reduce neuroinflammation in both HD and ALS.

Cytokine Inhibition: The use of cytokine inhibitors or modulators to reduce pro-inflammatory cytokine release is another promising approach. In HD, targeting TNF-α and

IL-1β has shown potential in preclinical models, while in ALS, the inhibition of IL-6 signaling could slow disease progression.

Immunomodulatory Therapies: Immunomodulatory agents such as minocycline, which has both anti-inflammatory and neuroprotective properties, have been explored for their potential to reduce microglial activation and slow neuronal degeneration in ALS and HD. Additionally, mesenchymal stem cell therapies are being investigated for their ability to modulate both the central and peripheral immune responses in neurodegenerative diseases.

Blood-Brain Barrier Stabilization: Restoring the integrity of the blood-brain barrier could be an effective way to limit peripheral immune cell infiltration and reduce neuroinflammation in both ALS and HD.

The dysregulation of the immune system—both centrally within the brain and peripherally throughout the body—plays a central role in the progression of neurodegenerative diseases like Huntington's and ALS. Immune system dysfunction, particularly the chronic activation of microglia, astrocytes, and peripheral immune cells, exacerbates neuronal damage, neuroinflammation, and tissue degeneration. The interplay between systemic and central immune responses in these diseases complicates their pathogenesis and offers potential targets for therapeutic intervention. By targeting immune system dysregulation, it may be possible to slow the progression of these devastating diseases and improve the quality of life for affected individuals. Continued research into the immune mechanisms underlying Huntington's disease and ALS is critical for developing more effective treatments that could potentially modify disease progression or even prevent its onset.

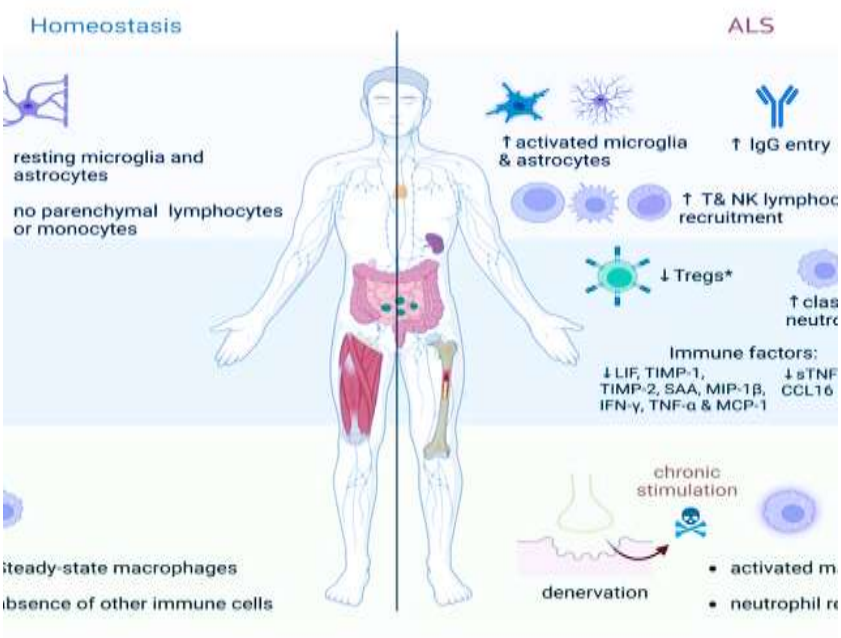


Figure:4 The image contrasts the states of homeostasis and ALS (Amyotrophic Lateral Sclerosis). In a healthy state, microglia and astrocytes are resting, with no immune cell infiltration. In ALS, there's activation of microglia and astrocytes, increased IgG entry, and recruitment of T and NK lymphocytes. This chronic stimulation leads to denervation and heightened immune responses, highlighting the disease's pathology and immune involvement.

An In-Depth Look at Key Molecules in the Inflammatory Cascade and Their Impact on Neuronal Function and Survival

Neuroinflammation is increasingly recognized as a central player in a wide array of neurological disorders, including neurodegenerative diseases such as Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis (ALS), as well as in acute conditions such as stroke and traumatic brain injury (TBI). While inflammation is an essential and protective response to injury or infection, the inflammatory cascade in the central nervous system (CNS) becomes maladaptive when it persists or becomes excessive. This dysregulated inflammation contributes significantly to neuronal dysfunction and death. At the core of neuroinflammation lies a complex network of signaling molecules—pro-inflammatory cytokines, chemokines, reactive oxygen species (ROS), and signaling enzymes—that orchestrate the inflammatory response. This article will explore the key molecules in the inflammatory cascade and their effects on neuronal function and survival, providing insights into how these molecules contribute to both acute injury and chronic neurodegeneration.

The Inflammatory Cascade in the Central Nervous System:The inflammatory response in the brain is largely mediated by resident immune cells such as microglia and astrocytes, as well as infiltrating peripheral immune cells when the blood-brain barrier (BBB) is compromised. Microglia, which are analogous to macrophages in the periphery, serve as the primary immune responders in the CNS. Under normal conditions, microglia are in a resting state, continuously surveying the environment for potential threats. When the brain is injured or infected, microglia become activated, transitioning to an amoeboid shape and releasing a plethora of inflammatory mediators that can affect surrounding neurons, glia, and the extracellular matrix.Astrocytes, the most abundant glial cells in the brain, also play a crucial role in the inflammatory response. They maintain homeostasis by regulating blood flow, the extracellular environment, and the blood-brain barrier. Astrocytes can become reactive in response to injury or disease, contributing to neuroinflammation and neuronal injury through the release of pro-inflammatory cytokines and chemokines.The inflammatory cascade begins with the activation of pattern recognition receptors (PRRs) on microglia, such as the Toll-like receptors (TLRs) and NOD-like receptors (NLRs), that recognize danger signals (known as damage-associated molecular patterns or DAMPs) from damaged cells, or pathogen-associated molecular patterns (PAMPs) from invading pathogens. Once activated, these receptors initiate a signaling cascade that leads to the production of a variety of pro-inflammatory mediators, including cytokines, chemokines, prostaglandins, and reactive oxygen species (ROS).

Cytokines are small proteins that play pivotal roles in the regulation of the immune response. In the CNS, microglia, astrocytes, and peripheral immune cells produce a variety of cytokines that influence neuronal function. These cytokines can have both beneficial and harmful effects on the brain, depending on their timing, concentration, and duration of action.

TNF-α is one of the most studied and potent pro-inflammatory cytokines in neuroinflammation. It is primarily produced by activated microglia and astrocytes in response to injury or infection. TNF-α has a dual role in the brain—it can promote protective responses such as tissue repair and regeneration in the early stages of inflammation, but when overproduced or sustained, TNF-α becomes neurotoxic. TNF-α contributes to neuronal dysfunction and death by inducing apoptosis, promoting oxidative stress, and increasing the

permeability of the blood-brain barrier. It also activates the NF-κB signaling pathway, which further amplifies the inflammatory response.

In diseases like Alzheimer's disease (AD), Parkinson's disease (PD), and amyotrophic lateral sclerosis (ALS), chronic elevation of TNF-α is observed and correlates with disease progression. In AD, TNF-α is implicated in the neurodegenerative process through the promotion of amyloid plaque formation and tau phosphorylation. In PD, TNF-α exacerbates dopaminergic neuron loss in the substantia nigra.

Interleukin-1β (IL-1β):IL-1β is another potent pro-inflammatory cytokine that plays a critical role in the initiation and propagation of the inflammatory response. IL-1β is primarily produced by microglia and astrocytes and is often upregulated in response to TLR activation. Like TNF-α, IL-1β has both protective and harmful effects on neurons. In the acute phase of neuroinflammation, IL-1β helps mediate tissue repair, but chronic production of IL-1β can lead to sustained neuroinflammation, synaptic dysfunction, and neuronal death.IL-1β contributes to neurodegeneration by disrupting neuronal signaling, promoting oxidative damage, and increasing the production of nitric oxide (NO). In AD, IL-1β exacerbates amyloid plaque deposition and tau aggregation. In neurodegenerative diseases such as ALS, IL-1β has been linked to motor neuron degeneration and progressive loss of motor function. Elevated levels of IL-1β also impair neurogenesis in the hippocampus, a region critical for learning and memory.

Interleukin-6 (IL-6):IL-6 is a cytokine with pleiotropic effects, playing roles in both inflammation and tissue repair. In the CNS, IL-6 is produced by microglia, astrocytes, and infiltrating immune cells such as macrophages. IL-6 signaling is mediated through its receptor, IL-6R, and activation of the Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway.While IL-6 is involved in immune responses to infection and injury, its chronic elevation in neurodegenerative diseases can lead to detrimental effects on neuronal function. In both HD and ALS, elevated IL-6 levels correlate with disease progression and motor dysfunction. IL-6 also promotes the production of other inflammatory mediators, amplifying the inflammatory response and contributing to neurodegeneration.In AD, IL-6 contributes to synaptic dysfunction and is involved in amyloid-β plaque formation. In ALS, IL-6 has been linked to the activation of astrocytes and microglia, driving neuroinflammation and motor neuron death.

Chemokines are a subset of cytokines that mediate the recruitment of immune cells to sites of inflammation. In the CNS, chemokines are primarily produced by microglia, astrocytes, and endothelial cells of the blood-brain barrier. Chemokines can influence neuronal survival by altering the balance between pro-inflammatory and anti-inflammatory responses.

Monocyte Chemoattractant Protein-1 (MCP-1/CCL2):MCP-1, also known as CCL2, is one of the key chemokines involved in the recruitment of peripheral monocytes and macrophages to sites of injury or infection. Elevated levels of MCP-1 have been observed in various neurodegenerative diseases, including AD, PD, and ALS. In AD, MCP-1 is implicated in the recruitment of peripheral macrophages to the brain, which further exacerbates neuroinflammation and neuronal damage. In ALS, MCP-1 is involved in the recruitment of inflammatory macrophages to the spinal cord, contributing to motor neuron degeneration.While MCP-1 plays a critical role in the immune response, its chronic overexpression in the brain contributes to sustained inflammation, promoting neuronal dysfunction and death. The persistent activation of monocytes and macrophages through MCP-1 signaling disrupts synaptic activity and impairs neuronal survival.

Interleukin-8 (IL-8/CXCL8):IL-8, or CXCL8, is another chemokine that is involved in immune cell recruitment and activation during inflammation. In the CNS, IL-8 is primarily produced by astrocytes and microglia in response to injury or infection. IL-8 attracts neutrophils and T lymphocytes to the site of inflammation, exacerbating neuroinflammation. In AD, IL-8 has been linked to the recruitment of neutrophils and the disruption of blood-brain barrier integrity, leading to further neuronal injury.IL-8 has been found to interact with several receptors, including CXCR1 and CXCR2, which mediate the infiltration of immune cells. While IL-8 plays a role in the acute immune response, its chronic activation results in sustained neuroinflammation that contributes to neuronal loss and dysfunction.

Reactive oxygen species (ROS) and nitric oxide (NO) are key molecular mediators of oxidative stress during neuroinflammation. ROS are highly reactive molecules that are produced by activated microglia, astrocytes, and peripheral immune cells, and they can damage cellular structures, including lipids, proteins, and DNA. NO is a free radical that is produced by inducible nitric oxide synthase (iNOS) in response to pro-inflammatory signals.

While ROS and NO are involved in the immune response to infection or injury, their overproduction during neuroinflammation leads to cellular damage and contributes to the pathogenesis of neurodegenerative diseases. In AD, the accumulation of ROS and NO promotes amyloid-β aggregation, tau hyperphosphorylation, and synaptic dysfunction. In ALS, ROS and NO contribute to motor neuron degeneration by inducing mitochondrial dysfunction and promoting apoptosis.

Oxidative stress plays a critical role in the progression of neurodegenerative diseases. In HD, increased ROS production is associated with mutant huntingtin protein aggregation, leading to neuronal dysfunction and death. In ALS, oxidative damage to motor neurons is a key feature of disease progression, and elevated ROS levels are correlated with the degeneration of the spinal cord and cortex.

Antioxidant defense mechanisms, such as superoxide dismutase (SOD) and glutathione peroxidase (GPx), are often overwhelmed during chronic neuroinflammation, exacerbating oxidative damage. Targeting oxidative stress with antioxidant therapies is a potential strategy to mitigate the impact of neuroinflammation on neuronal survival.

Prostaglandins are lipid mediators derived from arachidonic acid through the action of cyclooxygenase enzymes (COX-1 and COX-2). COX-2, in particular, is induced during inflammation and plays a significant role in the inflammatory cascade. Prostaglandins, including PGE2, contribute to the amplification of neuroinflammation by enhancing the production of pro-inflammatory cytokines and chemokines.In neurodegenerative diseases like AD and PD, COX-2 activity is upregulated, and prostaglandin production is associated with neuronal damage, synaptic loss, and cognitive decline. COX inhibitors, such as nonsteroidal anti-inflammatory drugs (NSAIDs), have been explored as potential therapies for neurodegenerative diseases, although their clinical efficacy has been variable.

The inflammatory cascade in the CNS involves a complex network of molecules, including cytokines, chemokines, reactive oxygen species, nitric oxide, and prostaglandins, all of which play pivotal roles in regulating neuronal function and survival. In the context of neurodegenerative diseases, this inflammatory response can become maladaptive, leading to neuronal dysfunction, synaptic loss, and neuronal death. Dysregulation of key inflammatory mediators, such as TNF-α, IL-1β, IL-6, ROS, and COX-2, contributes significantly to the progression of diseases like Alzheimer’s, Parkinson’s, Huntington’s, and ALS.Targeting

specific molecules in the inflammatory cascade offers promising therapeutic potential for slowing or halting disease progression. However, the challenge remains to modulate these inflammatory pathways without disrupting the normal immune surveillance that is essential for brain homeostasis.

Current and Emerging Treatments Aiming to Reduce or Regulate Neuroinflammation in Neurological Disorders

Neuroinflammation plays a pivotal role in the progression of numerous neurological disorders, including neurodegenerative diseases such as Alzheimer's, Parkinson's, multiple sclerosis, Huntington's disease, amyotrophic lateral sclerosis (ALS), and acute conditions like stroke and traumatic brain injury (TBI). While inflammation is an essential component of the body's response to injury or infection, chronic neuroinflammation contributes significantly to neuronal dysfunction and loss, exacerbating disease progression. As a result, targeting neuroinflammation has emerged as a promising therapeutic strategy. This article will explore the current and emerging treatments designed to reduce or regulate neuroinflammation, including immunomodulatory therapies, anti-inflammatory drugs, and innovative approaches targeting specific molecular pathways involved in the inflammatory cascade.

Understanding the Role of Neuroinflammation in Neurological Disorders:Neuroinflammation involves the activation of the brain's immune cells, including microglia, astrocytes, and infiltrating peripheral immune cells, in response to injury, infection, or neurodegenerative processes. Microglia, the resident immune cells of the central nervous system (CNS), continuously monitor the brain environment for potential threats. Upon activation, microglia release pro-inflammatory cytokines, reactive oxygen species (ROS), nitric oxide (NO), and other molecules that help defend against pathogens and promote tissue repair. However, when microglial activation becomes chronic or excessive, it leads to sustained neuroinflammation, which in turn can damage neurons, impair synaptic function, and accelerate disease progression.Chronic neuroinflammation has been implicated in the pathogenesis of various neurological disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), multiple sclerosis (MS), and amyotrophic lateral sclerosis (ALS). In these conditions, dysregulated immune responses cause the release of inflammatory mediators such as cytokines (e.g., TNF-α, IL-1β, IL-6), chemokines, and growth factors, which can disrupt neuronal function and survival. Therefore, controlling or modulating neuroinflammation has become a key therapeutic target in these diseases.

Current Strategies for Regulating Neuroinflammation

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used anti-inflammatory agents for various inflammatory conditions. NSAIDs, such as ibuprofen, aspirin, and naproxen, exert their effects by inhibiting the cyclooxygenase (COX) enzymes, particularly COX-2, which are responsible for the production of pro-inflammatory prostaglandins. In the brain, COX-2 is upregulated in response to injury or disease and is involved in the production of prostaglandins, which mediate neuroinflammation.Given the central role of COX-2 in neuroinflammation, NSAIDs have been investigated as potential treatments for neurodegenerative diseases, particularly Alzheimer's disease and Parkinson's disease. In preclinical studies, NSAIDs have shown the ability to reduce microglial activation, decrease pro-inflammatory cytokine production, and attenuate neuronal damage. However, clinical trials of NSAIDs in neurodegenerative diseases have yielded mixed results, with some studies showing limited benefit and others suggesting that long-term use

of NSAIDs may have adverse effects, such as gastrointestinal toxicity or cardiovascular risks.One significant limitation of NSAIDs is that they inhibit both COX-1 and COX-2 enzymes, leading to side effects like gastric ulcers, renal dysfunction, and bleeding. Therefore, selective COX-2 inhibitors, such as celecoxib, have been developed to minimize the gastrointestinal and renal side effects of traditional NSAIDs. However, even selective COX-2 inhibitors have not demonstrated strong efficacy in treating neurodegenerative diseases, and their use remains controversial.

Glucocorticoids, such as prednisone and dexamethasone, are powerful anti-inflammatory agents that act by suppressing the immune system and inhibiting the production of pro-inflammatory cytokines. Glucocorticoids are used clinically in conditions involving acute neuroinflammation, such as multiple sclerosis (MS), traumatic brain injury (TBI), and spinal cord injury. These drugs are particularly effective at reducing the acute inflammatory response and alleviating symptoms associated with exacerbations of MS or inflammation after brain injury.However, long-term use of glucocorticoids is associated with significant side effects, including osteoporosis, weight gain, glucose intolerance, and increased susceptibility to infections. The immunosuppressive effects of glucocorticoids can also increase the risk of opportunistic infections, making their long-term use in neurodegenerative diseases more challenging. Despite these drawbacks, glucocorticoids remain an essential tool in managing acute inflammation in certain neurological conditions.

Multiple sclerosis (MS) is a chronic inflammatory disease of the CNS in which the immune system attacks the myelin sheath, leading to demyelination, axonal injury, and neurodegeneration. One of the primary mechanisms of neuroinflammation in MS is the activation of T cells, which cross the blood-brain barrier and initiate an inflammatory cascade involving microglia and astrocytes. Current treatments for MS aim to modulate the immune response and reduce the frequency and severity of relapses.Disease-modifying therapies (DMTs) are the cornerstone of MS treatment and include drugs that target specific components of the immune system. Some of the most widely used DMTs include interferon beta, glatiramer acetate, and monoclonal antibodies such as natalizumab and ocrelizumab. These therapies work by suppressing immune cell activation and migration, reducing inflammation, and preventing further damage to the CNS.Interferon beta, for example, has been shown to reduce the activation of T cells and microglia in MS, thereby decreasing the frequency of relapses and slowing disease progression. Similarly, monoclonal antibodies such as ocrelizumab target B cells, which are involved in the production of antibodies that attack myelin. By depleting B cells, ocrelizumab helps reduce the autoimmune response and limit neuroinflammation in MS.While these therapies have proven effective in reducing disease activity and delaying progression in MS, they do not completely halt disease progression or reverse existing damage. As a result, researchers are investigating new strategies to target neuroinflammation more effectively and protect neurons from damage in MS and other neurodegenerative diseases.

Emerging Immunomodulatory Therapies

Microglial Modulation:Microglia are the resident immune cells of the CNS and play a crucial role in both the initiation and resolution of neuroinflammation. In neurodegenerative diseases, microglial activation can become chronic, leading to sustained inflammation and neuronal damage. Therefore, targeting microglial activation has become a promising strategy for modulating neuroinflammation.One potential therapeutic approach is to inhibit the activation of microglia by targeting specific receptors and signaling pathways involved in

their activation. For example, the P2X7 receptor, which is involved in the activation of the inflammasome and the release of pro-inflammatory cytokines, has been identified as a potential target for reducing neuroinflammation. Drugs that block P2X7 receptor activity have shown promise in preclinical models of Alzheimer's disease and Parkinson's disease by reducing microglial activation and improving neuronal survival.Another emerging strategy is to modulate the polarization of microglia. Microglia exist in two main states: the M1 pro-inflammatory phenotype, which exacerbates neuroinflammation, and the M2 anti-inflammatory phenotype, which promotes tissue repair and neuroprotection. Therapies that promote the M2 phenotype or inhibit the M1 phenotype are being explored as a means to regulate neuroinflammation in neurodegenerative diseases.

Monoclonal antibodies (mAbs) have revolutionized the treatment of various diseases, including cancer and autoimmune disorders. In the context of neuroinflammation, mAbs are being developed to target specific molecules involved in the inflammatory process. One notable example is anti-TNF-α monoclonal antibodies. Tumor necrosis factor-alpha (TNF-α) is a pro-inflammatory cytokine that plays a key role in neuroinflammation and neuronal injury. Drugs such as infliximab and adalimumab, which are widely used in autoimmune diseases like rheumatoid arthritis and Crohn’s disease, have shown promise in reducing neuroinflammation in animal models of neurodegenerative diseases. Although TNF-α inhibitors have not been universally successful in clinical trials for neurodegenerative diseases, they remain a potential area of interest for future therapeutic development.Another class of mAbs targets amyloid-β in Alzheimer's disease. Amyloid plaques are a hallmark feature of Alzheimer's, and they are associated with chronic microglial activation and neuroinflammation. Anti-amyloid antibodies, such as aducanumab and donanemab, aim to reduce amyloid plaque accumulation and modulate the associated inflammatory response. Although aducanumab was recently approved by the FDA, its clinical efficacy remains debated, and ongoing studies are investigating its long-term benefits and safety profile.

JAK/STAT Pathway Inhibitors:The Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway is a critical signaling pathway involved in the immune response. JAK inhibitors, such as tofacitinib, are already used in autoimmune diseases like rheumatoid arthritis and inflammatory bowel disease. These inhibitors work by blocking JAKs, which are enzymes that activate the STAT proteins involved in cytokine signaling.In the context of neuroinflammation, JAK inhibitors have shown potential in preclinical models of neurodegenerative diseases, such as Alzheimer's and multiple sclerosis. By inhibiting the JAK-STAT pathway, these drugs can reduce the production of pro-inflammatory cytokines and limit the activation of microglia and astrocytes. Ongoing clinical trials are evaluating the safety and efficacy of JAK inhibitors in treating neurodegenerative diseases.

Cannabinoid-Based Therapies:Cannabinoids, which act on the endocannabinoid system, have gained attention as potential modulators of neuroinflammation. The endocannabinoid system plays a crucial role in regulating immune responses in the CNS, and cannabinoids have been shown to reduce microglial activation and the release of pro-inflammatory cytokines in animal models.Cannabinoid-based therapies, such as cannabidiol (CBD) and Δ9-tetrahydrocannabinol (THC), are being explored for their potential to reduce neuroinflammation and protect neurons in conditions like multiple sclerosis, Parkinson's disease, and Alzheimer's disease. While some early studies have shown promise, further research is needed to determine the long-term safety and efficacy of these therapies.

Neuroinflammation is a key contributor to the pathogenesis of a wide range of neurological disorders, and controlling or modulating this inflammatory response offers a promising therapeutic approach. Current treatments, including NSAIDs, glucocorticoids, and disease-modifying therapies, have had varying degrees of success in managing neuroinflammation, particularly in conditions like multiple sclerosis. However, these therapies often come with significant side effects or limitations in efficacy.

Emerging immunomodulatory therapies, including microglial modulators, monoclonal antibodies, JAK inhibitors, and cannabinoid-based therapies, offer new avenues for regulating neuroinflammation. These approaches hold the potential to slow disease progression, improve neuronal survival, and reduce symptoms in patients with neurodegenerative diseases.Despite promising preclinical and early-phase clinical results, further research and clinical trials are needed to fully understand the long-term safety and efficacy of these emerging therapies. As our understanding of neuroinflammation deepens, more targeted and personalized treatments may emerge, offering hope for patients suffering from chronic neurological diseases.

Conclusion

In conclusion, neuroinflammation plays a central role in the pathogenesis of a wide range of neurological disorders, from chronic neurodegenerative diseases like Alzheimer’s and Parkinson’s to acute conditions such as stroke and traumatic brain injury. The activation of microglia, astrocytes, and the release of pro-inflammatory cytokines and reactive molecules exacerbate neuronal damage and contribute to disease progression. While inflammation is initially a protective response, its chronic or dysregulated state leads to harmful effects on neuronal function and survival. Current therapeutic strategies primarily focus on modulating this inflammatory response, but challenges remain in developing treatments that effectively balance the need for immune protection with the potential harm of sustained inflammation. Ongoing research into targeted therapies, such as microglial modulation, cytokine inhibitors, and novel immune modulators, offers hope for future treatments that can mitigate neuroinflammation and improve outcomes for patients with neurological diseases.

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USE OF PENTOXIFYLLINE IN VETERINARY MEDICINE

ABSTRACT

Pentoxifylline is a nonselective phosphodiesterase inhibitor methylxanthine derivative drug with hemorheological and anti-inflammatory effects. Pentoxifylline shows its effect by inhibiting the phosphodiesterase enzyme and increasing the level of cAMP, thus preventing platelet aggregation and cyclooxygenase activity. Thus, it reduces platelet adhesion to vascular walls, increases the flexibility and deformability of erythrocytes, reduces blood viscosity, and reduces plasma fibrinogen levels. Pentoxifylline has anti-inflammatory effects by suppressing proinflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-8) and leukotrienes. It also has anti-proliferative, anti-fibrotic, anti-diabetic, immunomodulatory, antiviral, bronchodilator, antiproteinuric, and antioxidant effects. Although pentoxifylline was first used in the treatment of claudication, it is now used in various diseases, including vasculitis, endotoxemia, sepsis, diabetic ulcers, cancer, acute respiratory system diseases, seizure disorders, and collagen disorders. Although pentoxifylline is not approved for use in animals, it is used off-label due to its effects. Pentoxifylline is used in conditions such as vasculitis, atopic dermatitis, contact allergy, dermatomyositis, and systemic lupus erythematosus in dogs; cutaneous vasculitis, laminitis, endometritis-placentitis, and septicemia in horses; and vasculitis, laminitis, endometritis-placentitis, and septicemia in cattle. It has also been stated that it may be useful in the treatment of cognitive disorders in geriatric dogs, uterine torsion in horses, and feline infectious peritonitis in cats. Although information on the side effects of pentoxifylline in animals is limited, it causes side effects, especially in the gastrointestinal system and central nervous system. In conclusion, pentoxifylline is widely used in animals due to its hemorheological and anti-inflammatory effects. However, its use is restricted by the fact that it is not approved in animals, and the appropriate dosage regimens and side effect profile are not fully known. Therefore, further studies are needed to demonstrate in detail the appropriate dosage regimen, therapeutic efficacy, and undesirable effects of pentoxifylline in animals.

VETERİNER HEKİMLİKTE PENTOKSİFİLİNİN KULLANIMI

ÖZET

Pentoksifilin, hemoreolojik ve antiinflamatuvar etkiye sahip, nonselektif fosfodiesteraz inhibitörü metilksantin türevi bir ilaçtır. Pentoksifilin fosfodiesteraz enzimini inhibe edip cAMP düzeyini artırarak etkisini gösterir ve böylelikle trombosit agregasyonunu ve siklooksijenaz aktivitesini önler. Böylelikle trombositlerin damar duvarlarına yapışmasını azaltır, eritrositlerin esnekliğini ve şekil verilebilirliğini artırıp kan viskozitesini düşürür ve plazma fibrinojen düzeyini azaltır. Pentoksifilinin proinflamatuvar sitokinleri (TNF-α, IL-1β, IL-6 ve IL-8) ve lökotrienleri baskılayarak antiinflamatuvar etki gösterir. Ayrıca anti-proliferatif, anti-fibrotik, anti-diyabetik, immünomodülatör, antiviral, bronkodilatör, antiproteinürik ve antioksidan etkilere de sahiptir. Pentoksifilin ilk olarak klodikasyon tedavisinde kullanılmasına karşın vaskülit, endotoksemi, sepsis, diyabetik ülserler, kanser, akut solunum sistemi hastalıkları, nöbet bozuklukları ile kollajen bozuklukları dahil olmak üzere çeşitli hastalıklarda kullanılır. Pentoksifilinin hayvanlarda kullanımı onaylanmamasına karşın sahip olduğu etkilerden dolayı etiket dışı olarak kullanılır. Pentoksifilin köpeklerde vaskülit, atopik dermatit, kontakt alerji, dermatomiyozit ve sistemik lupus eritematozusda, atlarda kutanöz vaskülit, laminit, endometrit-plasentit ve septisemide ve sığırlarda vaskülit, laminit, endometrit-plasentit ve septisemi gibi durumlarda kullanılır. Ayrıca geriatrik köpeklerde bilişsel bozukluklarının tedavisinde, atlarda uterus torsiyonunda ve kedilerde feline infeksiyöz peritonitiste faydalı olabileceği ifade edilmiştir. Hayvanlarda pentoksifilinin yan etkileri ile ilgili bilgiler sınırlı olmakla birlikte özellikle gastrointestinal sistem ve merkezi sinir sistemde yan etkilere neden olur. Sonuç olarak pentoksifilin sahip olduğu hemoreolojik ve antiinflamatuar etkilerden dolayı hayvanlarda yaygın olarak kullanılır. Ancak hayvanlarda onaylı olmaması ve uygun dozaj rejimlerinin ile yan etki profilinin tam olarak bilinmemesi kullanımını kısıtlamaktadır. Bu nedenle hayvanlarda pentoksifilinin uygun dozaj rejiminin, terapötik etkinliğinin ve istenmeyen etkilerinin detaylı olarak ortaya konulduğu daha fazla çalışmalara ihtiyaç vardır.

1. Giriş

Pentoksifilin (PTX) nonselektif fosfodiesteraz inhibitörü olan metilksantin türevi bir ilaçtır (Brie ve ark., 2016). Hemoreolojik ve antiinflamatuar özellikleri nedeniyle ilk olarak 1984 yılında aralıklı klodikasyon, daha sonra vaskülit, endotoksemi, sepsis, diyabetik ülserler, nöbet bozuklukları, kanser ve kollajen bozukluklarının tedavisinde kullanılmaya başlanmıştır (Samlaska ve Winfield 1994; Zhang ve ark., 2004). PTX, fosfodiesteraz, kalsiyuma bağımlı fosfoprotein fosfataz ve transglutaminazın inhibisyonu ve protein kinazın magnezyuma bağımlı aktivasyonu yoluyla hücre içi siklik adenosin monofosfat (cAMP) düzeyini artırırken kalsiyum miktarını azaltırarak etkinlik gösterdiği ifade edilmektedir (Aviado ve Porter,1984). Bu etkileri ile tümör nekroz faktörü (TNF)-α, interlökin (IL)-1β, IL-6 ve IL-8 salınımını azaltır (Çakmak ve ark. 2012). Buna ek olarak PTX, eritrositlerdeki sertliği azaltıp esnekliği arttırdığından eritrositlerin hasar olması engeller ve kanın akım hızını düzenlediğinden iskemik durumlarda mikrosirkülasyonu ve oksijenin taşınmasının sağlanmasında kullanılır (Ahmadi ve Khalili, 2015). Ayrıca protein kinaz (PKA1) sisteminin ve adenozini aktive etmesi ile tümör nekroz faktörü alfa (TNF-α) ve lökotrienlerin sentezini baskıladığı için anti-inflamatuar, anti-proliferasyon ve anti-fibrotik etkilere sahiptir (Bell, 2021). Bu etkilerine ek olarak anti-diyabetik, immünomodülatör, antiviral, bronkodilatör, antiproteinürik ve antioksidan etkilere sahiptir (Martin ve ark., 2003; Badri ve ark., 2011). Bütün bu etkilerine ek olarak gebelik döneminde kullanıldığından erken doğum öncesi intrauterin inflamasyonu azaltarak, fetal beyin hasarını önleyebileceği bildirilmiştir (Sezik ve ark. 2020).

PTX, antiviral, antineoplastik, immünomodülatör, antiinflamatuar, bronkodilatör, antidiyabetik, antioksidan, antifibrotik, antiproliferatif, anti-proteinürik, anti-akut akciğer hasarı ve antitrombotik olmak üzere pek çok etkiye sahiptir (Badri ve ark., 2011; Zagzoug ve ark., 2023; Mostafa-Hedeab ve ark., 2022; Rodríguez-Morán ve Guerrero-Romero, 2008). Beşerî hekimlikte PTX periferik arterlerin tıkayıcı hastalıkları ve arteriyosklerotik veya diyabetik nedenlerden meydana gelen arteriovenöz dolaşım bozukluklar, bacak ülseri ve gangren gibi trofik bozukluklar, serebral dolaşım bozuklukları ve dejeneratif vasküler süreç ile seyreden dolaşım bozuklukları tedavisinde kullanımı onaylanmıştır (Bell, 2021). Bu kullanımlarına ek olarak septik şok, endotoksemi, akut solunum sistemi hastalıklar, diyabet, deri enfeksiyonları ve kanser tedavisini, kronik kalp yetmezliği, aralıklı topallık, vaskülit, osteoradyonekroz, organ transplatasyonları, diyabetik ülserasyonlar, nöbet bozuklukları ile kollajen bozuklukları dahil olmak üzere çeşitli hastalıkların tedavisinde etiket dışı olarak kullanılmaktadır (Çorum ve ark., 2018; Zagzoug ve ark., 2023; Rivero ve ark., 2017; Windmeier ve Gressner, 1997; Shaw ve ark., 2009).

PTX trombosit aktivasyonunu inhibe ederek trombositlerin kan damarı duvarlarına yapışmasını ile eritrositlerin esnekliğini ve deformasyonu artırarak kan viskozitesini azaltır, plazma fibrinojen konsantrasyonunu azaltarak fibrinolizi destekler ve monositlerin ile polimorfonükleer filtrelenebilirliğini sağlar (Çorum ve ark., 2018). Bu etkilerine ek olarak prostasiklin düzeylerini artırarak vazodilatasyona neden olması olması periferik vasküler hastalık, hemorajik şok ve iskemik hasarını tedavi etmesinde kullanılmasına katkı sağlar (Genov'es ve ark., 2014). PTX'in antitrombotik etkisine prostasiklin sentezini indüklemesine ek olarak fosfodiesteraz E enziminin (PDE) inhibisyonu da katkı sağlamaktadır. Prostasiklin ve nitrik oksit (NO) güçlü vazodilatörler ve aynı zamanda trombosit agregasyon inhibitörleridir. Ayrıca fibrinolitik etkisinden kaynaklı kan viskozitesini azaltırarak (Ahmadi ve Khalili, 2015), çeşitli damar hastalıklarının tedavi etmesinde kullanılmaktadır (Zhang ve ark., 2004).

Diyabetik hastalıklarda PTX kullanılması ile durumunda birçok direkt ve dolaylı etki oluşturarak tedaviye katkıda bulunduğu ifade edilir. Başlıca PTX Langerhans pankreas adacıklarındaki beta hücre fonksiyonundaki iyileşme sağlayarak hepatik glukoz üretimini azaltır ve böylelikle insülin direncini orta derecede iyileştirir. Ayrıca diyabetik nefropatili hastalarda kullanıldığında renin-anjiyotensin-aldosteron sistemini bloke ettiği ve mikrosirkülasyonu teşvik ettiğinden böbrek hasarının önüne geçebileceği belirtilmektedir (Bell, 2021). Mikrovasküler kan akışını iyileştirici etkileri ayrıca diyabetik ayak ülseri de dahil olmak üzere diyabetle ilişkili çeşitli komplikasyonun tedavisinde kullanılmasının faydalı olabileceği düşünülmektedir (Campbell, 1993). PTX'in mikro dolaşım ve periferik oksijenasyon üzerindeki olumlu etkisi kaynaklı deneysel radyoterapide tümör oksijenasyonunu iyileştirdiği ve foton ışınlamanın radyolojik etkinliğine katkı sağlamaktadır (Böhm ve ark., 2003). PTX diyabetik böbrek hastalığına ek olarak kronik böbrek yetmezli hastalarda böbrek nekrozundan sorumlu hücrenin proliferasyonu ve inflamasyonu baskılar. Bu etkisinden kaynaklı hem insan hem de hayvanlarda yapılan araştırmalarda PTX'in geniş spektrumlu böbrek koruyucu etkilere sahip olduğunu ve dolayısıyla PTX'in bir anti-proteinürik ajan olarak kullanılabileceği gösterilmiştir (Badri ve ark., 2011). Ayrıca böbrek hastalıklarının yanı sıra böbrek nakli kullanıldığında böbreklerinin beslenmesini kolaylaştırdığı ve doku reddinin engellenmesine katkı sağlayıcı etkiye sahip olabileceği ifade edilmiştir (Chen ve ark., 2017).

Deri ilgili hastalıklarda da PTX etkin bir şekilde kullanılabileceği belirtilmektedir. PTX kemokin üretimini etkileyerek iltihaplı hücrelerin deriye girişini engelleyebileceğini ileri sürülmektedir. Yapılan çalışmalarda alerjik temas aşırı duyarlılık ve sedef hastalığı gibi yaygın görülen yangı ile karakterize deri hastalıklarında PTX'in etkili olduğu bildirilmiştir (Bruynzeel ve ark., 1998).

Pentoksifilinin Veteriner Hekimliğinde Kullanımı

Pentoksifilin beşerî hekimlikte birçok hastalığın tedavisinde kullanımı onaylanırken, veteriner hekimliğinde kullanımı onaylı değildir (Scagnelli, 2017). Ancak FDA (Amerika Birleşik Devletleri Gıda ve İlaç Dairesi) PTX'in veteriner hekimliğinde kullanımını güvenli ve etkili olabileceği ifade etmiştir (FDA). PTX etiket dışı olarak veteriner hekimliğinde kan akımı ile ilgili bozuklukları düzenleyici ve antiinflamatuar etkilerinden kaynaklı kan akımın bozulduğu ve yangının görüldüğü durumlarda kullanımı önerilir (Logas, 2021). Köpeklerde vaskülit, atopik dermatit, kontakt alerji, dermatomiyozit ve sistemik lupus eritematozus, atlarda kutanöz vaskülit, laminit, endometrit-plasentit, taylarda septisemi ve sığırlarda vaskülit, laminit, endometrit-plasentit ve septisemi gibi durumlarda kullanılabilir (Coşkun ve ark., 2022; Corum ve ark., 2018). TNF-α gibi birçok inflamatuar sitokini baskılamasından kaynaklı köpeklerde yaygın bir şekilde temas dermatitin tedavisinde kullanılabileceği düşünülmektedir (Logas, 2021). Ayrıca geriatrik köpeklerde bilişsel bozukluklarının tedavisinde kullanılabilir (Sykes, 2022). Atlarda uterus torsiyonu ve korioal lantoisin uterustan ayrılması durumlarında tedavi protokollerine PTX' in eklenmesi tedaviyi olumlu yönde etkileyebileceği bildirilmiştir (Dascanio ve McCue, 2021). Kedilerde ise feline infeksiyöz peritonitis (FİP) ile ilişkili vasküliti azaltmak için prednizolon ile birlikte kullanılmasının faydalı olduğu ifade edilmiştir (Plumb, 2018). Yapılan çalışmalarda PTX'in tedaviye eklenmesi ile FİP'li kedilerde önemli oranda ölüm azalttığı ortaya konulmuştur (Sykes, 2022). PTX kedi ve köpeklerde vaskülit ve vaskülopatilerin tedavisinde kullanılabilir. Buna ek olarak kedi ve köpeklerde deri hastalıkların tedavisinde kullanıldığını ve oldukça etki olduğu ifade edilmiştir. Özellikle atopik dermatit ve kontakt dermatit tedavisinde iyileşmeyi kolaylaştırdığı (Allerton, 2020), kaşıntının tedavisinde

glukokortikoidler ile birlikte tedaviye başlanıldığında birkaç hafta boyunca etkili olabileceği (Logas, 2021) ifade edilmiştir. Köpeklerde PTX uygulaması ile akciğer dokusunda pro-infalamatuvar sitokinlerden TNF-α ve IL-8 düzeyini azalttığından akciğerler üzerine koruyucu etkiye sahiptir (Duan ve ark., 2007). Yüksek kolesterollü diyetle beslenen tavşanlara PTX uygulaması sonucunda ortaya çıkan antiinflamatuar etkiden kaynaklı damar duvarında daralma yapıcı etkiyi engellediği ve aort plak alanını genişlettiği ifade edilmiştir (Prasad, 2007). Bütün bu etkilerine ek olarak tavuklarda eklemlerde amiloid A birikimini azaltırdığı (Swayne, 2013) ve farelerde endometritin tedavisinde faydalı olduğu (Mohammadzadeh ve ark., 2007) bildirilmiştir.

Köpeklerde deri hastalıklarında (dermatomiyozit, kulak kenarı sebore/nekrozu, kontakt dermatit ve atopi vb.) başlangıçta 10 mg/kg ile başlanır ve eğer cevap alınmazsa doz 15 mg/kg çıkarılır. Dermatomiyozit, kulak kenarı sebore/nekrozu, kontakt dermatit ve atopi gibi deri hastalıkların tedavisinde günde 3 defa kullanımı önerilir (Plump, 2018; Allerton, 2020). Köpeklerde kutanöz vaskülitin tedavisinde 15-20 mg/kg dozunda günde 3-4 defa kullanımı önerilir (Logas, 2021). Köpeklerde deri ile ilgili hastalıkların tedavisinde PTX'in 1-2 ay boyunca kullanılması gerekebileceği ifade edilmiştir (Tizard, 2021).

Kedilerde köpeklerde görülene benzer deri hastalıklarında kullanılabilir. Ancak kedilerde deri hastalıklarında günde 2 defa 100 mg dozunda kullanılması önerilir (Logas, 2021). FİP' li kedilerde vasküliti azaltmak amacıyla tek başına kullanılacaksa 2-4 mg/kg/gün dozunda PO yolla günde 2 defa kullanılması önerilirken, prednizolon ile kullanılacaksa iki haftada bir kullanımı önerilir (Plump, 2018). Atlarda endotoksemi tedavisinde 8 mg/kg dozunda PO yolla günde 3 kez, dermatitin tedavisi için 4-8 mg/kg dozunda PO yolla günde 2 defa, naviküler hastalığın tedavisi için gün bir defa 6 gr/hayvan dozunda PO yolla 6 hafta boyunca kullanımı önerilmektedir (Plump, 2018). Atlarda plasenta yangısında 7.5-8.4 mg/kg dozunda günde 2-4 defa kullanımı önerilmektedir (Plump, 2018; Dascanio ve McCue, 2021).

2. Yan etkileri

PTX insanlarda başta gastrointestinal, merkezi sinir sistemi ve kardiovasküler yan etkilere neden olabilir. Kullananların çok az kısmında baş dönmesi ve baş ağrısına yapabilir. PTX' in hayvanlarda neden olduğu yan etkiler ile ilgili bilgi oldukça sınırlıdır. Veteriner hekimliğinde PTX kullanımına bağlı görülen yan etkiler genellikle gastrointestinal sistem (kusma/iştahsızlık) ve merkezi sinir sistemi (heyecan, sinirlilik) ile ilgilidir (Plump, 2018). Köpeklerde genellikle iyi tolere edilir; ancak yüksek dozlarda (10mg/kg>) kullanıldığında genellikle bulantı, kusma ve ishal görülürken (Logas, 2021), nadiren de olsa köpeklerde eritema multiforme (Plump, 2018) görülebileceği ifade edilmiştir. Kedilerde ise aşırı uyarılma, taşikardi ve deride kızarık yapabilir (Logas, 2021). Atlarda intravenöz (IV) uygulama sonrası , geçici lökositoz, kas fasikülasyonları, terleme ve kalp atım hızında hafif artışlara neden olabilir (Plump, 2018). Koyunlarda yapılan bir çalışmada 40 mg/kg dozunda canlıda taşikardi ve hipersalivasyon (Çorum ve ark., 2018), sığırlarda 10 mg/kg dozunda damar içi uygulama sonrasında geçici salya artışı ve huzursuzluk (Üney ve ark. 2019) ve tavuklarda 100 mg/kg dozda abdominal solunum ve göz kapaklarında düşme (De Boever ve ark. 2005) görüldüğü ifade edilmiştir. Pentoksifilin fibrinolize neden olması nedeniyle kanama riski olan canlılarda kullanılmamalıdır. Karaciğer ve/veya böbrek yetmezliği hayvanlarda kullanılmamalıdır (Scagnelli, 2017).

3. Farmakokinetiği

PTX suda ve etanolde çözünür, plazma proteinlerine %70 oranında bağlanır ve eliminasyon yarılanma ömrü 0.4-0.8 saat arasında değişir (Harris ve ark., 2010). PTX gastrointestinal sistemden iyi emilir, çoğunlukla karaciğer ve eritrositlerde metabolize olup, böbrekler yoluyla atılmaktadır. Yiyecek ve sigara içmek pentoksifilinin ve özellikle aktif metaboliti hidroksi-pentoksifilinin plazma konsantrasyonunu azaltır (Frampton ve Brogden, 1995; Aviado ve Porter, 1984). PTX, hepatik sitokrom P-450 (CYP450) enzimleri tarafından yüksek oranda metabolize edilir ve metabolitleri büyük ölçüde idrarla atılır (Varanasi ve ark., 2008). PTX insanlarda ve hayvanlarda yüksek oranda metabolize edilir (Üney ve ark.,2019). Pentoksifilin metabolize olduktan sonra M-I, M-II, M-III, M-VI, M-V, M-VI ve M-VII olmak üzere en az yedi tane metaboliti oluşur. Dolaşımda başlıca M-I, M-IV ve M-V metabolitleri bulunmaktadır. Pentoksifilinin hemoreolojik etkilerine M-I ve M-V'inde katkısı vardır. M-I'in kan akışını artırır ve trombosit toplanmasını engeller, M-V ise kan akışını artırma yeteneğine sahiptir. Pentoksifilin metabolize olduktan sonra onun ve metabolitlerinin kandaki konsantrasyonu M-V>M-I>pentoksifilin>M-IV şeklindedir. Pentoksifilin indirgeme yoluyla M-I'e, oksidasyon yoluyla da M-IV ve M-V'e dönüşür. Karaciğerde pentoksifilin M-I'e dönüşümü geri dönüşümlüdür (Wen ve ark., 2017). Metabolit IV'ün %45'i ve metabolit III'ün %5'i böbrekler yoluyla atılmaktadır (Harris ve ark., 2010). M-I (hidroksi-pentoksifilin), PTX'in eritrositlerde ve karaciğerde metabolize olması sonucu oluşur (Çorum ve ark., 2018) ve PTX ile aynı farmakolojik etkiye sahiptir (Frampton ve Brogden, 1995). PTX' in teröpatik etkisi kendisi ve aktif metaboliti olan M-I' in plazma konsantrasyonlarıyla ilişkilidir (Frampton ve Brogden, 1995). İnsanlarda ve atlarda PTX ve M-I'in terapötik etkilerinin doza bağımlı olduğu bildirilmektedir (Çorum ve ark., 2018). PTX' in % 90'dan daha fazlası böbreklerle atılmasına rağmen kendisinin ve aktif metaboliti (M-I) idrarda önemli miktarda bulunmaz. İdrarda çoğunlukla M-V ve az miktarda M-IV bulunur (Frampton ve Brogden, 1995). PTX büyük ölçüde karaciğerde metabolize edildiğinden ve böbrekler yoluyla elimine edildiğinden, böbrek veya karaciğer fonksiyon bozukluğu olan hastalarda bu ilacın kullanımı önerilmemektedir (Martin ve ark., 2003). Yüksek oranda perisistemik eliminasyona (ilk geçiş etkisi) uğrar. Gıdalarla alınması PTX' in emilim hızını yavaşlatır fakat emilim miktarını değiştirmez (Campbell, 1993). Pentoksifilinin maksimum klinik etkiye ulaşması üç aya kadar sürebilir (Logas, 2021). Bazı hayvan türlerinde PTX' in farmakokinetiği ile ilgili bilgiler oldukça sınırlıdır (Sykes, 2022). Pentoksifilinin farmakokinetiği köpek ve at türlerinde incelenmiştir (Scagnelli, 2017). Köpeklerde PTX 'in oral biyoyararlanımı düşük, yarılanma ömrü kısadır ve 8 saatte bir uygulanması tavsiye edilmektedir (Sykes, 2022). Atlarda pentoksifilinin oral biyoyararlanımı değişiklik göstermektedir (Scagnelli, 2017).

4. Sonuç ve Öneriler

Pentoksifilin gerek veteriner hekimliği gerekse beşerî hekimliğinde pek çok alanda kullanılan fosfodiesteraz enzim inhibitörü bir ilaçtır. İnsanlarda özellikle hemoreolojik ve antiinflamatuar etkilerinden yararlanılması için ilk olarak aralıklı klodikasyon, daha sonra vaskülit, endotoksemi, sepsis, diyabetik ülserler, nöbet bozuklukları, kanser ve kollajen bozukluklarının tedavisinde kullanılmıştır. Zamanla birlikte PTX'in antiviral, antineoplastik, immünomodülatör, bronkodilatör, antidiyabetik, antioksidan, antifibrotik, antiproliferatif, anti-proteinürik, anti-akut akciğer hasarı ve antitrombotik etkilere sahip olduğu ortaya konulmuştur. PTX'in veteriner hekimliğinde ruhsatlanmamıştır, fakat beşerî hekimliğinde kullanılan birçok endikasyon için veteriner hekimliğinde de kullanılabilir. Ancak bu denli

çok etkiye sahip olmasına rağmen veteriner hekimliğinde etkinliğinin net olarak ortaya konulduğu çalışma sayısı çok azdır. Bu yüzden PTX'in farklı hayvan türlerinde etkilerin ortaya koyulması için daha fazla çalışmaya ihtiyaç vardır.

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ANTIDEPRESSANT USE IN DOGS

KÖPEKLERDE ANTİDEPRESAN KULLANIMI

ÖZET

Depresyon insanlarda ve hayvanlarda hayatı birçok yönden etkileyen önemli bir merkezi sinir sistemi hastalığıdır. Depresyonun etiyolojisi tam olarak bilinmemekle birlikte, altında yatan birçok faktör olduğu düşünülmektedir. Hayvanlarda ve insanlarda depresyonun patofizyolojisi ve görülme oranı birbirine oldukça yakındır. Bu nedenle insanlarda kullanılan birçok antidepresan ilaç köpeklerde de kullanım alanı bulmaktadır. Özellikle köpeklerde depresyon tedavisinde trisiklik antidepresanlar, monoamin oksidaz inhibitörleri ve seçici serotonin geri alım inhibitörleri sıklıkla kullanılmakta, ve buna ek olarak yeni nesil ve alternatif antidepresanlarında kullanıldığı görülmektedir. Bu derleme de köpeklerde depresyonun tedavisinde kullanılan bu ilaçların etki mekanizmaları, endikasyonları, dozaj rejimleri ve yan etkileri hakkında bilgi verilmeye çalışılmıştır.

Anahtar kelimeler: Antidepresan, Depresyon, Köpek.

1. GİRİŞ

Depresyon ruh hali değişikliği, enerji eksikliği, üzüntü, uykusuzluk, sürekli uyuma isteği ve hayattan tat alamama ile karakterize kronik bir hastalıktır (Cui, 2015). Yaşam kalitesinde azalmaya neden olan depresyon, insanların yaklaşık %4'ünde görülen önemli bir merkezi sinir sistemi hastalığıdır (Harsanyi ve ark., 2022). Depresyonun en önemli belirtileri arasında sürekli yalnız kalma isteği, intihar eğiliminde artma ve ölüm düşüncesi, gündelik hayat ile bağdaşmayan hareketler ve sosyal izolasyon yer alır (Dudek ve ark., 2019).

Depresyon oldukça karmaşık bir fizyopatolojiye sahiptir. Depresyonun temelinde stres, hipotalamik-hipofiz-adrenal (HPA) eksen, enfeksiyon, immün sistem ve bağırsak mikrobiyotasındaki değişimler yer almaktadır (Cruz-Pereira ve ark., 2020). Zihinsel ve fiziksel sağlık ayrılmaz bir bütündür. Zihinsel durumun iyi olması bireyin potansiyelini fark etmesi, stresle daha iyi baş edebilmesi, daha üretken olabilmesi ve topluma daha iyi katkı sağlamasına olanak sağlar (Herrman ve ark., 2005). Depresyonun gelişimde, tetiklenmesinde ve ilerlemesinde stres önemli bir rol oynar (Cruz-Pereira ve ark., 2020).

Antidepresanların çoğu sinapslara gelen mesajları güçlendirerek veya engelleyerek etkisini gösterir. Mesajlar aksonlar boyunca elektriksel uyarılar halinde sinapslara ulaşır, fakat sinapslar arası aralıktan geçebilmesi için seratonin, adrenalin, dopamin ve asetilkolin gibi nörotransmitter maddelere ihtiyaç vardır. Bu nörotransmitter maddeler salgılandıktan sonra sinapslarda uzun süre kalamazlar ve ya parçalanır ya da nöronların içinde depolanırlar. Bu durum canlıda normal ruhsal dengenin korunmasını sağlar. Seratonin canlının mutlu ve sakin kalmasında, dopamin kişinin motive olmasında ve gerçeği görmesinde, nöroadrenalin ise stresin yönetiminde rol oynar. Bu nörotransmiter maddelerinin seviyelerinin değişmesi canlıda psikolojik bozukluklara neden olur. Psikolojik bozuklukların düzeltilmesi amacıyla genellikle bu nörotransmitter maddelerin vücuttaki konsantrasyonunu arttıran veya aralarındaki dengeyi sağlamaya yönelik uygulamalar yapılır. Böylece hücreler arası mesajlaşma için daha fazla nörotransmitter madde ortaya çıkar ve canlının duygu-durumu bozukluğu düzeltilmeye çalışılır (Mitchell ve ark., 2004; Dudley, 2012).

Duygusal, davranışsal, bilişsel ve algısal birçok anormallik vardır. Psikiyatri genellikle akıl hastalıkları, öğrenme güçlükleri ve kişisel bozuklukları inceler. Hayvan psikopatolojisi, hayvanlardaki zihinsel ve davranışsal bozuklukları inceleyen bilim dalıdır. Günümüzde evcil hayvanların psikolojisi; başta hayvan sahibinin mutluluğu ve refahı olmak üzere pek çok kişinin hayatını etkilediği için önemi gün geçtikçe artmaktadır. Evcil hayvanlarda yeme bozukluğu (aktivite anoreksisi, pika), anksiyete, obsesif kompulsif bozukluklar, ayrılık anksiyetesi ve travma sonrası stres bozukluğu gibi bozukluklar yaygın olarak görülür. Hayvanlardaki davranış bozuklukları insanlardaki psikiyatrik bozukluklara oldukça benzerlik gösterir. Evcil hayvanlar ile insanlar arasındaki zihinsel bozukluklar ve bu bozuklarının fizyopatolojik yansıması oldukça benzerdir. Ayrıca köpeklerdeki depresyon oranı insanlara oldukça yakındır, hatta çevre değişimi gibi faktörlerden insanlardan daha fazla etkilenirler (Haq, 2017). Bu nedenle beşerî hekimlikte kullanılan birçok ilaç veteriner hekimliğinde de köpeklerinin zihinsel ve davranışsal bozukluklarının tedavisinde kullanılabilir.

2. DEPRESYONDA KULLANILAN İLAÇLAR;

Depresyonun tedavisinde kullanılan antidepresanlar genellikle serotonerjik ve adrenerjik sistemler üzerine etkinlik gösterir (Cruz-Pereira ve ark., 2020). Köpek ve kedilerde davranışsal bozuklukların tedavisinde en yaygın kullanılan ilaçlar antidepresanlar ve

anksiyolitiklerdir. Köpeklerde depresyonda kullanılan ilaçlar; trisiklik antidepresanlar, monoamin oksidaz inhibitörleri (MAOI), seçici serotonin geri alım inhibitörleri (SSRI), yeni (atipik veya ikincil nesil antidepresanlar) antidepresanlar, diğerleri (lityumlu antidepresanlar) ve alternatif antidepresanlar (sarı kantron, S-adenozilmetiyonin ve omega-3 yağları) olmak üzere 6 gruba ayrılır. Her grubun, merkezi sinir sistemindeki nörotransmiterler (serotonin, norepinefrin, epinefrin ve dopamin) üzerindeki etkileri farklıdır ve bu farklılık antidepresanın özgünlüğünü, etkinliğini ve potansiyel yan etkilerini belirler (Wismer, 2000).

Veteriner sahada davranış bozukların tedavisinde ruhsatlı ilaç sayısı oldukça sınırlıdır, bu yüzden tedavide kullanılan ilaçların birçoğu etiket dışı olarak kullanılır (Overall, 2019; Simpson ve Papich 2003). Bu tür bir kullanım bazı ülkelerde yasal olmakla birlikte, hasta sahibine bu durumun açıklanması gereklidir (Overall, 2019). Etiket dışı ilaç kullanımında; ilacın hedef türdeki metabolizmasının, reseptör duyarlılığının ve toksisitesinin bilinmemesi gibi zorluklar vardır (Simpson ve Papich, 2003). Bazı ilaçlar için bazı türlerde bu veriler elde edilmiş olabilir, ancak doza ve türe bağlı bu verilerde değişimler görülebileceği unutulmamalıdır. Bu nedenle köpeklerde etiket dışı kullanılan ilaçların farmakokinetik, farmakodinamik ve güvenilirlik çalışmalarının yapılması gereklidir (Overall, 2019).

2.1. TRİSİKLİK ANTİDEPRESANLAR (TCA)

TCA'lar psikiyatrik hastalıklarda kullanılan en büyük ilaç ailelerinden biridir ve özellikle endojen depresyon, panik atak, fobik ve obsesif durumlar, nöropatik ağrı ve pediatrik idrar kaçırma tedavisinde kullanılırlar (Overall, 2019; Wismer, 2000). TCA'lar ucuzdur ve iyi tolere edilir; bu nedenle evcil hayvanlarda davranış bozukluklarının tedavisinde kullanım alanı bulur. Genel olarak uyarıların ve kaygının azaltılmasında kullanılırlar (Simpson ve Papich, 2003). Kesin etki mekanizmaları bilinmemekle birlikte; nöronal membranda nöroadrenalin ve serotoninin geri alımını engelleyerek etki gösterdikleri düşünülmektedir (Wismer, 2000; Overall, 2019; Simpson ve Papich, 2003). Ayrıca güçlü antikolinerjik etkinliklere sahiptirler (Wismer, 2000). Muskarinik, alfa-1 adrenerjik ve histamin-1 ve -2 reseptörlerini de bloke ettikleri için ağız kuruluğu, sedasyon ve hipotansiyon gibi istenmeyen etkilere neden olurlar. Antidepresan etkileri dışında veteriner hekimliğinde kaşıntının giderilmesi, tükürük salgısının azaltılması ve idrar kaçırmanın engellenmesinde de kullanılırlar. TCA'lar lipofilik yapılarından dolayı sindirim sisteminden hızlı bir şekilde emilirler (30 ila 60 dakika içinde) ve geniş bir dağılım hacmine sahiptirler. Enterohepatik siklusa girdiklerinden biyolojik yarı ömürleri uzundur (Wismer, 2000). Bu grubun üyeleri arasında amitriptilin, amoksapin, klomipramin, desipramin, doksepin, imipramin, imipramin, maprotilin, nortriptilin, protriptilin ve trimipramin yer alır. Bu ilaç grubu veteriner hekimlikte sıklıkla kullanılmasına karşın hiçbiri FDA tarafından onaylanmamıştır (Overall, 2019; Wismer, 2000).

Evcil hayvanlarda davranış bozukluklarına bağlı kaşıntının giderilmesinde doksepininin kullanımı önerilir ve etkisi H_1 reseptör antagonisti olan difendramin'den 800 kat daha güçlüdür (Overall, 2019). Klomipramininde 6 aylıktan büyük köpeklerde davranış bozukluğu için kullanılabileceği belirtilmiştir (Overall, 2019).

TCA kullanımı genç ve sağlıklı bireylerde önemli yan etkilere neden olmazken, yaşlı ve hasta bireylerde yan etkiler sorun oluşturabilir (Simpson and Papich, 2003). Kullanımı sonucu ortaya çıkan yan etkilerin çoğuna antikolinerjik etkileri (ağız kuruluğu, kabızlık, idrar retansiyonu, taşikardi ve diğer aritmiler) aracılık eder. Buna ek olarak alfa-1 reseptörleri bloke etmesinden kaynaklı ortostatik hipotansiyon, senkop, oryantasyon

bozukluğu, uyuşukluk ve iştahsızlık gibi yan etkilere de görülebilir. Köpeklerde TCA kullanımı sonucu ortaya çıkan yan etkilerin görülme sıklığı oldukça azdır. Köpeklerde sedasyon, kabızlık, iştahta azalma ve taşikardi gibi geçici yan etkiler görülebilir (Overall, 2019). Kardiyovasküler bozukluğu olan hayvanlarda, TCA kullanılmadan önce kalp fonksiyonları tekrardan değerlendirilmelidir (Simpson and Papich, 2003). Yapılan bir çalışmada sağlıklı köpeklere klomipramin ve amitriptilin kullanılması sonrasında EKG'de herhangi bir anormallik görülmediği ifade edilmiştir (Reich ve ark., 2000). Ancak yaş ve hastalık/lar ile birlikte kardiyovasküler sistem üzerinde etkiler görülebileceği akılda tutulmalıdır (Simpson and Papich, 2003).

Evcil hayvanlarda bilinçli veya kazara yüksek dozda TCA kullanımı sonucu ciddi yan etkiler ortaya çıkabilir (Simpson and Papich, 2003). Bu gruptaki ilaçların toksik dozları birbirinden farklılık gösterir; çoğunun öldürücü dozu 15 mg/kg iken, klomipraminin ve amitriptilin hidroklorür için öldürücü doz sırasıyla 100 mg/kg ve 50 mg/kg'dır. Köpeklerde doz aşımı sonucu zehirlilik belirtileri yaklaşık 30 dakika içerisinde ortaya çıkar ve müdahale edilmezse 2 saat içinde ölüm görülebilir. Zehirlenme veya doz aşımı sonucunda ortaya çıkan ilk klinik belirti uyuşukluk ve ataksidir, bu belirtiler ortaya çıktıktan kısa bir süre sonra taşikardi, kusma, midriyazis, vazodilatasyon, hipotansiyon, aritmi, nefes darlığı, akciğer ödemi, nöbet ve koma görülebilir ve sonrasında ölüm şekillenir. Ayrıca TCA'ların doz aşımına bağlı olarak idiyosenkratik hiperaktivite de görülebilir (Wismer, 2000).

2.2. MONOAMİN OKSİDAZ İNHİBİTÖRLERİ (MAOI)

MAOI, hücre içi monoamin oksidaz (MAO) enziminin etkinliğini inhibe ederek etki gösterirler (Simpson ve Papich, 2003). MAO enzimi başta sinir dokusu olmak üzere, karaciğer, böbrek, bağırsak, trombosit ve plasentada bulunur (Wismer, 2000). Bu enzim monoamin nörotransmiterlerinin (seratonin, adrenalin, nöroadrenalin, dopamin ve tiramin gibi) yıkımlanmasında görevlidir (Wismer, 2000; Simpson ve Papich, 2003). MAO enziminin vücutta A ve B olmak üzere iki formu vardır. MAO-A çoğu nöronlarda bulunur ve seratonin, adrenalin ve nöroadrenalin gibi nörotransmitterlerin parçalamasından sorumludur. MAO-B ise astrositlerde bulunur ve dopaminin parçalamasından sorumludur (Mocchegiani, 2008). Bu grupta yer alan ilaçlar MAO enzimini inhibe ederek monoaminlerin merkezi sinir sistemindeki konsantrasyonunda artışına neden olarak etkinlik gösterirler (Wismer, 2000; Simpson ve Papich, 2003). Bu grubun üyeleri arasında fenelzin, tranilsipromin ve selegilin yer alır (Wismer, 2000).

Köpeklerde sinirsel bozukluklar sonucunda ortaya çıkan davranışsal ve bilişsel bozuklukların tedavisinde kullanımı onaylanmış ilk ilaç selegilindir (L-deprenyl, Anipryl). Selegilin MAO-B'yi seçici ve geri dönüşümsüz bir şekilde inhibe eder. Ayrıca dopaminerjik, adrenerjik ve kolinerjik nöronlar üzerinde koruyucu etkilere sahiptir (Landsberg, 2006; Simpson ve Papich, 2003). Yaşlı köpeklerde sosyal etkileşimin azalması, kafa karışıklığı ve uyku döngüsünde değişikliklerle karakterize bilişsel bozukluklarının tedavisinde kullanımı onaylanmıştır (Simpson ve Papich, 2003). Bu amaç için selegilin her sabah 0.5-1 mg/kg dozda 30 gün boyunca kullanılması önerilir ve bu süre zarfında iyileşme görülmezse, tedaviye 1 ay daha devam edilmesi önerilir (Landsberg, 2005).

Köpeklerde yan etkileri nadirdir, ancak yüksek dozlarda hiperaktiviteye ve stereotipik davranışlara neden olabilirler (Simpson ve Papich, 2003). MAO inhibitörlerinin doz aşımında tansiyonda düzensizlik, depresyon, ataksi, huzursuzluk, taşikardi, aritmi, koma, nöbet, solunum depresyonu, ateş ve şok görülebilir. Bu belirtiler genellikle bir veya iki saat içinde görülür, ancak bazı vakalarda 12 ila 24 saat sonra da görülebileceği ifade edilmiştir.

Doz aşımı durumunda MAO inhibitörlerinin spesifik bir antidotu yoktur, bu yüzden genel zehirlenme tedavisi yapılmalıdır (Wismer, 2000).

2.3. SEÇİCİ SERATONİN GERİ ALIM İNHİBİTÖRLERİ (SSRI)

SSRI, sinir hücresine serotoninin geri alımını bloke edip sinir hücreleri arasında serotonin seviyesini artırırlar (Lee, 2011) SSRI'lar özellikle serotonin 1A (5-HT1A) reseptörlerine bağlanıp, seratoninin geri alımını seçici bir şekilde bloke ederler. Beşerî hekimlikte depresyon, obsesif kompulsif bozukluklar, panik atak, anksiyete ve psikojenik ağrı gibi çeşitli psikolojik hastalıklar ile alkolizm, obezite ve migren tedavisinde kullanılırlar (Overall, 2019; Fitzgerald ve Bronstein, 2013). Veteriner hekimliğinde (köpeklerde) ayrılma kaygısı, kompulsif davranışlar ve baskınlık tipi saldırganlığın yönetimi için kullanılırlar (Simpson ve Papich, 2003). Fluoksetinin köpeklerde ayrılık kaygısının tedavisinde kullanımı onaylanmıştır (Overall, 2019). Veteriner hekimlikte SSRI'lar terapötik dozlarda kullanıldığında bile sedasyon, merkezi sinir sistemi uyarımı, iştahsızlık ve uyuşukluk gibi yan etkileri görülmektedir (Lee, 2011). Bu grup üyeleri arasında fluoksetin, fluvoksamin, nefazodon, paroksetin ve sertralin yer alır (Wismer, 2000).

Köpeklerde fluoksetin saldırganlık, ayrılma kaygısı, panik ve obsesif kompulsif bozuklukların tedavisinde kullanılırken, paroksetin depresyon, anksiyete ve depresyonla ilişkili huzursuzluk tedavisinde kullanılır. Sertalin ise panik atak ve anksiyete gibi bozukluklarının tedavisinde kullanılabileceği ifade edilmiştir (Overall, 2019).

TCA veya MAO'lara göre SSRI'larının antikolinerjik, sedatif ve kardiyovasküler yan etkileri oldukça azdır (Wismer, 2000). SSRI'larda doz aşımı durumlarında merkezi sinir sisteminde artan seratonin kaynaklı; letarji veya huzursuzluk, kusma, ataksi, titreme, nöbetler, hipertansiyon ve taşikardi görülebilir (Simpson, 2003). Köpeklerde saldırganlık, fobi, depresyon, korku ve kaygının tedavisinde sertalinin 1–2 mg/kg dozunda günde 2 kez kullanımı önerilirken; fluoksetinin günde 1 kez kullanımı önerilir (Denenberg, 2020). Ayrıca köpeklerde sertalinin LD_{50} değeri 80 mg/kg iken, fluoksetinin 100 mg/kg'dan fazladır (Simpson, 2003).

2.4. YENİ (ATİPİK) ANTİDEPRESANLAR (İkinci Nesil Antidepresanlar)

2.4.1. Bupropion

Sinir ucundan dopamin taşıyıcı pompayı inhibe ederek, dopaminin emilmesini engeller ve seviyesini artırır (Stahl, 2013). Başlıca yan etkileri; huzursuzluk, uyuşukluk, gastrointestinal bozukluklar ve hipertansiyondur (Denenberg, 2020). Beşerî hekimlikte depresyonun tedavisinde ve sigarayı bırakmak için kullanılır. Doz aşımı sonucunda 1-4 saat içinde titreme ve nöbetler görülebilir (Wismer, 2000). Köpeklerde anksiyete, depresyon ve kaygının tedavisinde 0.5–1.5 mg/kg dozunda günde 1 kez kullanımı önerilir (Denenberg, 2020).

2.4.2. Venlafaksin

Bu madde sinirlerde seratonin, nöroadrenalin ve düşük oranda dopaminin geri alımını engelleyerek etki gösteren bir seratonin-nöroadrenalin geri alım inhibitörüdür. Beşerî hekimliğinde depresyon ve anksiyete gibi duygu durum bozukluklarının tedavisinde ve kronik ağrıda kullanılır (Denenberg, 2020; Mitchell, 2004). Ayrıca narkolepsi ve katapleksinin tedavisinde de kullanılabileceği bildirilmiştir (Delucchi and ark., 2010). Köpeklerde kaygı, korku, fobi ve depresyonun tedavisinde 1–2 mg/kg dozunda günde 2-3 kez kullanımı önerilir (Denenberg, 2020).

2.4.3. Mirtazapin

Serotonerjik nöronlar aynı zamanda presinaptik alfa-2 hetero reseptörlere de sahiptir. Nöroadrenalin bu reseptörlere bağlandığında seratonin salınımını engeller (Stahl, 2013). Mirtazapin bu reseptörlere bağlanıp seratonin salınımını arttırarak etki gösterir. Aynı zamanda 5-HT1 reseptörlerini uyarırken, 5-HT2 VE 5HT3 reseptörlerini güçlü bir şekilde inhibe eder (Denenberg, 2020). Antikolinerjik yan etkilere oldukça azdır. Yarılanma ömrü 20-40 saattir, günde bir kez kullanımı önerilir. Başlangıç dozu 15 mg/gün'dür ve 45 mg/gün'e kadar doz artırılabilir. En sık görülen yan etkileri; uyku hali, baş dönmesi, sedasyon, iştah artışı ve kilo alımıdır (Buschmann and ark., 2007). Köpeklerde iştah acıcı olarak, anksiyete ve depresyonun tedavisinde 0.2–0.5 mg/kg dozunda günde 1 kez kullanımı önerilmektedir (Denenberg, 2020).

2.4.4. Trazodon

Veteriner hekimliğinde zihinsel ve davranışsal bozukluklarının tedavisinde en sık kullanılan serotonin geri alım inhibitörüdür. Düşük dozlarda (0,05-1 mg/kg) 5HT2A ve 5HT2C reseptörlerini bloke ederken, yüksek dozlarda (6-8 mg/kg) serotonin geri alınımını inhibe eder (Stalh,2013; Wismer,2000). Köpeklerde farklı anksiyete bozukluklarının tedavisinde kullanılır. Köpeklerde kaygı ve korku durumlarında 5–10 mg/kg dozunda günde 1-2 defa kullanımı önerilir (Denenberg, 2020). Köpeklerde oral LD_{50} dozu 500 mg/kg'dır (Wismer, 2000).

2.4.5. Nefazadon

Seratoninin geri alımını inhibe ederek etki gösterir, aynı zamanda seratonin-2 reseptör antagonistidir. C_{maks}'a ulaşma süresi 20-40 dakikadır. Köpeklerde yarılanma ömrü 6.8-14.2 saattir (Wismer, 2000).

2.5. DİĞERLERİ

2.5. Lityumlu bileşikler

Lityum fosfatidilinositol fosfatazları, adenil siklazları, glikojen sentazkinaz 3 ve G proteinlerini inhibe ederek etkisini gösterir. Ancak bu etkilerinden hangisinin antidepresan etkinlikten sorumlu olduğu bilinmemektedir (Buschmann and ark., 2007). Canlılarda konvülsiyon, bipolar hastalıklar ve duygu durum bozuklukları ve depresyonda kullanılır. Bulantı, huzursuzluk, el titremeleri, kilo alımı, sık susama ve idrara çıkma en belirgin yan etkileridir (Mitchell ve Triggle, 2009).

2.6. ANTİDEPRESAN ALTERNATİFLER

Yüzyıllardır bitkisel ürünler psikolojik hastalıkların tedavisinde kullanılır. Depresyon tedavisine cevap vermeyen bireyler veya antidepresan ilaçlara karşı duyarlılığı olan bireylerde bitkisel-doğal maddeler iyi bir alternatif olabilir (Mischoulon, 2004).

2.6.1. Sarı kantron (St. John's Wort (Hyperıcum)) (SJW)

Sarı kantron, sıcak iklimlerde yetişen küçük ve otsu bir çalıdır. Bitkinin tüm kısımları (tomurcuğu, sapı ve yaprakları) depresyon tedavisinde kullanılır (Mitchell ve Triggle, 2009). Psikolojik etkilerinden yapısında bulunan hiperisin, psödohiperisin ve hiperforinin sorumlu olduğu düşünülmektedir. Düşükte olsa serotonerjik etkileri vardır ve MAO enzimini inhibe eder. Aynı zamanda sitokin üretiminde azalmaya neden olduğu için antiinflamatuar etkiye

de sahiptir (Macalusa ve Preskorn, 2019). Sarı kantronun 300-1.800 mg/gün dozlarında günde 2-3 kez kullanımı önerilir. Bu doz kullanılan preparatlara göre farklılık gösterebilir (Mischoulon, 2009). Sarı kantron genellikle güvenlidir ve iyi tolere edilmektedir, en sık görüler yan etkileri ağız kuruluğu, baş dönmesi ve kabızlıktır (Rodriguez-Landa ve Contreras, 2003).

2.6.2. S-adenozilmetiyonin (SAMe)

SAMe, folik asit ve B12 vitaminini de içeren tek karbonlu metabolik döngünün bir ara ürünüdür (Macalusa ve Preskorn). Metilen tetrahidrofolat redüktaz enzimiyle etkin hale gelir. Genetik polimorfizmler bu enziminin yapısını bozabilir, buda tek karbon döngüsünün bozulmasına bağlı nörotransmiterlerin sentezinin azalmasına ve dolayısıyla depresyona katkıda bulunabilir (Mischoulon and ark., 2012). Bu nedenle depresyonun tedavisinde seratonin, dopamin ve adrenalin sentezinin uyarılması amacıyla kullanılmaktadır (Macalusa ve Preskorn). Aynı zamanda bu maddelerin (B12 ve folik asit) eksikliği depresyonla ilişkilendirilmektedir. Depresyonlu hastalara folik asit ve vitamin B12 uygulaması iyileşme sağladığı için depresyonun tedavisinde kullanım alanı bulmaktadır (Mischoulon, 2007).

2.6.3. Omega-3 Yağları

Omega-3'ler başlıca deniz ürünlerinde bulunan doymamış bir yağ asididir. Zihinsel ve davranışsal bozuklukların tedavisinde başlıca eikosapentaenoik asit (EPA) ve dokosaheksaenoik asit (DHA) kullanılmaktadır (Appleton ve ark., 2016). Etki mekanizması tam olarak bilinmemekle birlikte; depresyonun oluşmasında etkili olan enzim ve nörotransmiterler ile kalsiyum kanalları üzerine etkili olduğu bilinmektedir (Mischoulon, 2007). Depresyonun tedavisi için beşerî hekimlikte 1-2 g/gün dozda kullanımı önerilir (Sublette and ark., 2011).

3. SONUÇ VE ÖNERİLER

Depresyon insanlarda ve hayvanlarda önemli merkezi sinir sistemi problemleri arasında yer alır ve canlının hayatında hem fiziksel hem de psikolojik açıdan önemli sorunlara neden olur. İnsanlarda en belirgin depresyon semptomları arasında depresif ruh hali, sürekli intihar etme ve ölüm düşünceleri, dengesizlik ve sosyal izolasyon yer almaktadır. Depresyonun etiyolojisi tam olarak bilinmemekle beraber, bazı nörotransmiter maddelerin vücutta ki dengesinin bozulmasına bağlı olarak ortaya çıktığı düşünülmektedir. Özellikle insan ve köpeklerde depresyon benzer patofizyolojiye sahiptir, bu nedenle insanlarda kullanılan ilaçlar köpeklerde de kullanılabilir. Başta; trisiklik antidepresanlar, monoamin oksidaz inhibitörleri, seratonin geri alım inhibitörleri ve yeni (atipik) ilaçlar olmak üzere pek çok ilaç depresyon tedavisinde kullanım alanı bulur. Bu ilaçların merkezi sinir sisteminde depresyondan sorumlu olan nörotransmiterler üzerine etkinlikleri, özgünlükleri ve yan etki profilleri farklılık gösterir.

İnsanlarda depresyonun tedavisinde kullanımı onaylanmış birçok madde varken hayvanlarda kullanılacak onaylı ilaç sayısı oldukça sınırlıdır. Bu kullanılan maddelerden sadece selergilin, köpeklerde depresyonun tedavisi için onaylanmıştır. Depresyonun köpeklerde önemli bir davranışsal ve zihinsel sorun olduğu düşünüldüğünde köpeklerde antidepresanların etkinliklerini ve güvenilirliklerini ortaya koyan çalışmaların yaygınlaştırılmasına ihtiyaç vardır.

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RATIONAL USE OF ANTIBIOTICS IN CHILDREN

ABSTRACT

In this study, the importance of the rational use of antibiotics, particularly those commonly used in the pediatric age group, is addressed. It is emphasized that the inappropriate and unnecessary use of antibiotics leads to numerous serious health problems and economic burdens, especially antimicrobial resistance (AMR). According to data from the World Health Organization, nearly half of all medications are used incorrectly, which accelerates the development of resistance to antibiotics. Although infections frequently encountered during childhood are often viral in origin, unnecessary antibiotic use remains widespread due to parents' lack of knowledge, pressure on physicians to prescribe, and the easy accessibility of antibiotics. Rational antibiotic use becomes possible through treatment plans based on accurate diagnosis, appropriate dosage and duration, cost-effectiveness, and individualization. Findings in the literature show that educational programs for parents, in-service training for healthcare personnel, and age-appropriate educational materials for children (such as illustrated storybooks) are effective in promoting rational antibiotic use. In this context, increasing awareness about antibiotic use in childhood illnesses is a vital necessity not only for individual health but also for public health. It is concluded that national strategies supporting rational antibiotic use, the widespread adoption of rapid diagnostic tests, and the implementation of institutional policies can contribute to taking effective steps in the fight against antibiotic resistance.

Keywords: Rational use of drugs, antibiotics, pediatrics.

ÇOCUKLARDA AKILCI ANTİBİYOTİK KULLANIMI

ÖZET

Bu çalışmada, özellikle pediatrik yaş grubunda yaygın olarak kullanılan antibiyotiklerin akılcı kullanımının önemi ele alınmıştır. Antibiyotiklerin uygunsuz ve gereksiz kullanımının, antimikrobiyal direnç (AMD) başta olmak üzere birçok ciddi sağlık sorununa ve ekonomik yüke neden olduğu vurgulanmaktadır. Dünya Sağlık Örgütü'nün verilerine göre, ilaçların yarıya yakını hatalı şekilde kullanılmakta, bu da antibiyotiklere karşı direnç gelişimini hızlandırmaktadır. Çocukluk çağında sık karşılaşılan enfeksiyonlar genellikle viral kaynaklı olmasına rağmen, ebeveynlerin bilgi eksikliği, hekim üzerindeki reçete baskısı ve kolay erişilebilir antibiyotikler nedeniyle gereksiz antibiyotik kullanımının yaygın olduğu görülmektedir. Akılcı antibiyotik kullanımı; doğru tanıya dayalı, uygun doz ve sürede, maliyet-etkin ve bireye özgü tedavi planlarıyla mümkün hale gelmektedir. Literatürdeki bulgular, ebeveynlere yönelik eğitim programlarının, hizmet içi sağlık personeli bilgilendirmelerinin ve çocuklara yönelik yaşa uygun eğitim materyallerinin (örneğin resimli hikaye kitapları) akılcı antibiyotik kullanımının benimsenmesinde etkili olduğunu göstermektedir. Bu bağlamda, çocuk hastalıklarında antibiyotik kullanımına ilişkin farkındalığın artırılması, sadece bireysel sağlık değil, aynı zamanda toplum sağlığı açısından da hayati bir gerekliliktir. Akılcı antibiyotik kullanımını destekleyen ulusal stratejiler, hızlı tanı testleri ve kurum içi politikaların yaygınlaştırılması ile antibiyotik direnci ile mücadelede etkin adımlar atılabileceği sonucuna varılmıştır.

Anahtar Kelimeler: Akılcı ilaç kullanımı, antibiyotikler, çocuklar.

Introduction

In ancient times, humans used plants in various ways to treat diseases; today, they have learned to manufacture drugs from plants, enhance their efficacy by adding new chemicals, and thus achieved the development of modern scientific medicines (Kırılmaz & Doğanyiğit, 2021). The World Health Organization (WHO) defines a drug as "any substance or product intended or expected to modify or explore physiological systems or pathological states for the benefit of the recipient" (Özkan et al., 2024). Medications are of great importance for human health and well-being and play a critical role in the prevention and treatment of diseases (Seğmenoğlu, 2022). According to WHO data, approximately 50% of medications worldwide are prescribed, sold, or used incorrectly. Moreover, more than half of all patients experience difficulties in using medications properly (Sel et al., 2025). In this regard, the WHO emphasizes the need for healthcare professionals and medicine users to utilize medications consciously and correctly to reduce morbidity and mortality rates and control pharmaceutical expenditures (Kalmaz & Temel, 2024).

Rational and Irrational Use of Medicines

Rational Use of Medicines (RUM) is defined as "the use of medications that meet the clinical needs of patients, in doses that suit their individual requirements, for an adequate period of time, and at the lowest cost to them and their community" (Sağır & Parlakpınar, 2014). The RUM process begins with identifying the patient's problems, determining treatment goals, and choosing a proven effective and reliable treatment option from among various alternatives. At this stage, an appropriate prescription is written, and the patient is informed and guided throughout the treatment process. The outcomes of the treatment are then regularly monitored and evaluated (İlhanlı Yaramış & Ulupınar, 2021). The stages of RUM include accurate diagnosis, prognosis assessment, setting treatment objectives, evaluating treatment options, selecting the appropriate treatment, and, if necessary, writing and following up on a correct prescription (Aydın & Gelal, 2012). Irrational use of medicines, a major issue in both developed and developing countries, includes practices such as using expensive or irrelevant medications unnecessarily, misuse of antibiotics, overdosing, or irrational self-medication by individuals (Tosun & Hoşgör, 2021). Unconscious and non-prescribed drug use poses serious health risks and may even lead to death. These improper practices are defined as "Irrational Use of Medicines" (IUM) (Bozdemir & Filiz, 2021). The main causes of irrational drug use include: easy access to prescription drugs in the market, the widespread availability of over-the-counter drugs, patient pressure on physicians to prescribe medication, inadequate knowledge among trainee physicians or medical students, lack of awareness, increased workload of healthcare professionals, improper drug promotions and advertisements (influence of profitable marketing programs by pharmaceutical companies), and drug-use advice from non-healthcare individuals such as friends and relatives (Alptekin et al., 2021). Irrational use of medicines can result in several negative consequences, including adverse drug interactions, delays in treatment, increased adverse events, development of drug resistance, decreased patient compliance, and increased treatment costs. Additionally, issues like drug dependency may arise (Uçman & Uysal, 2021). In a study conducted by Dağtekin et al. (2018) on adults attending a primary healthcare facility in Turkey, the rate of irrational drug use was found to be 53.4%. According to data from the Pharmaceutical Industry Employers' Union, 2.06 billion boxes of medications were consumed in Turkey in 2015, and this figure increased by 24% to 2.55 billion boxes in 2022. The same report notes that the monetary value of drugs rose from 17.6 billion TL in 2015 to 109.8 billion TL in 2022, marking a 525.6% increase (Kıraç & Yağcı

Özen, 2025). Thus, the primary goal of rational drug use should be the prevention of physiological, biological, and psychological harm caused by improper medication use and the minimization of its social and economic impacts (Kan & Sevim, 2023).

Rational Use of Antibiotics

Antibiotics play a critical role in the treatment of bacterial infectious diseases and are of great importance for human health. Therefore, they are widely used in societies (Doğan et al., 2021). They are among the most commonly used medications worldwide (Seğmenoğlu, 2022). Rational use of antibiotics can be defined as the cost-effective use of antibiotics with appropriate indications, correct dosage and duration, based on clinical findings and individual characteristics, to achieve the most effective outcomes in the treatment or prevention of infectious diseases (Doğan et al., 2021). The rational use of antibiotics begins with an accurate diagnosis and the formulation of a suitable treatment plan. It involves correctly selecting the appropriate antibiotic, writing a proper prescription, initiating the treatment process, informing the patient, providing necessary warnings, monitoring the treatment progress, and scheduling follow-up appointments (Çakıröz Dede & Tuğrul, 2021). The use of antibiotics affects the normal bacterial flora in humans and frequently leads to the emergence of antibiotic-resistant bacteria (Akçam, 2021). Antibiotic resistance is defined as the failure of certain microbial strains to respond to antibiotics, or the acquisition of resistance by previously susceptible strains through various mechanisms (Araz et al., 2022). Irrational use of antibiotics leads to widespread resistance among microorganisms to commonly used antibiotics; this, in turn, results in treatment failures, prolonged hospital stays, increased treatment costs, loss of workforce, and higher mortality rates (Alay et al., 2021). Infections caused by antibiotic-resistant microbes become very difficult, and sometimes impossible, to treat. If antibiotics—one of the cornerstones of modern medicine—lose their effectiveness, we risk losing the ability to treat infections and protect public health (Doğan et al., 2021). Moreover, essential medical procedures such as surgeries and immunosuppressive therapies could become increasingly hazardous. Antimicrobial resistance (AMR) currently causes approximately 700,000 deaths annually, and if urgent measures are not taken, it is projected to cause 10 million deaths per year and an economic loss of 100 trillion USD by 2050 (Findik, 2022). The overuse and misuse of antibiotics contribute to bacterial resistance, increased side effects, emergence of resistant infections, and significant financial burdens on healthcare systems. This has become a major global public health issue with the potential to affect future generations (Tokur et al., 2023). The World Health Organization (WHO) has reported that antibiotic resistance has reached alarming levels globally. In other words, antibiotic resistance has become a serious health concern faced by all countries (Atik, 2022). In Turkey, at least three out of every ten prescriptions contain antibiotics, and due to this high rate of use, Turkey ranks second after Greece and first among OECD countries in terms of resistance development (Gürkan, 2023). In a study conducted by Beder et al. (2024), the resistance rates of antibiotics were examined over time, and significant statistical differences were found in the resistance rates of antibiotics such as piperacillin/tazobactam, ceftazidime, cefepime, imipenem, meropenem, and levofloxacin.

Rational Use of Antibiotics in Children

The pediatric age group represents one of the periods in which antibiotics are most frequently used. Although upper respiratory tract infections (URTIs), which are common among children, are generally caused by viral agents, research shows that antibiotics are still widely

used in their treatment (Güngör, 2019). Children with weakened immune functions become more susceptible to infectious diseases, making them one of the groups that frequently use antibiotics, which raises concerns regarding medication safety (Hu et al., 2021). While appropriate antibiotic treatment is vital, it is equally important to limit inappropriate use that contributes to antimicrobial resistance (Nguyen, 2023). Parents' lack of sufficient knowledge regarding the rational use of antibiotics in the treatment of childhood illnesses can lead to misuse and the development of resistance (Gürkan, 2023). One of the causes of antibiotic overuse is parents demanding antibiotics based on past experiences or personal beliefs. Additionally, initiating antibiotic treatment without medical consultation constitutes a significant public health issue (Güngör, 2019). On the other hand, many physicians report feeling compelled to prescribe antibiotics due to parental pressure (Gürkan, 2023).

A study conducted by Alajami et al. (2022) in Saudi Arabia aimed to assess the rate of antibiotic use reported by parents of children and identify parental factors affecting antibiotic use. A 27-question survey was administered to 284 parents. The results showed that 81% of participants had given their children at least one course of antibiotics, and 71% had done so without consulting a physician. The researchers emphasized the concerningly high rates of antibiotic use among children and suggested that additional interventions may be necessary to limit such use.

The study conducted by Çalışır et al. (2020) aimed to assess the attitudes of mothers of hospitalized children regarding the rational use of medicines. The findings revealed several behaviors, including giving non-prescription medications without consulting a doctor, failing to administer antibiotics for the recommended duration, administering suspension drugs without proper measuring tools, mixing medications with food, and storing leftover medications. Based on these findings, it was recommended that mothers be provided with regular education and counseling services to enhance awareness and encourage appropriate behaviors concerning rational medicine use. It was also emphasized that nurses should address rational drug use during discharge education.

In another study, Bruns et al. (2022) noted that critically ill children represent a patient group that requires more informed decision-making regarding antibiotic treatment. They identified key considerations in achieving appropriate antibiotic therapy, such as diagnostic approaches to identify pathogens and guide treatment, timing of antibiotics, empirical versus targeted therapy, and therapeutic drug monitoring. To support clinical decision-making, they developed a framework consisting of six essential questions to be addressed before initiating antibiotic treatment in critically ill children, thus contributing to the literature.

A study by Okoye et al. (2022) evaluated the medication use patterns of pediatric patients under 12 years of age who visited the outpatient pediatric clinic at Bingham University Teaching Hospital in Nigeria. The study found that 81% of patients were prescribed antibiotics, with amoxicillin/clavulanic acid being the most frequently prescribed. The authors emphasized the need for national strategies targeting pediatric clinics and addressing non-standard prescribing practices in the pediatric population.

Thi et al. (2024) emphasized that if the infection is viral, rapid and accurate diagnostic tests for viruses and bacteria should be an essential part of a physician's diagnostic plan to avoid the indiscriminate use of antibiotics. Additionally, education on the limited risks and benefits of antibiotic use must be further encouraged to reduce resistance. Diagnostic tools based on molecular techniques and the application of these and other rapid methods outside hospital

settings can help more precisely determine which patients require antibiotics (Alfayate Miguélez et al., 2020).

In a study conducted by Bakaruddin et al. (2022), the effectiveness of illustrated storybook reading–video interventions on children's knowledge about rational medicine use was evaluated. The results showed that these interventions effectively improved children's understanding of rational medicine use. The authors emphasized the importance of prioritizing education and awareness regarding antibiotic use.

Conclusion

Rational use of antibiotics is critically important for preserving individual health and ensuring the sustainability of public health. Particularly in the pediatric age group, the widespread and often unnecessary use of antibiotics accelerates the development of antimicrobial resistance, resulting in serious public health problems. Among the main causes of this issue are parental lack of knowledge, pressure on physicians to prescribe antibiotics, easy access to over-the-counter antibiotics, and challenges in accurate diagnosis. In this context, antibiotics should only be used in children when clinically necessary, based on a correct diagnosis, and within the framework of appropriate dosage and treatment duration. An effective educational process must be established among physicians, parents, and children. Awareness-raising initiatives targeting parents and continuous professional development programs for healthcare providers are essential. Furthermore, the widespread implementation of rapid and accurate diagnostic tests will play a key role in preventing unnecessary antibiotic prescriptions. In conclusion, through national strategies, educational materials, and systematic practices that support rational antibiotic use in children, it is possible to reduce antibiotic resistance and ensure effective public health management. Building awareness regarding rational medicine use will help preserve the effectiveness of antibiotics and safeguard the health of future generations.

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CLIMATE CHANGE LITIGATION: TRANSNATIONAL LEGAL MOBILIZATION AND THE EVOLUTION OF GLOBAL CLIMATE GOVERNANCE

ABSTRACT

As the global climate crisis intensifies, climate change litigation has emerged as a powerful tool in shaping environmental policy and holding governments and corporations accountable for climate inaction. With the increasing failure of traditional political mechanisms to adequately address climate change, courts are becoming vital arenas for advancing climate justice. Transnational legal mobilization, where legal strategies, arguments, and actors transcend national boundaries is playing a pivotal role in reinforcing global climate governance. This form of litigation is not only redefining the relationship between law and environmental policy but is also enabling a more participatory and rights-based approach to climate governance. Despite the rising prevalence of climate lawsuits across jurisdictions, a significant research gap remains in understanding how transnational legal mobilization influences the evolution of global climate governance structures, particularly in the Global South. Existing literature often focuses on litigation in high-income countries, overlooking the dynamics, barriers, and innovations emerging from less-developed regions that are disproportionately affected by climate impacts. Furthermore, the interplay between international legal norms and national court decisions remains underexplored. This study aims to bridge this gap by analyzing climate change litigation through a comparative doctrinal lens, focusing on transnational legal mobilization and its role in shaping global climate governance. The research adopts a qualitative methodology, incorporating case law analysis, policy documents, and academic literature from multiple jurisdictions, with particular attention to landmark cases such as *Urgenda Foundation v. The Netherlands*, *Juliana v. United States*, and ongoing climate suits in countries like India, South Africa, and the Philippines. Interviews with legal practitioners and climate activists complement the doctrinal review to capture practice-based insights. Key findings reveal that climate litigation is increasingly leveraging international human rights norms and scientific consensus to frame climate change as a legal harm, thereby pressuring states to align domestic policies with global climate commitments. Courts are progressively recognizing intergenerational equity, the right to a healthy environment, and state accountability for emissions, even in jurisdictions lacking explicit climate laws. The study also highlights the diffusion of legal strategies and the influence of global civil society in supporting litigation across borders.

The implications of this research are substantial. It underscores the potential of transnational litigation to drive normative convergence in climate law, democratize environmental governance, and serve as a catalyst for policy change. Ultimately, the evolution of global climate governance will increasingly depend on the synergistic relationship between legal activism, judicial innovation, and international cooperation.

Keywords: Climate Change Litigation, Transnational Legal Mobilization, Global Climate Governance, Environmental Justice, Comparative Legal Analysis

Introduction

Climate change is no longer a future threat looming on the horizon—it is an urgent and escalating global crisis with far-reaching consequences for ecosystems, biodiversity, public health, economic stability, and fundamental human rights. From rising sea levels and extreme weather events to food insecurity and forced displacement, the multifaceted impacts of climate change are being felt across every region of the world. Despite the growing scientific consensus and the intensifying severity of these effects, governmental responses through traditional legislative and executive mechanisms have often proven inadequate, delayed, or politically constrained. In this context, an increasing number of citizens, civil society groups, and environmental organizations are seeking recourse through the judiciary. Climate change litigation has rapidly emerged as a potent legal tool to enforce environmental obligations, challenge regulatory inaction or insufficient ambition, and hold both state and non-state actors particularly fossil fuel corporations accountable for their role in exacerbating climate risks.

This paper critically examines the growing phenomenon of transnational legal mobilization, defined as the strategic deployment of legal arguments, litigation strategies, and activist networks that transcend national borders. This form of mobilization seeks not only to achieve justice within domestic legal systems but also to contribute to the development of cohesive, rights-based, and science-informed global climate governance. As climate change increasingly challenges the sufficiency of traditional legal doctrines, courts are being called upon to interpret and enforce laws through a transboundary and intergenerational lens. Historically, legal dispute particularly environmental ones, were addressed predominantly within national legal frameworks, often limited by domestic statutes and judicial doctrines. However, the inherent global nature of climate change has blurred these jurisdictional boundaries, demanding a legal response that is equally expansive and interconnected. Contemporary climate litigation increasingly invokes international environmental treaties (e.g., the Paris Agreement), authoritative scientific assessments such as those from the Intergovernmental Panel on Climate Change (IPCC), and universally recognized human rights frameworks, including the right to life, health, and a clean and sustainable environment. This evolution in legal reasoning reflects a paradigmatic shift toward integrating global legal norms into domestic adjudication processes.

Through a doctrinal and comparative lens, this paper investigates how national courts are engaging with international legal principles and how landmark cases in one jurisdiction are shaping litigation strategies, judicial reasoning, and policy innovation in others. By exploring this dynamic interaction between local legal systems and global normative structures, the study aims to illuminate the transformative role of transnational legal mobilization in the evolution of global climate governance.

Literature Review

1. Joana Setzer & Catherine Higham (2021) – *Global Trends in Climate Litigation*: Setzer and Higham's report for the Grantham Research Institute provides one of the most extensive empirical overviews of global climate litigation. It documents the exponential rise in climate-related lawsuits, particularly post-2015, and categorizes them based on actors (state, non-state), objectives (mitigation, adaptation), and legal bases (human rights, constitutional law, tort). The study emphasizes the increasing

trend of transnational influence, whereby landmark rulings in the Global North shape legal narratives in developing nations. However, the authors note a persistent gap in Global South representation and suggest the need for greater international collaboration. This work is foundational for understanding how litigation contributes to the emerging infrastructure of global climate governance.

2. Hari Osofsky (2005) – *The Geography of Climate Change Litigation***:** In this pioneering article, Osofsky argues that climate litigation cannot be fully understood without considering geographic and jurisdictional dimensions. She emphasizes that transnational legal mobilization is not merely about exporting legal arguments but involves adapting them to different political, cultural, and institutional settings. Osofsky highlights early litigation efforts in the U.S. and their global influence, laying the groundwork for understanding how strategic litigation travels across borders. Her work has been instrumental in establishing litigation as both a legal and geopolitical tool in climate fighting.
3. Jacqueline Peel & Hari Osofsky (2018) – *Climate Change Litigation: Regulatory Pathways to Cleaner Energy*: Peel and Osofsky's book bridges the gap between litigation and energy governance. They present climate litigation not only as a form of legal redress but also as a regulatory tool that pushes governments and corporations toward decarbonization. The authors introduce the concept of "polycentric governance," arguing that litigation contributes to shaping energy policy by fostering accountability across regulatory scales. Their interdisciplinary approach shows how litigation intersects with market forces, technological shifts, and political structures—offering a nuanced understanding of its role in global climate governance.
4. Lavanya Rajamani (2020) – *Legal Form and Climate Change*: Hard, Soft, and Non-Obligations: Rajamani analyzes the legal architecture of the Paris Agreement and its hybrid nature mixing binding and non-binding obligations. She explores how courts globally interpreting and invoking these provisions in domestic rulings, despite their formally non-binding status. Her work is significant in understanding how transnational legal mobilization operationalizes international law, particularly through litigation. Rajamani's insights highlight how flexible legal norms are instrumental in enabling domestic courts to enforce global climate targets, making her work central to the discussion of legal norm diffusion.
5. United Nations Environment Programme (UNEP) – Global Climate Litigation Report (2023): The 2023 UNEP report provides a comprehensive, global-scale mapping of climate litigation. It identifies trends such as the rise of rights-based cases, increased litigation against corporations, and the growing role of youth and indigenous plaintiffs. The report emphasizes transnational legal mobilization, noting how legal arguments rooted in international law and environmental science are diffusing across legal systems. It also highlights strategic litigation's potential to bridge governance gaps in countries where political will is lacking. This document serves as an authoritative policy and legal benchmark for ongoing research.
6. David Boyd (2012) – *The Environmental Rights Revolution*: Boyd's comparative analysis of environmental constitutionalism across jurisdictions explores how constitutional provisions are increasingly invoked in climate litigation. He highlights the evolution of environmental rights from aspirational declarations to enforceable legal norms, especially in Latin America and South Asia. His work underlines the importance of constitutional litigation as a mechanism for translating global climate obligations into actionable national mandates. Boyd's focus on judicial innovation

and rights discourse enriches our understanding of transnational legal mobilization's normative underpinnings.

7. Margaretha Wewerinke Singh (2019) – *State Responsibility, Climate Change, and Human Rights*: Wewerinke Singh investigates the interface between international human rights law and state responsibility in the context of climate change. She argues that human rights-based litigation is an effective strategy for establishing legal accountability, particularly when legislative and executive avenues have failed. The book critically assesses landmark cases and posits that transnational human rights frameworks offer a legal scaffold for courts to enforce climate justice. Her work contributes significantly to the evolving understanding of climate litigation as a vehicle for holding states accountable to both international law and their citizens.

Research Methodology

This research adopts a qualitative doctrinal methodology supported by comparative case study analysis. The study examines landmark climate litigation cases across jurisdictions (e.g., the Netherlands, USA, India, South Africa, and the Philippines) and uses document analysis of court rulings, legal filings, international conventions, and policy briefs. In addition, expert interviews with legal scholars and climate advocates provide practice-based insights into the dynamics of transnational legal mobilization. The approach allows for a detailed understanding of how climate litigation contributes to legal and policy development across jurisdictions.

The Rise of Climate Litigation: A Global Overview

Over the past two decades, climate change litigation has witnessed an exponential rise, emerging as a pivotal legal tool in the global response to the climate crisis. What began as isolated legal challenges have now developed into a global movement involving diverse actors, legal arguments, and jurisdictions. As scientific consensus on anthropogenic climate change has solidified most notably through the authoritative findings of the Intergovernmental Panel on Climate Change (IPCC) courts have increasingly been called upon to adjudicate complex legal questions surrounding state responsibility, corporate accountability, and intergenerational equity. According to the United Nations Environment Programme (UNEP) Global Climate Litigation Report 2023, over 2,400 climate-related legal cases have been filed across more than 80 countries, a figure that more than doubled since the previous report in 2017. These cases span a wide array of claims, including but not limited to: failures by governments to meet greenhouse gas (GHG) emissions reduction targets; inadequate adaptation planning; challenges to fossil fuel infrastructure projects; lawsuits against corporations for misrepresentation or “greenwashing”; and claims invoking constitutional and human rights violations due to environmental degradation.

One of the most influential milestones in this global wave was the *Urgenda Foundation v. State of the Netherlands (2015)* case, wherein the Dutch District Court in The Hague ruled that the Dutch government had a legal obligation to cut GHG emissions by at least 25% below 1990 levels by 2020. The court based its decision on domestic tort law as well as the European Convention on Human Rights (ECHR), asserting that insufficient climate action endangered the rights to life and well-being. This case marked the first time a court imposed a binding emissions reduction target on a national government, setting a powerful

international precedent. The ruling was subsequently upheld by the Court of Appeals and the Dutch Supreme Court, strengthening its authority and inspiring similar suits globally.

In the United States, the landmark case *Juliana v. United States (2015)* was brought by 21 youth plaintiffs who argued that the federal government's promotion of fossil fuel industries violated their constitutional rights to life, liberty, and property. Though ultimately dismissed on procedural grounds in 2020, the case broke new ground by framing climate change as a constitutional and intergenerational justice issue. It sparked a new wave of youth-led litigation and placed a spotlight on the government's fiduciary duty to protect natural resources for future generations, which is also known as the *public trust doctrine.* In the Global South, climate litigation has begun to gain traction, often fueled by novel legal strategies and grounded in pressing environmental realities. A notable example is *Leghari v. Federation of Pakistan (2015),* where a farmer successfully sued the Pakistani government for failing to implement its national climate change policy. The Lahore High Court held that climate inaction violated fundamental constitutional rights, including the rights to life and dignity. In the Philippines, the Carbon Majors Petition initiated by Greenpeace Southeast Asia seeks to hold 47 of the world's largest fossil fuel companies accountable for human rights violations arising from climate-induced harm. This case is particularly significant for its attempt to link corporate emissions to human rights impacts, potentially reshaping liability frameworks for multinational enterprises.

Despite these advancements, climate litigation in the Global South faces distinct structural and institutional challenges. Many legal systems lack robust environmental jurisprudence or access to specialized environmental courts. Resource constraints both financial and technical, which can limit plaintiffs' ability to mount effective cases. Moreover, political resistance and threats to judicial independence often pose additional barriers. Nevertheless, civil society organizations, indigenous communities, and youth activists are increasingly turning to the courts, adapting successful transnational legal strategies to their local contexts. The cumulative effect of these lawsuits is a growing body of jurisprudence that is shaping how courts worldwide interpret environmental duties and state obligations in the context of climate change. As legal arguments become more sophisticated and internationally harmonized by relying on scientific evidence, human rights law, and global treaties such as the Paris Agreement, the role of the judiciary in climate governance is becoming increasingly pronounced. The rise of climate litigation is not only a response to policy failures but also a proactive mechanism for accelerating legal and institutional innovation in the face of an escalating global crisis.

Transnational Legal Mobilization: Concepts and Strategies

Transnational legal mobilization refers to the strategic use of legal tools, principles, and networks that transcend national boundaries to advance climate-related litigation and environmental justice. It is a process through which lawyers, activists, NGOs, and affected communities leverage international legal norms, comparative jurisprudence, and global solidarity to challenge climate inaction and hold both states and non-state actors accountable.

This mobilization is defined by several interrelated strategies:

- ***Invocation of international legal instruments:*** Legal practitioners increasingly rely on globally ratified treaties and agreements, such as the *Paris Agreement* (2015), the

UN Framework Convention on Climate Change (1992), and human rights treaties like the *International Covenant on Civil and Political Rights* (ICCPR), to frame domestic legal claims. These instruments provide a normative foundation for arguing that inadequate climate action violates both global obligations and individual rights.

- ***Citing foreign jurisprudence:*** Landmark rulings such as the *Urgenda case* in the Netherlands, are frequently cited in climate litigation around the world. Courts in countries like Ireland, Germany, Colombia, and South Korea have referenced or echoed reasoning from such cases, demonstrating a judicial willingness to adopt and adapt persuasive legal precedents from other jurisdictions.
- ***Formation of cross-border legal networks:*** Transnational legal mobilization thrives on the exchange of litigation strategies, legal expertise, and technical resources across borders. Organizations such as ClientEarth, Earthjustice, the Global Legal Action Network (GLAN), and Greenpeace International facilitate knowledge-sharing and build capacity among legal practitioners in both developed and developing nations.
- ***Strategic litigation supported by civil society coalitions:*** Public interest law groups, youth movements, indigenous communities, and environmental NGOs collaborate across regions to launch or support litigation that aligns with broader climate justice goals. These collaborations create a *"norm cascade,"* where legal norms and doctrines gain traction globally through successive court endorsements, influencing both domestic jurisprudence and international policymaking.

Transnational legal mobilization not only enhances the legal repertoire available to litigants but also empowers underrepresented actors—particularly from the Global South—to participate meaningfully in shaping global climate governance norms and policies.

Key Cases in Transnational Climate Litigation

A growing body of landmark judicial decisions exemplifies how climate litigation has crossed borders, influenced legal standards and prompting policy shifts. Some of the most influential cases include:

- ***Urgenda Foundation v. State of the Netherlands (2015, 2019):*** In a groundbreaking ruling, Dutch courts held the government legally accountable for failing to adequately reduce greenhouse gas emissions. Invoking Articles 2 and 8 of the *European Convention on Human Rights* (right to life and right to private and family life), the court ordered the Dutch state to reduce emissions by at least 25% by 2020 compared to 1990 levels. This was the first case globally where a court mandated national emissions reductions based on human rights obligations.
- ***Juliana v. United States (2015–2020):*** Youth plaintiffs argued that the U.S. government's continued support for fossil fuel industries violated their constitutional rights to life, liberty, and property under the *Due Process Clause*. While the Ninth Circuit ultimately dismissed the case on procedural grounds—holding that the claims presented political rather than justiciable questions—it nonetheless galvanized youth-led climate activism and established the public trust doctrine as a legal argument in climate cases.
- ***Leghari v. Federation of Pakistan (2015):*** This landmark case in Pakistan resulted in the Lahore High Court recognizing climate inaction as a violation of constitutional

rights, including the right to life and dignity. The court compelled the government to implement its *National Climate Change Policy*, marking a rare instance of successful climate litigation in South Asia and demonstrating the viability of judicial intervention in developing countries.

- ***Greenpeace Southeast Asia v. Carbon Majors (Philippines, ongoing):*** A petition filed before the *Philippine Commission on Human Rights* seeks to hold 47 fossil fuel companies responsible for contributing to climate change and violating the human rights of Filipinos. This quasi-judicial inquiry represents an innovative approach, linking corporate emissions directly to human rights impacts and potentially setting a precedent for transnational corporate liability.
- ***Milieudefensie et al. v. Royal Dutch Shell (Netherlands, 2021):*** The Hague District Court ruled that Shell must reduce its global carbon emissions by 45% by 2030, in line with the Paris Agreement. The court held Shell responsible not only for its direct emissions but also for those across its supply chain and end-user consumption. This landmark decision marked a historic shift by extending climate accountability to multinational corporations under tort law and human rights frameworks.

These cases illustrate the judiciary's evolving willingness to reinterpret constitutional, environmental, and human rights law in the context of climate change, pushing the boundaries of traditional legal doctrines to address planetary-scale challenges.

Interplay between International Norms and Domestic Courts

A defining feature of modern climate litigation is the increasing reliance of domestic courts on international legal norms and global governance instruments. Courts are integrating provisions from treaties such as the *Paris Agreement*, *UNFCCC*, and international human rights covenants into their reasoning, even in jurisdictions lacking robust national climate legislation.

This interplay manifests in several ways:

- Courts use soft law instruments like the *Paris Agreement*, which, while not strictly enforceable, provide normative benchmarks for evaluating state conduct.
- Human rights norms are increasingly invoked to ground claims of environmental harm, especially concerning the rights of future generations, indigenous peoples, and vulnerable communities.
- Scientific evidence, including IPCC reports and planetary boundary frameworks, is used to substantiate claims and frame the urgency of state action or corporate mitigation.

The growing trend of *"judicial transnationalism*" where domestic courts look beyond national law to incorporate global norms, suggests a convergence in legal reasoning and supports the emergence of a unified, albeit decentralized, climate governance framework.

Barriers and Challenges to Transnational Legal Mobilization

While transnational legal mobilization has reshaped the legal landscape of climate action, several barriers continue to hinder its full realization:

- ***Jurisdictional limitations:*** National courts are often hesitant to adjudicate cases involving transboundary emissions or global corporations, citing the lack of direct jurisdiction or political question doctrines. This limits the scope of redress in cases involving diffuse or extra-territorial harm.
- ***Resource constraints:*** Complex climate litigation often requires extensive expert evidence, international legal expertise, and prolonged litigation timelines. Developing countries frequently lack institutional capacity, financial resources, or legal infrastructure to support such efforts, creating asymmetries in legal mobilization.
- ***Political resistance and judicial conservatism*:** Climate litigation may be perceived as challenging state sovereignty or interfering in policy domains reserved for the executive or legislature. As a result, courts may exhibit restraint, particularly in politically sensitive environments, thus diluting the transformative potential of litigation.
- ***Implementation and enforcement gaps:*** Even when climate cases are successful, the lack of effective enforcement mechanisms can render judicial victories symbolic rather than substantive. Governments may delay implementation, or courts may lack the means to monitor compliance, undermining the intended impact.

Overcoming these challenges requires sustained international collaboration, capacity-building in judicial institutions, and the continued engagement of civil society in advancing legal accountability for climate action.

The Role of Civil Society and Youth Movements

Civil society organizations (CSOs) and youth-led movements have emerged as indispensable actors in the landscape of climate change litigation. Operating both as initiators and supporters of legal action, these groups bridge the gap between affected communities, legal systems, and international climate governance frameworks. Their roles extend beyond courtroom advocacy to include awareness-building, legal capacity enhancement, media engagement, and policy advocacy.

Prominent organizations such as *ClientEarth, Earthjustice,* and the *Global Legal Action Network (GLAN)* have spearheaded numerous strategic climate lawsuits globally. These groups provide technical legal expertise, conduct impact litigation, and develop innovative legal arguments that incorporate environmental science, human rights principles, and international treaty obligations. For instance, ClientEarth has successfully litigated against European governments for failing to meet air quality standards and has launched legal challenges against fossil fuel companies for inadequate climate disclosures under corporate law. Youth-led movements have also become powerful forces for legal mobilization. Inspired by figures such as Greta Thunberg and the Fridays for Future campaign, young people have taken their demands for climate justice from the streets to the courts. Notable examples include *Juliana v. United States*, in which youth plaintiffs sought constitutional

recognition of their right to a stable climate system, and *Youth for Climate Justice v. Austria and Others*, a case currently before the European Court of Human Rights. These initiatives highlight a broader trend of intergenerational equity being used as a legal and moral principle in litigation, emphasizing the rights of future generations to inherit a livable planet. Additionally, grassroots CSOs and indigenous groups have played vital roles in mobilizing legal actions, particularly in the Global South, where environmental degradation often intersects with violations of land rights, cultural heritage, and community livelihoods. By forging transnational alliances and participating in global forums such as the UN Climate Conferences (COPs), civil society actors are also instrumental in shaping the normative and political environment in which climate litigation takes place. Therefore, civil society and youth-led movements serve as catalysts for legal innovation, multipliers of public pressure, and agents of normative transformation in climate governance. Their involvement democratizes access to environmental justice and strengthens the legitimacy and effectiveness of judicial responses to climate change.

Implications for Global Climate Governance

The growing body of climate litigation is having profound and far-reaching implications for the evolution of global climate governance. By expanding the scope of legal accountability and enabling diverse actors to challenge insufficient climate action, litigation is increasingly shaping not only domestic legal landscapes but also international policy norms.

1. ***Driving Accountability and Transparency:*** Climate litigation forces governments and corporations to justify their climate policies or lack thereof before impartial judicial bodies. Legal challenges often compel the disclosure of emissions data, risk assessments, and climate adaptation plans, thereby increasing transparency in climate governance. Courts serve as watchdogs where political processes have failed to deliver adequate climate ambition or enforce regulatory commitments.

2. ***Promoting Intergenerational Equity and the Right to a Healthy Environment:*** Many recent legal cases explicitly invoke the principle of intergenerational justice, emphasizing that current inaction burdens future generations with irreversible environmental harm. Courts are increasingly recognizing environmental rights as extensions of existing constitutional or human rights, including the right to life, health, and dignity. The recognition of a right to a clean and sustainable environment as a justiciable right has become a cornerstone of emerging climate jurisprudence, reinforcing the moral and legal imperative for action.

3. ***Influencing Corporate Behavior through ESG and Fiduciary Duties:*** Litigation is pushing corporations, particularly those in high-emissions sectors making them accountable for their environmental impact. Legal actions related to greenwashing, climate disclosures, and carbon emissions are influencing corporate governance and investment practices. Institutional investors and regulators are increasingly integrating Environmental, Social, and Governance (ESG) criteria into their decision-making, in part due to the legal risks spotlighted by climate litigation.

4. ***Encouraging Norm Diffusion Across Jurisdictions:*** As courts in one jurisdiction adopt progressive rulings or expand legal interpretations in favor of climate action, these decisions are often cited or adapted elsewhere, contributing to a process known as norm diffusion. For example, the success of the Uganda case in the Netherlands has influenced litigation in countries such as Belgium, France, Germany, and even South Korea. This cascading effect facilitates a convergence of climate-related legal standards and helps to harmonize legal approaches across different legal systems.

Collectively, these trends signal a paradigm shift in global climate governance. Judicial bodies, traditionally sidelined in international environmental diplomacy, are now emerging as **co-**regulators of climate responsibility. They complement and, in some cases, compensate for the inertia or dysfunction of multilateral institutions such as the UNFCCC. As litigation becomes an increasingly global phenomenon, it reinforces the rule of law, promotes international legal accountability, and strengthens the foundational pillars of a just and sustainable climate order

Conclusion

Transnational climate litigation has emerged as one of the most significant legal and socio-political developments in the global response to climate change. It represents not just a reaction to governmental and corporate inertia but a transformative force that is reshaping how climate justice, accountability, and environmental governance are conceptualized and operationalized across jurisdictions. By leveraging international legal instruments, scientific consensus, and cross-border networks, climate litigants are actively challenging traditional, state-centric notions of environmental governance. They are demanding that both public and private actors adhere to their commitments to their climate and uphold the fundamental rights of present and future generations.

Key Findings

1. Global Proliferation of Litigation: Over 2,400 climate-related cases have been filed in more than 80 countries, demonstrating an accelerating global trend toward judicial intervention in climate matters.
2. Transnational Legal Mobilization as a Strategic Tool: Legal strategies, such as citing foreign precedents and invoking international human rights treaties like the ICCPR, Paris Agreement, have enabled litigants to build powerful transnational narratives and legal arguments.
3. Judicial Innovation: Courts are increasingly interpreting constitutional rights like the right to life, dignity, and a healthy environment through a climate lens, expanding the scope of enforceable rights.
4. Empowerment through Civil Society and Youth Movements: Civil society organizations and youth-led initiatives have catalyzed climate litigation, mobilizing public support and shifting discourse toward intergenerational justice.
5. Diffusion of Legal Norms: Landmark rulings, such as Uganda case, Milieudefensie v. Shell, have transcended national borders, influencing litigation strategies and policy reforms in both developed and developing legal systems.
6. Challenges in Enforcement and Access: Many jurisdictions, particularly in the Global South, face barriers such as weak enforcement mechanisms, jurisdictional limitations, political resistance, and limited legal or financial resources.

These findings underscore a significant evolution in the structure of global climate governance, where courts, litigants, and non-state actors are assuming critical roles in advancing environmental protection. In doing so, they are complementing and at times compensating for the shortcomings of multilateral institutions like the UNFCCC. As litigation becomes increasingly transnational and rights-based, the legal system is becoming a crucial arena for enforcing climate accountability and shaping future climate policies.

Recommendations and Suggestions

To harness the full potential of transnational climate litigation and overcome its limitations, the following strategic actions are recommended:

1. Institutionalize Climate Jurisprudence Training: National judiciaries especially in the Global South, should receive targeted training on climate science, international environmental law, and human rights frameworks to strengthen the adjudication of climate cases.
2. Create a Global Climate Litigation Observatory: Establishing an open-access, multilingual database of climate-related jurisprudence would support legal harmonization, facilitate knowledge exchange, and empower litigants with precedent-based strategies.
3. Strengthen Legal Aid Mechanisms: Governments and international institutions should fund legal aid programs and NGOs that support vulnerable communities and youth groups in pursuing strategic climate litigation.
4. Codify Environmental Rights Constitutionally: Countries should recognize the right to a healthy environment as a fundamental right within their constitutions to ensure justiciability and enhance enforceability of climate claims.
5. Enhance Enforcement Mechanisms: Judiciaries should be equipped with clearer enforcement tools, such as climate compliance commissions, special implementation officers, or judicial monitoring bodies, to ensure that court orders are effectively followed.
6. Foster Multi-Stakeholder Collaboration: Strategic partnerships between NGOs, academics, bar associations, and international law firms can provide the multidisciplinary expertise required for complex climate litigation.
7. Promote Public Engagement and Education: Raising awareness about climate rights and legal remedies through public campaigns and school curricula can democratize access to climate justice and strengthen citizen participation.

Concluding by stating that as climate change intensifies manifesting in more severe natural disasters, ecological disruptions, and human rights violations, the judiciary will increasingly function as a cornerstone of global climate governance. Empowered by transnational legal mobilization and supported by a robust network of civil society actors, courts can ensure that climate obligations are not mere aspirations, but enforceable mandates grounded in law and ethics. The future of planetary stewardship depends not only on political will and technological innovation but also on the ability of legal systems to deliver timely, equitable, and just climate outcomes.

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THE IMPORTANCE OF miRNAS IN CYSTIC ECHINOCOCCOSIS

ABSTRACT

Objective: This study aims to evaluate the diagnostic, therapeutic, and immunological roles of microRNAs (miRNAs) in cystic echinococcosis (CE).

Method: Current scientific literature on Echinococcus granulosus-induced CE was reviewed, with a specific focus on the biomarker potential of parasite- and host-derived miRNAs, as well as their regulatory effects on the immune response.

Results: CE is a zoonotic parasitic disease that primarily affects the liver and lungs, leading to cyst formation and significant clinical outcomes in both humans and animals. miRNAs are key post-transcriptional regulators whose expression patterns vary during the progression of the disease, offering potential diagnostic value. Certain parasite-specific miRNAs have been detected in host blood and may contribute to early-stage diagnosis and monitoring of treatment response. Furthermore, these molecules can modulate immune functions, potentially influencing disease severity and progression.

Conclusion: miRNAs present a promising avenue for the early diagnosis and immunological evaluation of CE. Further research into their roles could enhance our understanding of host-parasite interactions and contribute to the development of novel strategies for disease management and control.

Keywords: Cystic echinococcosis, microRNA, biomarker, immune response, diagnosis

KİSTİK EKİNOKOKKOZDA miRNA' LARIN ÖNEMİ

ÖZET

Amaç: Bu çalışma, kistik ekinokokkoz (KE) olgularında mikrornaların (miRNA) tanısal, terapötik ve immünolojik rollerini değerlendirmeyi amaçlamaktadır.

Yöntem: Echinococcus granulosus kaynaklı KE ile ilgili güncel bilimsel literatür gözden geçirilmiş; özellikle parazit ve konağa ait miRNA'ların biyobelirteç potansiyeli ile bağışıklık yanıtı üzerindeki düzenleyici etkileri incelenmiştir.

Bulgular: KE, esas olarak karaciğer ve akciğerleri etkileyen, kist oluşumuna ve hem insanlarda hem de hayvanlarda önemli klinik sonuçlara yol açan zoonotik bir paraziter hastalıktır. miRNA'lar, hastalığın ilerlemesi süresince değişen ifade desenleriyle potansiyel tanısal değer sunan önemli post-transkripsiyonel düzenleyicilerdir. Bazı parazite özgü miRNA'lar, konak kanında tespit edilmiş olup erken evre tanısı ve tedavi yanıtının izlenmesine katkı sağlayabilir. Ayrıca bu moleküller, bağışıklık fonksiyonlarını düzenleyerek hastalığın şiddetini ve seyrini etkileyebilir.

Sonuç: miRNA'lar, KE'nin erken tanısı ve immünolojik değerlendirilmesi için umut vadeden bir alan sunmaktadır. Bu moleküllerin rollerine yönelik ileri araştırmalar, konak-parazit etkileşimlerini daha iyi anlamamıza katkı sağlayabilir ve hastalığın yönetimi ile kontrolü için yeni stratejilerin geliştirilmesine olanak tanıyabilir.

Anahtar Kelimeler: Kistik ekinokokkoz, mikrorna, biyobelirteç, bağışıklık yanıtı, tanı

1. GİRİŞ

Echinococcus granulosus parazitinin neden olduğu bir enfeksiyon hastalığıdır. Zoonotik bir parazittir. Erişkin formu, köpek ve tilki gibi etçil hayvanların ince bağırsaklarında bulunur. İnsanlar, dışkıyla kirlenmiş su veya gıda yoluyla enfekte olur. Parazitin larvaları, insanlarda karaciğer ve akciğer gibi organlarda su dolu kistler oluşturur.

Kistler büyüme özelliğinde-insan kafası büyüklüğüne kadar ulaşabilir. Kistlerin yırtılması Tip-I anaflaktik şok-ölüme neden olur. Teşhis US, BT, MR gibi görüntüleme yöntemleriyle olur. Tedavi, cerrahi müdahale, drenaj veya antiparaziter ilaçlarla gerçekleştirilir.

2. DÜNYADAKİ DAĞILIM

KE, Orta Asya, Güney Amerika, Akdeniz ve Doğu Afrika'da endemik olup Güney Amerika'da yılda 5.000 yeni vaka görülmeye devam etmektedir.

KE Türkiye'de hem koyun-sığır hem de insanlarda yaygın olan bir parazit enfeksiyonudur. Önemli bir halk sağlığı sorunudur. Özelikle bölgemizde yaygınlık yüksektir %12-30'dur. Hatta Malatya'da %45 oranındadır.

3. miRNA NEDİR?

miRNA'lar, hücrelerde 20-22 nükleotid uzunluğunda küçük yapıdadır. Serum ve plazmada sabit kalır ve mRNA'ya bağlanarak biyolojik süreçlerde rol alır. Hücre büyümesi, gelişimi ve stres tepkileri gibi süreçlerde etkilidir. Bağışıklık sistemini düzenleyerek enfeksiyonlarla mücadele eder. Hastalıkların erken evrelerinde tespit edilme hassasiyetine sahiptir. Genlerin ne zaman aktif olacağını veya ne zaman duracağını düzenlerler.

4. miRNA'LARIN BİYOBELİRTEÇ OLARAK KULLANIMI

Biyobelirteçler, vücuttaki biyolojik süreçleri ve hastalıkları takip eden göstergelerdir. miRNA'lar, yüksek özgüllükleri nedeniyle biyobelirteç olarak kullanılabilirler. Erken teşhis sağlar ve hastalığın ilerlemesini durdurabilir. Kanser, kalp hastalıkları, sinir hastalıkları ve enfeksiyonlarda miRNA seviyeleri, hastalığın gidişatını gösterebilir.

5. KE ENFEKSİYONUNDA MİRNA BİYOBELİRTEÇLERİ

Parazit miRNA'ları, yaşam döngülerinde işlevsel rol oynar. Bu yüzden son yıllarda, parazit ve miRNA ilişkili çalışmaları önem kazanmaktadır. *Echinococcus granulosus'un* gelişim evrelerinde çok sayıda miRNA ifade edilmektedir. miRNA'lar, parazitin yerleştiği organa ve hastalığın evresine göre farklı ekspresyon gösterirler. Aynı zamanda KE'ye özgü miRNA'ların tespit edilmesi, daha az invaziv ve yüksek özgüllük sağladığından tanıda ve enfeksiyonun takibinde önemlidir.

6. GÜNCEL ARAŞTIRMALAR VE GELECEK PERSPEKTİFLERİ

Ojha ve ark. (2019) yaptığı çalışmada dolaşımdaki miRNA'ların enfeksiyon hastalıklarının tanısında biyobelirteç olarak oynadığı kritik rol ele alınmıştır. Sepsis, inflamatuvar bağırsak hastalığı, grip, arbovirüs ve hepatit gibi enfeksiyonlarda çeşitli miRNA'lar tanı ve prognoz amaçlı kullanılmaktadır. Günümüzde non-invaziv tanı yöntemleri, miRNA'lar gibi biyobelirteçlerin yardımıyla erken teşhiste belirleyici bir konuma sahiptir. Gelecekte, dolaşımdaki miRNA'ların biyobelirteçler olarak kullanımı, insan enfeksiyonlarının hızlı ve etkili bir şekilde tedavi edilmesine olanak sağlayacaktır.

miR-2, miR-71 ve miR-125, parazitin gelişiminde önemlidir. miR-125, MiR-96 yalnızca parazitin erken aşamasında bulunur

Alizadeh ve ark. (2020) yaptığı çalışmada, KE takibinde parazit kökenli miRNA'ların biyobelirteç olarak kullanılma potansiyelini değerlendirmiştir. Egr-miR-71 ve egr-let-7 miRNA'ları, KE'li hastaların plazmalarında tespit edilmiş ve ameliyat sonrası üç ve altı ayda bu miRNA'ların seviyelerinde belirgin bir düşüş gözlemlenmiştir. Özellikle egr-miR-71, hidatidozun erken teşhisi ve takibi için umut verici bir biyobelirteç olarak öne çıkmaktadır.

Mariconti ve ark. (2019) yaptığı çalışmada, 84 miRNA'nın ekspresyon seviyelerini mikroarray yöntemi ile araştırılmıştır. Aktif kist grubunda sekiz miRNA (let-7g-5p, let-7a-5p, miR-26a-5p, miR-26b-5p, miR-195-5p, miR-16-5p, miR-30c-5p, miR-223-3p) inaktif kist grubuna göre anlamlı şekilde daha fazla ifade edilmiştir. Bu bulgular, aktif kistlerin varlığının bu miRNA'larla ilişkili olduğunu göstermektedir.

KE tanısı almış 50 hasta ve 20 sağlıklı kontrol grubunda miRNA (let-7, miR-71 ve miR-10) plazma seviyeleri araştırılmıştır. CE1 kist tipinde miR-71, CE2 kist tipinde ise let-7'de belirgin bir artış gözlemlenmiştir.

Örsten ve ark. (2020) yaptığı çalışmada, aktif ve inaktif KE hastalarında bazı miRNA'ların kontrol grubuna kıyasla daha az üretildiğini söylüyor. Bu miRNA'ların miktarı, önemli bir değişim gösteriyor, yani hastalık sırasında miRNA seviyeleri düştüğü gözlemlenmiştir

7. KE VE KANSER İLİŞKİSİ

Parazit enfeksiyonları, bazı kanser türlerinin gelişiminde. Parazitler, konak hücrelerinin gen ekspresyonunu düzenler. miRNA'lar, hücre büyümesi ve ölümünü etkileyerek kanser gelişimini tetikleyebilir. miRNA'lar, parazit enfeksiyonları ile ilişkili kanser türlerinin tanısında kullanılabilir. Kanser teşhisi genellikle gecikir; bu, kanserin ilerlemesine neden olabilir. Tümör evreleri için bilgi verebilir.

Chakraborty ve ark. (2023) yaptığı bir çalışmada, let-7g, miR-15b, miR-155 ve miR-328 yüksek seviyelerde bulunduğunda, ileri kolon kanseri olan hastalarda hastalığın daha kısa sürede nüks etme potansiyeli bulunmaktadır. Özellikle, miR-328'in yüksek seviyeleri, kolon kanseri hastalarında karaciğer metastazı ile ilişkili bulunmuştur. Bu miRNA'lar, kolon kanserinin nasıl ilerlediğini ve yayıldığını etkileyebilir

Örsten ve ark. yaptığı çalışmada, aktif KE hastalarında, apoptoz, hücre-hücre etkileşimleri ve hücre döngüsü ile ilişkili altı miRNA'nın düşüş gösterdiği belirlenmiştir. Bu miRNA'lar, kanser gelişiminde önemli bir rol oynayabilecek moleküller olarak değerlendirilmektedir.

Özellikle, hsa-miR-4659a-5p ve hsa-miR-181b-3p gibi miRNA'ların kanser gelişimi ile ilişkilendirildiği bilinmektedir

Mohammadi ve ar. (2021), yaptığı bir çalışmada, hidatik kist sıvısında bulunan miR-365'in melanom kanseri üzerindeki etkilerini araştırmıştır. miR-365, önemli bir tümör baskılayıcı miRNA olarak öne çıkmaktadır. Kanser hücrelerinin büyümesini ve yayılmasını engellerken, tümör gelişimini de baskılar. Hidatik kist sıvısı, miR-365'in ifadesini artırır hücre ölümünü tetikler. Hidatik kist sıvısı ile tedavi edilen melanom hücrelerinde miR-365'in yüksek düzeyde ifade edilmiştir.

miRNA çalışmaları, kanser (KE) tanısı ve hatta erken teşhisinde önemli bir rol oynayarak daha etkili tedavi stratejileri geliştirilmesine katkı sunacaktır. Bu nedenle, farklı organ ve dokulardaki kanser enfeksiyonlarının miRNA profili üzerine yeni çalışmalara ihtiyaç duyulmaktadır.

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GOAT RECOMBINANT DNA: AN OVERVIEW

ABSTRACT

Sheep and goats have become crucial model animals in agricultural, pharmacological, and biological research because of their appropriate size, short gestation period, and copious milk secretion. Currently, it is feasible to generate or extract desired genes and transfer them across cell membranes using mechanical, electroporation, or viral vectors. Because they produce large quantities of milk and require less capital and care than cows, goats are an especially effective way for making recombinant proteins. There are a number of benefits to producing complex recombinant proteins in transgenic animals' milk, including the ability to obtain vast quantities of proteins that are typically correctly folded, assembled, cleaved, and glycosylated.

Keywords: Goats, recombinant DNA, recombinant proteins

1. Introduction

As scientific knowledge has grown and technology has advanced, molecular cloning technologies have advanced significantly. This has facilitated the expansion of recombinant DNA technology into new domains. Recombinant DNA technology has been widely used in a variety of industries, including agriculture, healthcare, and the sustainable environment. Recombinant DNA technology is crucial to the development of biopharmaceuticals, vaccines, gene therapy, molecular diagnostics, and other medical technologies. Recombinant DNA technology has been used in the environmental field to develop a number of bioremediation methods and bioindicators. Recombinant DNA technology has made significant contributions to the agricultural sciences, including improved crop output, tolerant crops, and nutritional enhancement. In addition to this, a wide range of industries use this technology to produce their goods (Vipra et al., 2022).

Recombinant DNA (rDNA) technique involves expressing genes in a host (often E. coli) by recombining genes from various sources in a novel way. It became feasible to "cut" DNA at particular spots with known base sequences after restriction endonucleases were discovered. These enzymes identify specific locations in foreign DNA that can infect the bacterial cell, including viruses and plasmids. They are quite particular to the locations where they operate on DNA rather than cleaving it at random. The enzymes are known as restriction sites because of their ability to "restrict" the entry of foreign DNA. By identifying DNA methylation, these restriction enzymes are able to distinguish "self" from "non-self," such as the human immune system. The bacterial cell methylates its own DNA shortly after it is synthesized, thus protecting it from attack by restriction endonucleases. Foreign DNA is not methylated, resulting in its cleavage and subsequent degradation (Pelley, 2007).

The recombinant proteins were first expressed in yeast and bacteria in the field of genetic engineering. Since human proteins do not experience post-translational changes in bacteria, it was later demonstrated that a number of human recombinant proteins might not be generated effectively in such systems. Furthermore, the changes those proteins experience in yeast cells differ from those that take place in human cells. Because of these factors, creating expression systems that guarantee proper post-translational modifications in recombinant proteins was a significant task. Studies to date have shown that transgenic animals have appealing benefits for producing recombinant proteins, including good protein quality and inexpensive production costs (Houdebine, 2009).

2. Transgenic farm animals

The ancient practice of selectively breeding genetic anomaly animals over many generations to improve production attributes is the basis for the modification of animal genomes. Nevertheless, there are drawbacks to selective breeding, the most significant of which are the need for a beneficial trait to exist in the population, the low heritability of traits, and the lengthy period needed for mating across several generations in order to "fix" the trait within a population. There is an urgent need for animal agriculture to be more accurate and responsive than selective breeding because of the requirement to sustainably grow animal production in order to feed planet by 2030 and the threat posed by climate change. This involves making use of every resource available, including genome editing and transgenesis (Talluri & Telugu, 2022).

Since its inception in 1981, animal transgenesis has undergone a revolution in terms of efficiency, cost, and speed (Yamashita & Melo, 2023). The use of biotechnology in livestock

includes a range of molecular biology-based reproductive methods. DNA mass transfer and microinjection into the pronucleus of fertilised oocytes are two methods used to transfer gene constructs. The last one can be created using retroviral vectors in cell lines or sperm, which transfer the integrated gene construct into the ovum during fertilisation. To guarantee that the conceptus develops into a transgenic animal, the foreign DNA must be present in the gametes or one-cell embryos before transgenic lines may be established. Depending on the kind of domestic animal being used and its biological capabilities, many techniques and procedures can be employed to transfer foreign genes in order to achieve this goal. The commercial availability of transgenic protein products for therapeutic use is believed to be approaching, and transgenic animals are currently widely employed as models for human disease throughout the world. Advanced research is being done in fields including better animal production and the development of organs for transplantation into humans. Transgenic animals offer an authentic in vivo setting for assessing the processes via which gene expression is altered in both adults and during development. “Animal pharming”, the process of using transgenic animals to produce pharmaceutical proteins for human use, is staking its claim in a lucrative world market since the inserted gene, enables an animal to generate the targeted pharmaceutical protein in its milk, urine, blood, sperm, or eggs, or to grow rejectionresistant organs for transplant (Collares et al., 2018).

3. Goat recombinant DNA

Goats seem like a very exceptional model when taking into account the benefits and drawbacks of livestock species. Furthermore, transgenic goat milk was used to generate antithrombin (AT), the first biological medication for humans to receive commercial approval (Lavine, 2009). Traditionally, a DNA construct is microinjected into the pronuclei of early embryos for producing transgenic goats. By employing somatic cell nuclear transfer (SCNT), which enables the introduction of a DNA construct into target cells in culture through lipid-mediated transfection and the subsequent selection of appropriately integrated donor cells for transfer, new advancements in the production of transgenic goats were achieved (Freitas et al., 2016).

Since they can provide meat, milk, fibre, and other byproducts, goats are an important livestock species. Sheep and goats have become crucial model animals in agricultural, pharmacological, and biological research because of their appropriate size, short gestation period, and copious milk secretion. Research on sheep and goats has made extensive use of genome editing. The two main methods used to generate genetically engineered sheep and goats are pronuclear injection and somatic cell nuclear transfer. Additional aided tools have been developed to improve genetic modification's effectiveness and make the process to produce genetically modified ancestors easier. Goats are an important livestock animal because they may produce meat, milk, fibre, and other byproducts. Because of their suitable size, short gestation period, and abundant milk production, sheep and goats have emerged as essential model animals in biological, pharmaceutical, and agricultural research. Genome editing has been widely used in sheep and goat research. Somatic cell nuclear transfer and pronuclear injection are the two primary techniques utilised for generating genetically modified sheep and goats. To increase the efficacy of genetic modification and facilitate the production of genetically modified ancestors, more assisted technologies have been developed. These tools are used for developing gene-edited sheep and goats, which offer useful models for studying gene functions, enhancing animal breeding, generating pharmaceuticals in milk, increasing animal disease resistance, simulating human diseases, and serving as hosts for the development of human organs. Furthermore, other intriguing

CRISPR system derivative tools have surfaced, such as base editors, which allow single-base changes to be induced without the need for a DNA donor or homology-directed repair. These accurate editors are useful for identifying desired traits and fixing single-base-controlled genetic disorders (Kalds et al., 2019).

There are a number of benefits to using recombinant somatic cell lines for nuclear transfer, including the ability to introduce transgenes using conventional transfection techniques, 100% transgenic animal production efficiency, and the ability to get around founder mosaicism. Furthermore, transgenic founders produced by pronuclear microinjection may also be cloned via somatic cell nuclear transfer techniques (Freitas et al., 2016).

PTHrP gene expression was effectively suppressed by recombinant adenoviruses that target goat parathyroid hormone–related protein (PTHrP) in mammary epithelial cells and transport short hairpin RNA (shRNA) (Zheng et al., 2013). Xu et al. (2008) produced TATCre recombinase, a recombinant cell-permeable fusion protein, by combining the Cre/loxP recombination system with protein transduction technology. By using this recombinant protein, the cytotoxic and genotoxic consequences of the integration and continuous expression of Cre recombinase-expressing vectors were eliminated, and the delivery efficiency was increased. Shadanloo et al. (2010) confirmed that transgenic goat embryos could be generated via Sperm-Mediated Gene Transfer (SMGT). The intracytoplasmic sperm injection (ICSI) technique was used by the authors of this paper to improve the approach. This study demonstrated that embryo growth, transgenic transmission, and expression are influenced to some degree by the technique (in vitro fertilisation vs. ICSI), sperm status (motile vs. live-immotile vs. dead), and DNA concentration.

4. Market for recombinant proteins from goats

The global protein therapeutics market reached US$ 138.3 billion in 2012 and this market is expected to increase to nearly US$ 179.1 billion in 2018 (Freitas et al., 2014). Businesses that are interested in using the "goat model" as a bioreactor may find this to be an intriguing topic. But despite the fact that it was always regarded as a highly-perspective method, there are still only two new commercial recombinant proteins that have made it to market (Kues & Niemann, 2011). The first explanation for this is the degree of technology used in transgenic animal production. Even though there have been many advancements and improvements, it still takes a long time to determine and verify which mammary expression system design should be employed to generate a certain protein. Some efforts in this regard have yet to be successful, particularly when it comes to highly active human proteins or those with intricate posttranslational modifications (Montesino et al., 2008).

The patents on all of the "blockbusters" of the recombinant protein market, which are still being made in various systems like bacteria or Chinese Hamster Ovary (CHO) cells, are the second reason. This aspect, presumably, forced industry pioneers to focus on orphan medications. An orphan medication made by a transgenic animal required more work to get to market than a blockbuster made in a standard expression system, but it typically had less commercial advantage, making it a hazardous enterprise. This is well demonstrated by the fact that several businesses have filed for bankruptcy since the start of the transgenic animal bioreactor era. They all struggled, even the most famous. A major player in the market, GTC-Biotherapeutics (USA), which was the first to bring goat-derived recombinant human AT (ATryn®) to the market, recently had to cut off roughly fifty of its employees and take out two loans from "LFB Biotechnologies," a French partner firm. GTCBiotherapeutics declared

in January 2013 that it had been purchased by LFB and rebranded as "rEvo (Freitas et al., 2014).

The human ATIII mentioned above is still the only goat-derived recombinant human protein available for purchase. But according to the information that is currently accessible, goats produced a small number of different recombinant proteins. Several of these proteins were claimed to advance to the clinical trial stage, while it is unclear what became of some of these efforts. Thus, transgenic goats have been producing blood clotting factors since the 1990s. The majority of the recombinant blood proteins listed were developed in the United States by GTC-Biotherapeutics. This is not surprising at all, considering the largest business in the market, GTCBiotherapeutics, holds a U.S. patent covering the manufacture of all therapeutic proteins in the milk of transgenic mammals. The patent was issued in 2006 and expires in 2021. But research in this area is also done in other nations, such Iran, where goats that express human factor IX were developed (Amiri Yekta et al., 2013).

Goats that express human monoclonal antibodies against the CD20 receptor, CD137 receptor, tumour necrosis factor (TNF), and epidermal growth factor receptor (EGFR) already exist, despite the fact that published articles hardly contain any information on transgenic goats producing monoclonal antibodies (Freitas et al., 2014). Additionally, techniques have been established for the separation of recombinant antibodies from goat milk (Baruah et al., 2006).

Given their high biological activity and potential to negatively impact transgenic animal health, recombinant hormones, growth factors, and cytokines present a more challenging task (Serova et al., 2012). However, transgenic goats expressing EPO (Montesino et al., 2008) and G-CSF (Freitas ve ark., 2012) had already been generated. There is considerable interest in the development of other commercially significant proteins expressed in transgenic goats. Consequently, a number of organisations have documented producing transgenic goats that exhibit elevated amounts of human lactoferrin (Goldman et al., 2012).

Pronuclear microinjection and SCNT continue to be the most popular methods to generate transgenic goats, despite the development of novel approaches for lab animals. In summary, there is currently no ideal transgenic design that can be relied upon to deliver accurate tissue-specific transgene expression at a high level (Freitas et al., 2014).

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THE PROTECTIVE EFFECT OF LYCOPENE IN LIVER DISEASES

ABSTRACT

Lycopene, a carotenoid predominantly present in tomatoes and other red fruits, has demonstrated significant potential as a therapeutic agent for the treatment of liver diseases. Its robust antioxidant and anti-inflammatory activities are fundamental to its hepatoprotective mechanisms. Lycopene effectively scavenges reactive oxygen species and reduces oxidative stress, a key contributor to the pathogenesis of liver disorders, including NAFLD, hepatic fibrosis, and drug-induced liver injury. Experimental and clinical evidence indicates that lycopene exerts its effects through the modulation of key molecular pathways, including the downregulation of pro-inflammatory cytokines as well as the inhibition of the nuclear factor kappa B (NF-κB) signaling pathway. Moreover, lycopene has been demonstrated to reduce lipid accumulation, enhance liver enzyme profiles, and protect against hepatocellular injury, underscoring its potential as a natural therapeutic agent for managing hepatic metabolic dysfunction. Given its excellent safety profile and accessibility through dietary intake, plant extraction, and biotechnological production, lycopene emerges as a promising candidate for adjunctive therapy targeting oxidative stress and inflammation in liver diseases. This review evaluates the current body of evidence regarding the hepatoprotective effects of lycopene across a range of liver disorders.

Keywords: Apoptosis, inflammation, liver, lycopene, oxidative stress

Introduction

Lycopene (LCP) is distinguished among natural compounds for its broad range of biological activities (Zhu et al., 2020, Sharma et al., 2021) and exhibits potent antioxidant, anti-apoptotic, and anti-inflammatory properties (Albrahim et al., 2021). The curative potential of LCP in various neurological disorders, including neurodegenerative conditions. Additionally, LCP has shown beneficial effects in the management of hepatic diseases (Kulawik et al., 2023).

Oxidative stress is a key contributing factor in the development and progression of liver diseases. Reactive oxygen species (ROS) initiate a cascade of oxidative events that impair mitochondrial function, leading to lipid peroxidation, cellular and membrane damage, and ultimately culminating in cell death (Handa et al., 2016). LCP possesses a highly conjugated double-bond system that underlies its potent antioxidant properties. This structural feature enables LCP to effectively scavenge free radicals, quench ROS, attenuate oxidative stress, and modulate inflammatory processes (Lucas et al., 2020, Singh and Goyal, 2008). The antioxidant activity of LCP is further evidenced by its capacity to reduce levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG), a biomarker of oxidative DNA damage. This reduction was consistently observed following treatment with low, medium, and high concentrations of LCP, indicating that LCP effectively scavenges ROS and thereby mitigates oxidative stress (Bazyel et al., 2019).

LCP exhibits strong anti-inflammatory effects by inhibiting the nuclear translocation of nuclear factor kappa B (NF-κB), thereby suppressing the activation of this key inflammatory signaling pathway (Donghia et al., 2024). Additionally, LCP has been shown to attenuate systemic inflammation in obesity by reducing circulating levels of TNF-α, IL-6 (Baz et al., 2022). Lycopene (LCP) is well-recognized for its anti-apoptotic properties. In a study by Albrahim (2022), LCP administration significantly reduced renal cell apoptosis through the downregulation of caspase-3 and Bax, accompanied by an upregulation of Bcl-2. Furthermore, the suppression of caspase-3 has been associated with the prevention of hepatocellular injury, inhibition of cell death, and attenuation of pro-inflammatory signaling pathways (Thapaliya et al., 2014). As LCP shows lots of beneficial properties for the treatment, it is better to understand their contributions to diseases.

Lycopene in Liver Diseases

Lycopene (LCP) is the carotenoid found in tomatoes, and the majority of dietary. LCP is efficiently absorbed and subsequently accumulated in hepatic tissue, where it exerts its physiological and bioactive functions (Zhao et al., 1998). Compared to other carotenoids, LCP exhibits superior antioxidant efficacy and a pronounced capacity to neutralize free radicals both in vitro and in vivo. This enhanced activity confers a greater ability to scavenge ROS. LCP has demonstrated potent anti-inflammatory and hepatoprotective effects, primarily through the downregulation of pro-inflammatory cytokine activity (Luvizotto et al., 2013, Róvero Costa et al., 2019). Lycopene inhibits NF-κB signaling pathway, a principal regulator of inflammatory responses (Donghia et al., 2024). Furthermore, lycopene treatment has been demonstrated to attenuate inflammation by decreasing the concentration of markers, including TNF-α, IL-6, and leptin, in models of high-fat diet (HFD)-induced obesity (Baz et al., 2022).

A growing body of preclinical evidence highlights LCP's protective role against various forms of hepatic injury through its capacity to counteract oxidative stress and modulate lipid metabolism. Chang et al. (2023) demonstrated that LCP administration significantly attenuated titanium dioxide (TiO_2)-induced hepatic injury in SPF-grade ICR mice by enhancing total antioxidant capacity (TAC) and glutathione (GSH) levels, increasing the activity of superoxide dismutase (SOD), and reducing malondialdehyde (MDA) concentrations. Similarly, Bandeira et al. (2017) reported that LCP mitigated acetaminophen-induced hepatotoxicity in C57BL/6 mice by reducing oxidative stress and liver damage.

LCP has shown considerable potential in the management of nonalcoholic fatty liver disease (NAFLD), a common metabolic condition marked by hepatic fat accumulation and chronic inflammation. Studies by Abenavoli (2022) and Jiang et al. (2016) demonstrated that LCP supplementation significantly lowered serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglycerides (TG), and total cholesterol in obese rodent models of NAFLD. Furthermore, LCP treatment alleviated hepatic steatosis, reduced free fatty acid accumulation, and downregulated proinflammatory markers such as TNF-α, along with cytochrome P450 enzymes. At the molecular level, LCP's efficacy has been attributed to its ability to modulate key signaling pathways; Ahn et al. (2012) demonstrated that it reduces hepatic steatosis by downregulating fatty acid-binding protein 7 via microRNA-2 regulation, while Chung et al. (2012) reported that the LCP metabolite apo-10'-lycopenoic acid exerts hepatoprotective effects by increasing SIRT1 gene expression and enzymatic activity in ob/ob mice. Collectively, these findings underscore LCP's potential as a therapeutic agent in mitigating oxidative liver damage and metabolic liver diseases such as NAFLD.

Interestingly, LCP has been demonstrated to confer protective effects against N-nitrosodiethylamine (NDEA)-induced hepatocarcinogenesis through multiple biochemical and molecular mechanisms. Gupta et al. (2013) reported that lycopene administration significantly decreased ROS production, and lipid peroxidation (LPO) levels. Notably, LCP supplementation attenuated tumor development by reducing tumor burden and frequency, delayed the appearance of aggressive tumor nodules, and improved the overall survival rate of NDEA-treated mice. Complementing these findings, Sahin et al. (2014) demonstrated that LCP effectively restored biochemical alterations in NDEA-treated rats, enhancing antioxidant defenses by increasing the activities of catalase (CAT) and SOD. Collectively, these studies highlight the chemopreventive potential of LCP against hepatic carcinogenesis via modulation of oxidative stress and tumor-associated biomarkers.

Conclusion

Lycopene, a carotenoid predominantly found in tomatoes, has demonstrated efficacy in alleviating metabolic impairments, inflammation, and apoptosis triggered by oxidative stress. Consequently, an in-depth understanding of lycopene's biological activities is crucial for exploring its therapeutic potential in the treatment of liver diseases.

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THE CHONDROGENIC EFFECT OF KARTOGENIN ON MESENCHYMAL STEM CELLS

ABSTRACT

Kartogenin (KGN) is a small molecule that exerts significant chondrogenic effects on MSCs, making it a promising candidate for cartilage repair. Upon treatment with KGN, MSCs exhibit enhanced differentiation into chondrocytes, as evidenced by increased expression of key chondrogenic markers such as SOX9, COL2A1, and Aggrecan. Additionally, KGN promotes the synthesis of cartilage-specific extracellular matrix components, including COL II and glycosaminoglycans. These molecular and biochemical changes contribute to the formation of cartilaginous tissue in vitro. KGN also supports long-term maintenance of the chondrogenic phenotype without inducing hypertrophy, which is critical for the stability of regenerated cartilage. Collectively, these effects suggest that KGN plays a crucial role in directing MSC fate toward chondrogenesis and holds strong potential for non-surgical approaches to cartilage repair. This review evaluates the chondrogenic effects of Kartogenin on MSCs and cartilage regeneration.

Keywords: Chondrogenesis, kartogenin, mesenchymal stem cells

Introduction

Kartogenin (KGN) is a low-molecular-weight bioactive molecule initially identified for its capacity to promote chondrogenic differentiation in bone marrow-derived mesenchymal stem cells (MSCs) (Johnson et al., 2012). Its mechanism of action entails the disruption of the interaction between core-binding factor β (CBFβ) and filamin A, thereby facilitating the nuclear translocation of CBFβ. Within the nucleus, CBFβ associates with RUNX1, leading to the transcriptional upregulation of key chondrogenic markers, including type II collagen (COL II) and aggrecan. In addition, KGN has been reported to support cartilage nodule formation and synovial joint development during limb morphogenesis, partially through activation of the transforming growth factor-beta (TGFβ) signaling pathway (Decker et al., 2014).

Thanks to its advantageous physicochemical characteristics, KGN is widely regarded as both a chondrogenic and chondroprotective compound and has been the focus of extensive research for its potential in promoting cartilage repair and regeneration (Cai et al., 2019). Numerous studies have shown that KGN can stimulate chondrogenic differentiation in mesenchymal stem cells (MSCs) obtained from a range of species, including humans, rabbits, and rats (Huang et al., 2017; Li et al., 2016; Liu et al., 2018; Spakova et al., 2018; Zhang & Wang, 2014; Zhou et al., 2017).

Remarkably, in a rabbit model with articular cartilage defects, treatment with a KGN-loaded hydrogel led to significantly better cartilage regeneration compared to controls that received no treatment (Chen et al., 2022). Similarly, intra-articular injection of KGN in a mouse model of osteoarthritis effectively reduced cartilage erosion and joint inflammation (Hou et al., 2021). These findings highlight the therapeutic promise of KGN in the context of regenerative medicine.

Kartogenin Structure

Kartogenin (KGN) is a small, heterocyclic molecule with a molecular weight of 317.3 g/mol. Its chemical structure includes a 4-aminobiphenyl (4-ABP) component and phthalic acid (PA), linked together by an amide bond. KGN is hydrophobic, which allows it to dissolve in dimethyl sulfoxide (DMSO) but makes it insoluble in water (Chen and Liao, 2023). The molecule features hydroxyl (–OH) groups that act as reactive sites, enabling interactions with acidic substances to form ester derivatives. This esterification process allows KGN to be attached to drug carriers or chemical moieties, which can influence its release profile and chemical stability (Liu et al., 2024).

In 2012, Johnson et al. identified more than 22,000 structurally varied heterocyclic pharmacophore compounds and singled out KGN as a small molecule with the ability to stimulate chondrogenesis, inhibit cartilage breakdown, and enhance joint weight-bearing capacity in animals in a dose-dependent fashion (Johnson et al., 2012). Thanks to its favorable physicochemical characteristics and the presence of the 4-ABP component (Zhang et al., 2019), KGN has been recognized as having strong chondrogenic potential and protective effects on cartilage. Since then, it has been widely investigated for its use in biological therapies aimed at repairing cartilage defects (Cai et al., 2019).

The Chondrogenic Effect of Kartogenin on Mesenchymal Stem Cells and Cartilage Regeneration

Kartogenin (KGN) is a small heterocyclic compound that has demonstrated significant potential in promoting the regeneration of articular cartilage by modulating the differentiation pathways of mesenchymal stem cells (MSCs). Notably, KGN can redirect the differentiation process from terminal hypertrophic maturation back toward chondrogenesis, thereby favoring cartilage regeneration (Valiani et al., 2017). Mechanistically, KGN binds to the intracellular signaling molecule filamin A, thereby inhibiting its interaction with the core-binding factor β (CBFβ) subunit. This inhibition activates the CBFβ-RUNX1 transcriptional pathway, which in turn promotes chondrogenesis (Jiang et al., 2022). Furthermore, KGN promotes MSCs to differentiate into chondrocytes by upregulating chondrogenic markers such as COL II, SOX-9, aggrecan, and TIMPs, while concurrently downregulating Runx2 and its associated hypertrophic downstream genes (Asgari et al., 2020; Gillogly et al., 1998).

Additionally, the controlled release of KGN has been shown to enhance the chondrogenic differentiation of peripheral blood-derived MSCs and promote extracellular matrix (ECM) production, which supports defect repair and cartilage formation in vivo (Chen et al., 2022). In vivo studies have demonstrated that KGN injection can induce the formation of cartilage-like tissue at the site of injection, as seen in the intact rat patellar tendon (Zhang & Wang, 2014), and during mouse limb development, where it promotes cartilage nodule formation via upregulation of hedgehog and TGF-β1 pathway-related genes (Decker et al., 2014). Moreover, KGN has been shown to stimulate the chondrogenic differentiation of synovial fluid-derived MSCs (SF-MSCs) while simultaneously protecting native chondrocytes from degeneration (Im, 2017). This protective effect is partially mediated through the inhibition of IL-1β-induced ECM and aggrecan degradation, as well as the stabilization of hyaluronan-CD44 interactions, which help preserve cartilage homeostasis (Ono et al., 2014).

Growth factors such as BMP-2, BMP-7, BMP-13, and TGF-β1 are known to enhance chondrogenic differentiation of MSCs and stimulate the accumulation of lubricin, a key glycoprotein involved in cartilage lubrication and protection (Oshin and Stewart, 2007; Jones and Flannery, 2007). KGN may act synergistically with these growth factors, as suggested by in vitro studies assessing lubricin synthesis under combined treatments with TGF-β1, BMP-7, and KGN (Liu et al., 2015).

Injection of KGN markedly reduced pain intensity and joint damage in the MIA-induced osteoarthritis (OA) model. KGN stimulated the production of IL-10 and exerted a protective effect on cartilage by suppressing the expression of matrix metalloproteinases (MMP3 and MMP6) as well as pro-inflammatory mediators, including IL-6, TNF-α, and IL-1β (Kwon et al., 2018). Additionally, KGN has been reported to activate Stat3 signaling through its interaction with gp130, a receptor for interleukin-6 (IL-6), which upregulates chondrocyte-specific gene expression and supports tissue repair during the late inflammatory phase (Liu et al., 2020).

Collectively, KGN promotes chondrogenic differentiation by upregulating critical cartilage-related genes, including Acan, Col2a1, Sox9, and TIMP-1, while suppressing the expression of hypertrophic markers such as Col X. This regulatory shift favors the transition from pre-hypertrophy to a pre-differentiated, proliferative state, ultimately contributing to improved cartilage repair and regeneration (Lairson et al., 2013; Yuan et al., 2016). These multifaceted

effects make KGN a promising therapeutic agent for cartilage tissue engineering and regenerative medicine applications.

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DETERMINING SOCIAL NETWORK FATIGUE LEVELS OF STUDENTS AT A PUBLIC UNIVERSITY BASED ON THEIR USE OF SOCIAL PLATFORMS

ABSTRACT

The purpose of this study is to determine the reasons why students at a public university use social networking sites. The study group consists of 387 students studying at the School of Health Services of a public university in the spring semester of the 2024-2025 academic year and using social networks. A survey consisting of questions on social network fatigue, social network overload, and social network victimization was used in the study. In addition, information on the socio-demographic characteristics of the participants participating in the study and the use of social networking platforms were also collected. The study examined which social networking platforms the participants used, the duration of social networking, and whether the daily average time spent on these platforms varied according to the time variable.

Keywords: Sosyal Ağ, Sosyal Platformlar, Sosyal Ağ Yorgunluğu, Sosyal Ağ Mağduriyeti.

BİR KAMU ÜNİVERSİTESİNDEKİ ÖĞRENCİLERİN SOSYAL PLATFORMLARI KULLANIM DURUMUNA GÖRE SOSYAL AĞ YORGUNLUK DÜZEYLERİNİN BELİRLENMESİ

ÖZET

Bu çalışmanın amacı bir kamu üniversitesindeki öğrencilerin sosyal ağ sitelerini kullanım nedenlerini belirlelemektir. Araştırmanın grubu bir kamu üniversitesinin Sağlık Hizmetleri Meslek Yüksekokulunda 2024-2025 akademik yılında bahar döneminde öğrenim gömekte olan ve sosyal ağları kullanan 387 öğrenci oluşturmaktadır. Araştırmada sosyal ağ yorgunluğu, aşırı sosyal ağ yüklenmesi, sosyal ağ mağduriyeti sorularından oluşan bir anket kullanılmıştır. Ayrıca araştırmaya katılan katılımcıların sosyo-demografik özellikleri ile sosyal ağ platformlarının kullanımına ait bilgiler de toplanmıştır. Araştırmada katılımcıların hangi sosyal ağ platformlarını kullandıkları, sosyal ağ kullanım süreleri, günlük ortalama bu platformlarda geçirilen zaman bu platformları zaman değişkenine göre farklılık gösterip göstermediği incelenmiştir.

Anahtar Kelimeler: Sosyal Ağ, Sosyal Platformlar, Sosyal Ağ Yorgunluğu, Sosyal Ağ Mağduriyeti.

GİRİŞ

Günümüzde teknoloji sosyal ve kültürel hayata olan etkisi artık tartışılamaz bir durumadır. Bunu sebebi olarak teknolojilerin ve internetin hızlı bir şekilde artması olarak gösterebiliriz ve internetin hızlı hızlı değişimlerin, bir sonucu olarak toplumda yaşayan bireylerin de iletişim kurma alışkanlıklarında da değişikliklere sebep olmuştur. Dolayısıyla iletişim teknolojisi dönüştürücü bir güce sahiptir diyebiliriz. Bu güçle bireylerin hatta toplumların iletişim alışkanlığını da kendisine uyarlamaya başlamıştır. Bunun sonucu olarak yeni bir sosyalleşme yapısı ortaya çıkmıştır. Özellikle 2000'li yıllarda akıllı telefonların hızlı bir şekilde gelişimi ve kullanımın artması ile genç nüfusun sosyal ağları kullanımı daha kolay hale gelmiş ve kullanımda bir artış olduğu da görülmüştür. Ayrıca sosyal ağ platformlarının üyelik sayısının her geçen gün artması ve bu platformlarda özellikle gençlerin geçirdiği süreler göz önünde bulundurulunca sosyal ağlarla iletişim artık bir iletişim biçimi olarak toplumda önemli bir yer aldığının önemli göstergelerinden biridir (Karaoglan Yilmaz, Yilmaz, R. 2018).

Sosyal medya kavramı ilk olarak yine 2000'li yılların başında ortaya çıkmıştır. Ardından 2003 yılında ise başta Facebook ve Twitter gibi çok sayıda sosyal medya platformlarının ortaya çıkması birlikte kullanımları artmıştır. Sosyal ağ Platformları, kullanıcılarına bir profil oluşturma ve platformda profil oluşturan diğer kullanıcılarla etkileşimde bulunmasına izin veren ağlardır. Günümüzde kullanımları hızlı yaygınlaşan sosyal platformlar, özellikle üniversite öğrencilerinin günlük olarak hem kişisel iletişimlerine olanak sağlayan, özellikle pandemi döneminde eğitim-öğretim süreçlerine katkıda bulunmuştur. Bunun yanında eğlence, alışveriş, iş bulma, ticaret yapma ve bunun yanında daha sayamadığımız birçok alanda kullanıcılarına olanak tanıdığı için kişilerin hayatına hakim olmuştur. (Karaoglan Yilmaz, Yilmaz, R. 2018.).

Dijital Türkiye 2025 raporunda yer alan verilere göre We are Social ve Meltwater tarafından hazırlanan rapora bakacak olursak; Türkiye'de internet kullanan kişi sayısının 77 milyona ulaştığı, Sosyal ağ kullanıcı sayısının son 1 yıl içerisinde % 1,7 artarak 58,6 milyona ulaştığı görülmektedir. Sosyal ağ kullanıcı sayılarının cinsiyet durumuna göre değerlendirildiğinde % 46,5'sının kadın, %53,4'ünün ise erkek olduğu görülmektedir. İnternet kullanıcılarının günlük olarak ortalama 7 saat 13 dakikayı internette geçirdiği, bunun 2 saat 43 dakikasını ise sosyal medyada aktif kullancı olarak geçirdikleri görülmektedir. Bunun yanında aylık ortalamaolarak 6-7 sosyal medya platformunun kullanıldığı görülmektedir. Türkiyede sosyal platformlardan en çok zaman geçirilen platformun Instagram olduğu tespit edilmiştir. Ayrıca aynı çalışmada sosyal medya kullanıcılarının, sosyal medya hesaplarını daha çok arkadaşlarını, aile üyelerini, tanıdıklarını, ya da satın almak istedikleri ürünleri takip amaçlı kullandığı görülmüştür. (https://datareportal.com/reports/digital-2025-global-overview-report.ErişimTarihi:15.05.2025)

Türkiye 2025 dijital raporuna göre kullanıcı sayısının en yüksek olduğu sosyal ağ platformunun 58,5 milyon kişi ile Instagram olduğu, Instagram'ın ardından 57,4 milyon kişi ile YouTube, arından ise 40,2 milyon kullanıcı ile TikTok takip ettiği raporlanmıştır. Söz konusu raporda Facebook'un kullanıcı sayısının 34,7 milyon kişi X platformunun kullanıcı sayısının ise 19,6 milyon kişinin kullandığı görülmektedir. Raporda kullanım süreleri ise ayda ortalama 32 saat 35 dakika ile en çok Instagram'da zaman geçirdiği ardından TikTok'ta 26 saat 27 dakika , YouTube'da ise aylık ortalama sürenin 23 saat 31 dakika olduğu belirtilmiştir. Geri kalan sosyal sırasıyla Facebook'ta süre 9 saat 46 dakika, X'te ise 5 saat 3

dakika olduğu belirlenmiştir.(https://www.meltwater.com/en/2025-global-digital-trends.ErişimTarihi:15.05.2025)

Yayınlanan rapora göre Instagram, Facebook ve X platformu kullanıcısının kullanım sayısında artışı olduğu görülse bile bunun yanı sıra sosyal medya kullanıcıların bazı nedenlerden dolayı sosyal platformlardan uzaklaştığı gözlemlenmiştir. Bu durumözellikle sosyal platform sağlayıcıları tarafından farkedilmiş ve bu düşüşü engellemek için sosyal platformlarda bir takım güncellemeler yapmışlarve platform kullanıcılarını geri kzanmaya çalışmışlardır. Örnek olarak Facebook bir çok farklı ara yüz eklemiş ve video sürelerinin uzatılması, canlı yayın gibi yenilikler getirmiş ve kullanıcılarını geri kazanmaya çalışmıştır. Hatta Facebook 'arkadaş etiketleme' gibi özellikler eklemiş fakat kişisel veriler ve gizlilik endişesi bu durumu değiştirmemiş aksine kullanıcıların uzaklaşmasına sebep olmuştur. (Acar, N.2025)

Gartner Dijital Danışmanlık şirketi yaptıkları pazar araştırmaları sonucunda 2010-2011 yıllarında düşüşü fark etmişlerdir. Araştırmaraporlarına göre; katılımcıların %23'ünün sosyal ağları ve sosyal platformları önceki yıllara göre daha az kullandığını ortaya çıkarmıştır. Bunun yanında Paw araştırma şirketi 2013 yılında yapılan diğer bir araştırmada ise; kullanıcıların %60'nın sosyal platformlarını bir süreliğine dondurduğu görülmüştür. Özellikle Çin de sıkça kullanılan ve tercih edilen QQ Zone isimli sosyal platformun son 3 yılda 60 milyondan fazla kullanıcı kaybettiği ve yine Çin'e popüler olan sosyal ağ platformlarından olan Renren, son 10 yıl boyunca 31 milyona yakın kullanıcısının hesaplarını sildiğini ortaya çıkarmıştır. Bu durumu Pazar şirketleri 'Sosyal Ağ Yorgunluğu' olarak yorumlamıştır. Sosyal ağ ile ilgili akademik açlışmaların 2012 yılında yapılmaya başlandığı görülmüş ve bu duruma zemin hazırlayan sebepler belirlenmeye çalışılmıştır.(Başoğlu D., Yanar Ş. 2017)

Araştırmanın Amacı

Bu araştırmanın amacı literatürde yeni olarak yer alan sosyal ağ yorgunluğu ve sebeplerini belirlemeye çalışmaktır. Bu amaçla sosyal ağ kullanıcılarının sosyal ağ yorgunluğunu hangi düzeyde ve hangi baskın olarak yaşadığını bulmaya çalışmaktır. Buradan yola çıkarak aşağıdaki araştırma soruları ve hipotezleri değerlendirebiliriz.

H1: Katılımcıların sosyal ağ yorgunluk düzeyleri ile cinsiyetleri arasında anlamlı bir fark bulunmaktadır,

H2: Katılımcıların sosyal ağ yorgunluk düzeyleri, yaşa göre anlamlı bir fark bulunmaktadır,

H3: Katılımcıların sosyal ağ yorgunluk düzeyleri ile haftada kullanım gün sayısı, arasında anlamlı bir fark vardır,

H4: Katılımcıların sosyal ağ yorgunluk düzeyleri ile sosyal platform dondurm, arasında anlamlı bir fark vardır,

H5: Katılımcıların sosyal ağ yorgunluk düzeyleri ile gün içi kullanım süresi arasında anlamlı bir fark vardır,

Araştırmanın Önemi

Bu çalışma; - "Sosyal Ağ Yorgunluğu" gibi yeni bir kavramın açıklanmasına yönelik bir çalışma olması,

- literatüre yeni giren “Sosyal Ağ Yüklenmesi” gibi yeni kavramların tanımlanması ve çerçevesinin belirlenmesi

- Sosyal Platform kullanıcılarının sosyal ağlara yönelik kullanım tutumlarının belirlenmesi

-Sosyal ağ platformlarının hem kullanıcılar hem de sektörde yer alanlara gelecekteki kullanım durumu hakkında fikir vermesi bakımından önem taşımaktadır.

Sınırlılıklar

-Araştırmanın uygulama kısmının sadece bir kamu üniversitesinin sağlık hizmetleri meslek yüksekokulundaki öğrenciler ile sınırlandırılmıştır.

Araştırmanın Yöntemi

Araştırmanın evrenini bir kamu üniversitesinin Sağlık Hizmetleri Meslek Yüksekokulunda öğrenciler oluşturmaktadır. Sağlık Hizmetleri Meslek Yüksekokulunda aktif kayıtlı olarak 1800 öğrenci olduğu öğrenci işlerinden bilgi alınarak belirlenmiştir. Sağlık Hizmetleri Meslek Yüksekokulunda 2024-2025 Bahar döneminde öğrenim gören öğrenciler oluşturmaktadır.

Krejcie ve Morgan (1970) yılında önermiş olduğu örneklem hesabından yararlanılmıştır. Tabloda, %95 güven aralığı dikkate alındığında; olayın görülme p=0,5 ve görülmeme sıklığının q=0,5 olmasına göre olması halinde araştırmaya en az 387 kişinin katılmasının yeterli olacağı belirlenmiştir Yine bu 1800 öğrenciden bir örneklem grubu seçilerek %95 güven aralığında 387 öğrenciye rastgele ulaşılmış ve ankete katılımları sağlanmıştır.

Sosyal Ağ Yorgunluğu Ölçeği (SAYÖ) 2012 yılında Maier ve diğerleri tarafından pazar şirketlerinin aynı yıl ortaya attığı platformların kullanıcı sayılarındaki düşüş iddiasını araştırmak üzere hazırlanmıştır.

Araştırmada toplam 51 sorudan oluşan 3 farklı ölçek kullanılmıştır. Çalışmamızın ilk kısmında sosoyal ve demografik özellikleri belirlemeye yönelik sorular yer almıştır. Çalışmaya katılan katılımcılara sosyal ağ kullanım sıklıkları, süre ve türleri ile gelecekteki sosyal ağ kullanım amaçlarını belirlemek için de sorular sorulmuştur. Böylece çalışmamız toplamda 64 sorudan oluşan bir form haline gelmiştir.

Araştirmanin Hipotez Sonuçlari ve Bulgulari

Araştırmamız dört bölümden oluşmaktadır. İlk bölümünde, katılımcılardan demografik bilgilerine yönelik veriler elde edilmeye çalışılmış ve bunu belirleyen sorular yer almaktadır. İkinci bölümünde ise öğrencilerin haftalık, günlük ve bir oturumdaki kullanım süreleri ile ilgili kullanım sürelerine ulaşılmaya çalışılmıştır. Üçüncü bölümde ise sosyal medya kullanım alışkanlıkları tespit edilmeye çalışılarak hangi sosyal ağları kullandıkları, saptanmaya çalışılmıştır. Bunun yanında sosyal paltformları dondurmaeğilimlerinin sosyal ağ yorgunluğu ileilişkisinin olup olmadığına bakılmıştır

Tablo:1

Değişkenler	f değeri	%
Erkek	82	25,0
Kız	305	75,0
Total	**387**	**100,0**

Bir haftada ne kadar süre sosyal ağ platformlarını ziyaret ediyorsunuz			
		Frekans	Yüzde
Süre	Haftada 1 gün	7	1,8
	Haftada 2-3 gün	22	5,7
	Haftada 4-5 gün	39	10,1
	Her gün düzenli	319	82,4
	Toplam	**387**	**100,0**

Yaş			
		Frekans	Yüzde
	18 Yaşında	50	12,9
	19 Yaşında	74	19,1
	20 Yaşında	113	29,2
	21 Yaşında	68	17,6
	22 Yaşında	37	9,6
	23 Yaş ve Üzerinde	45	11,6
	Toplam	**387**	**100,0**

Normal bir günde ne kadar süre sosyal ağ kullanıyorsunuz		
Süre	Frekans	Yüzde
1-3 Saat Arası	55	14,2
3-5 Saat Arası	153	39,5
5-7 Saat Arası	107	27,6
7 Saat ve Daha Fazla	72	18,6
Toplam	**387**	**100,0**

Bir oturumda genelde kaç dakika sosyal ağ platformlarını ziyaret ediyorsunuz			
		Frekans	Yüzde
Süre	1-10 Dakika Arası	33	8,5
	10-30 Dakika Arası	138	35,7
	30-50 Dakika Arası	126	32,6
	60 Dakika ve Üzeri	90	23,3

Tablo:2 Sosyal Ağ Platforma Kullanıcı dağılımı

INSTAGRAM	352
SNAPCHAT	92
WHATSAPP	324
TİKTOK	157
YOUTUBE	228
X PLATFORMU	44
FACEBOOK	3
LINKEDIN	4

Tablo:3 Cinsiyete Göre Sosyal Ağ Yorgunluğu

Cinsiyet		**N**	**Ort.**	**St. Sapma**	**St. Hata Ort.**	**P**
	Kadın	**305**	**2,3974**	**,64171**	**,03674**	**0,02**
	Erkek	**82**	**2,2019**	**,77594**	**,08569**	

Cinsiyet ile sosyal ağ arasında anlamlı bir farklılık vardır ($p<0.05$). Farklılığın kaynağı olarak erkek katılımcılar oluşturmaktadır. Erkek öğrencilerin, kız öğrencilere göre daha az bir oranda sosyal ağ yorgunluğu yaşadığı görülmektedir.

Tablo :4 Yaşa Göre Sosyal ağ yorgunluğu

Yaş					
	Kareler Top.	**df**	**Ort. fark**	**F**	**P**
Gruplar arası	**2,953**	**5**	**,591**	**1,297**	**,264**
Gruplar içi	**173,469**	**381**	**,455**		
Toplam	**176,422**	**386**			

Yaş aralığımız birbirine yakın olduğu için yaşa göre sosyal ağ yorgunluğu düzeyinde anlamlı bir fark bulunamamıştır.

Tablo:5 Bir haftada sosyal ağ kullanım süresi

Haftalık gün sayı					
	Kareler Top.	**df**	**Ort. Fark**	**F**	**Sig.**
Gruplar arası	**2,147**	**3**	**,716**	**1,573**	**,196**
Gruplar içi	**174,275**	**383**	**,455**		
Toplam	**176,422**	**386**			

Bir haftada sosyal platformlarda geçirilen gün sonuçlarına göre anlamlı bir fark yoktur. Haftadaki kullanım gün sayısı arttıkça kullanım süresi artmasına rağmen bu artış istatistiki olarak anlamlı bulunmamıştır.

Tablo:6 Sosyal Platformları dondurma

Sosyal Platform Dondurma süresi	Kareler Toplamı	df	Ortalama Fark	F	Sig.
Gruplar arası	,767	4	,192	,417	,796
Gruplar içi	175,655	382	,460		
Toplam	176,422	386			

Sosyal platform hesaplarını dondurma ve sosyal ağ yorgunluğu arasında anlamlı bir fark bulunamamıştır.

Tablo:7 Sosyal Platformlarda gün içi geçirilen süre

Günlük süre	Kareler Toplamı	df	Ortalama Fark	F	Sig.
Gruplar arası	3,658	3	1,219	2,703	,045
Gruplar içi	172,764	383	,451		
Toplam	176,422	386			

Bir günde sosyal ağ kullanımı ile sosyal ağ arasında anlamlı bir farklılık vardır ($p<0.05$). Farklılığın kaynağı ise 1-3 saat kullananlara göre 7 saat ve daha fazlasında kullananlar oluşturmaktadır.

Tartışma Sonuç ve Öneriler

Yapılan çoğu araştırmalarda çıkan sonuçlara baktığımız zaman çdaha çok iç sebepler olan demografik sebeplere dayalı olduğu görülmektedir. Literatürü incelediğimizde Ravindran ve diğerleri (2013), Ravindran ve diğerleri (2014) ile Lee ve diğerleri (2014) sosyal ağ yorgunluğunun iç sebeplerin; kişilik özellikleri olarak tanımlamışlardır. Sosyodemografik özellikleri ise bu sebepler grubunda tanımlayabiliriz. Buna rağmen çoğu araştırmacılar (Ravindran vd., 2013) sosyal ağ yorgunluğunun iç etmenlerinin hala tam olarak belirlenmediğini göstermişlerdir. Çünkü Ravindran ve diğerleri 2016 yılında yaptığı literatür çalışmalarında özellikle kişilerin cinsiyet ve yaş gibi sosyo-demografik özelliklerine göre sosyal ağ yorgunluğunun açıklanabilir derken Zhang ve diğerleri (2016) sadece cinsiyet ve yaşın sosyal ağ yorgunluğunda belirleyici bir neden olduğunu yaptıkları çalışmalarda ortaya koymuşlardır. Yine genel literatür çalışmalarına baktığımızda sosyal ağ yorgunluğunun belirlenmesi amacıyla yapılan çalışmalarda özellikle yaş ve cinsiyete ile ilgili çalışmaların yapıldığı göze çarpmaktadır. Gou ve diğerlerinin 2020 yılında yaptığı araştırmada araştırmaya katılanları cinsiyet ve yaşlarının yanında çalışma durumu gelir ve eğitimin de bağımsız değişken olarak etkilediğini belirtmişlerdir. Fakat çalışmamızın kısıtlılıklarında

belirttiğimiz gibi öğrenci grubumuz olduğu için bu değişkenler göz önünde bulundurulmamıştır.; Shi ve diğerleri, Yu ve diğerleri (2020) ile Lin ve diğerlerinin (2021) elde ettiği sonuçların aksine bu çalışmamızda çalışmaya katılan grubumuzda sosyal ağ yorgunluklarının cinsiyet açısından anlamlı bir fark olduğu ortaya çıkmıştır. Bu farklılığın sebebi olarak ise erkek öğrenciler olduğu görülmektedir. Yine çalışmamızda sosyal ağ yorgunluğuna kız öğrencilerin erkek öğrencilere oranla daha fazla sosyal ağ yorgunluğuna maruz kaldığını görmekteyiz. Çalışmamızın diğer bir bağımsız değişkeni olarak ise yaş üzerinde yapılmıştır. İlk olarak Zhang ve diğerleri (2016) araştırmalarına baktığımızda yaş arttıkça sosyal ağ yorgunluğunun da arttığın her ne kadar görsek ise de çalışmamızda katılımcıların üniversite öğrencisi olmaları ve yaş gruplarının birbirine çok yakın olması yaşın sosyal ağ yorgunluk üzerinde anlamlı bir etkisinin olmadığını görmekteyiz.

Araştırmamızdaki katılımcılara en çok hangi platformu kullanıyorsunuz sorusuna birbirinden irinden farklı platformları kullandıklarını görmekteyiz. Buna rağmen ilk sırada Instagram ikinci sırayı WhatsApp ve yine üçüncü sırayı ise YouTube olduğunu görmekteyiz. Her ne kadar 2025 yılı dijital raporumuzda en çok kullanılan platformlarda ilk üçte Tik Tok olduğu görülse de çalışmamızda ilk üçte yer alamamaktadır.

Fu ve diğerleri 2020 yılında yaptığı bir araştırmada kullanılan platform olan Facebook ile sosyal ağ arasında ilişki varımdır sorusuna anlamlı bir ilişki olmadığı görülmüştür. Yapılan çalışmamızda kullanılan platform türü ile sosyal ağ yorgunluğunun arasında bir ilişkiye rastlanmadığı görüşmüştür.

Çalışmamızın diğer bir sonucu ise kullanım süreleri ile ilgilidir. Çalışmamızda haftalık ve günlük sosyal platformlarda kullanım sürelerinde haftalık bazda sosyal platformun her gün düzenli olarak kullanıldığı, günlük bazda ise süreler ise kullanıcıların bir günde ortalama 3 ile 5 saat arası sosyal ağlarda zaman geçirdiğini göstermektedir. Sürenin bu kadar fazla olmasından dolayı sosyal yorgunluğun doğru orantıda arttığını görmekteyiz.

Genel bir sonuç değerlendirmesi yapacak olur isek sosyal medya kullanımı zamanla kullanıcıların çok fark edemediği bir "yorgunluk" haline dönüşmüştür. Çalışmamızda sosyal ağ yorgunluğunu çeşitli boyutlarıyla ele alınmaya çalışılmıştır. Bununla birlikte genel olarak diyebiliriz ki yorgunluğa neden olan sorunların başında, genellikle aşırı ve gereksiz bilgi yüklenmesine maruz kalmak, teknolojiye vazgeçilmez boyutta olan bağımlılığı sayabiliriz.

Kullanıcılarda, platformlarda yer alan bilgi kaynağına ve hızına yetişmeye çalışması, aşırı sosyalleşme çabası bunun yanında kendini gelişmeleri takip etmek zorunda hissetmesi gibi iletişim aktiviteleri, sosyalleşme çabaları bir stres kaynağı haline geldiğini görmekteyiz bunun yanında dış çevresel uyaranların çokluğu eklenince sosyal yorgunluğun kaçınılmaz bir durum olduğu görülmektedir.

Çalışmamızın bir bölümü olan sosyal mağduriyette başlıca sosyal yorgunluk etmenleri arasındadır. Sosyal platformlarda yaşanan fiziksel ve psikolojik zorbalanmalar diğer sosyal yorgunluğu arttıran etmenlerdendir.

Özellikle sosyal ağ yorgunluğu konusunun akademisyenlerinin araştırma yapmaları gerken alanlara arasında yer alması, sosyal ağ yorgunluğunun yapılan çalışmalar sonucu görüşleri ve önerileri çerçevesinde tartışılmasını ve araştırılmasını gerektiği düşünülmektedir. Sosyal ağ yorgunluğunun altında yatan nedenleri ortaya çıkarmak bu nedenleri önleyici çözümleri geliştirmek ve bu sosyal ağ yorgunluğu ile başa çıkma konusunda kuşkusuz en önemli sonuçlardan biri olduğu düşünülmekedir.

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ALEXITHYMIA IN EPILEPSY

ABSTRACT

People with epilepsy may experience various physical problems, and over time these problems can also affect their emotional and mental areas. Alexithymia is a concept that focuses on the difficulties individuals experience in recognizing, understanding and expressing their emotions, as well as the limited capacity to dream. When the concept was first put forward, it was observed that alexithymic individuals showed a large number of physical symptoms, had difficulty using their imagination, and had difficulty finding appropriate words to express their feelings. The conversations of these individuals are often full of repetitive details. It has been stated that they rarely dream, and they tend to exhibit either an overly dependent or distant attitude in their interpersonal relationships. In the literature, many chronic diseases such as asthma, allergies, essential hypertension, cancer, myocardial infarction, angina pectoris with coronary spasm, diabetes and inflammatory bowel disease have been found to be associated with alexithymia. Individuals with alexithymic characteristics have difficulty in distinguishing emotional arousal from physical arousal so they often use physical symptoms to express their emotions. Studies examining alexithymia in individuals with epilepsy have shown that individuals with epilepsy often experience difficulties in identifying emotions, emotional dysregulation, and especially issues such as rejection. It is known that alexithymia and emotion disorder negatively affect the quality of life of individuals with epilepsy and it is reported that it affects the suicidal tendencies of individuals. Alexithymia, defined as emotional blindness and the inability to identify and describe emotions, is commonly observed in the epileptic population, and it has been reported that these patients have more difficulty in recognizing and expressing their emotions compared to the healthy population. It is known that uncontrolled seizures inherent in epilepsy cause depression-induced alexithymia. In this review, the condition of alexithymia in individuals with epilepsy will be discussed.

Keywords: Epilepsy, Alexithymia, Nursing.

EPİLEPSİDE ALEKSİTİMİ

ÖZET

Epilepsili kişiler çeşitli fiziksel sorunlar yaşayabilir ve zamanla bu sorunlar duygusal ve zihinsel alanlarını da etkileyebilir. Aleksitimi, bireylerin duygularını tanıma, anlama ve ifade etmede yaşadığı güçlüklerin yanı sıra hayal kurma kapasitesinin sınırlılığına odaklanan bir kavramdır. Kavram ilk ortaya atıldığında aleksitimik bireylerin çok sayıda fiziksel belirti gösterdiği, hayal gücünü kullanmakta zorlandığı, duygularını ifade edecek uygun kelimeleri bulmakta güçlük çektiği gözlemlenmiştir. Bu bireylerin konuşmaları genellikle tekrarlayan detaylarla doludur. Nadiren rüya gördükleri belirtilmiş ve kişilerarası ilişkilerinde ya aşırı bağımlı ya da mesafeli bir tutum sergileme eğiliminde oldukları belirtilmiştir. Literatürde astım, alerjiler, esansiyel hipertansiyon, kanser, miyokard enfarktüsü, koroner spazmlı angina pektoris, diyabet ve inflamatuar bağırsak hastalığı gibi birçok kronik hastalığın aleksitimiyle ilişkili olduğu belirlenmiştir. Aleksitimik özelliklere sahip bireyler duygusal uyarılmalarını fiziksel uyarılmalardan ayırt etmekte zorlandıkları için duygularını ifade ederken çoğunlukla bedensel belirtileri kullanmalarıyla dikkat çekerler. Epilepsili bireylerde aleksitimiyi inceleyen çalışmalar, epilepsili bireylerin duyguları tanımlamada zorluk, duyguların düzensizliği, özellikle kabul etmeme gibi durumların yaygın olduğunu göstermektedir. Aleksitimi ve duygu düzensizliğininin epilesili bireylerin yaşam kalitesini olumsuz etkilediği bilinmekte ve bireylerin intihara yönelimlerine etki yaptığı bildirilmektedir. Duygu körlüğü ve duyguları tanımlama ve açıklama yetersizliği olarak tanımlanan aleksitimi, epilepsili popülasyonda sıklıkla görülmektedir ve bu hastaların sağlıklı popülasyona kıyasla duygularını tanıma ve ifade etmede daha fazla zorluk çektikleri bildirilmektedir. Epilepsinin doğasındaki kontrolsüz nöbetlerin depresyon kaynaklı aleksitimiye neden olduğu bilinmektedir. Bu derlemede, epilepsili bireylerde aleksitimi durumu ele alınacaktır.

Anahtar Kelimeler: Epilepsi, Aleksitimi, Hemşirelik.

GİRİŞ

1. Epilepsi-Aleksitimi

Epilepsi, beyin kaynaklı nörolojik bir bozukluk olup tekrarlayıcı nöbetlerle karakterizedir. Son yıllarda epilepsinin sadece nöbetlerle sınırlı kalmadığı, psikososyal ve duygusal zorluklarla da yakından ilişkili olduğu gösterilmiştir.[1] Bu çerçevede, aleksitimi, epilepsi hastalarında sıkça görülen, duyguların tanınması ve ifade edilmesinde yaşanan zorluklarla kendini gösteren bir durum olarak dikkat çekmektedir. [2] Bu derlemede, epilepsi hastalarında aleksitiminin yaygınlığı, etkileri ve olası nedenleri güncel bilimsel kaynaklar doğrultusunda ele alınmaktadır.

Aleksitimi terimi, Yunanca kökenli olup literatüre ilk kez Sifneos tarafından kazandırılmıştır ve "duygulara dair sözcüklerin yokluğu" anlamına gelmektedir.[3] Bireyin duygularını tanımlamada, bedensel duyumlardan ayırt etmede, duygularını ifade etmede ve soyut düşünme becerisinde yaşadığı güçlükler aleksitimi kavramıyla açıklanmaktadır.[4] Aleksitiminin kökeni ve niteliğiyle ilgili farklı görüşler bulunmakta olup; bazı araştırmacılar bunu kişisel bir eğilim, sosyal desteğin yetersizliği sonucu gelişen bir durum, psikolojik bir rahatsızlık, klinik bir belirti, psikosomatik bir hastalık, bilişsel bir yetersizlik, kişilik özelliği ya da nörolojik bir bozukluk olarak değerlendirmektedir.[5] Nörolojik temelli bu yapı, özellikle ön singulat korteks, insula ve prefrontal alanlardaki disfonksiyonlarla ilişkilendirilir.[6] Bu beyin bölgeleri aynı zamanda epilepside sıkça etkilenen alanlardır; özellikle temporal lob epilepsisi olan hastalarda duygusal işlemleme bozuklukları sıkça görülmektedir.[7] Batı toplumlarında yaşan bireyler duygularını kolaylıkla ifade edilebilirken, doğu toplumlarında yaşayan bireyler duyguları ifade etmek yerine bastırmayı tercih edebilmektedir.[4] Türkiye bu açıdan duyguların ifade edilemediği ve bedenselleştirildiği toplumlar arasında yer almaktadır.[8] Aleksitimik bireylerin duygusal uyarılmaları, fiziksel uyarılmalardan ayırt edememeleri, duygularını ifade ederken sıklıkla bedensel belirtilere başvurmalarıyla kendini göstermektedir.[9] Bu bireylerin, duygularını sözel olarak dile getirmekte zorlandıkları ve yaşadıkları duygusal deneyimleri fiziksel şikayetler, özellikle de ağrılar yoluyla dışa vurdukları düşünülmektedir.[10-13]

2. Epilepsi ve Aleksitimi İlişkisi

Epilepsili bireylerde aleksitimi prevelansı %30-%50 aralığında değişmekle birlikte sıklıkla görülen bir durumdur.[14,15]

2.1 Temporal Lob Epilepsisi ve Aleksitimi

Temporal lob epilepsisi (TLE), aleksitimi ile en sık ilişkilendirilen epilepsi türüdür. Bu hastalarda, özellikle sağ hemisfer kaynaklı nöbetlerin, duygusal farkındalık üzerinde daha fazla bozulmaya neden olduğu bildirilmiştir.[16] TLE hastalarında yapılan çalışmalarda, Toronto Aleksitimi Ölçeği (TAS-20) ile ölçülen aleksitimi puanlarının, sağlıklı bireylere kıyasla anlamlı derecede yüksek olduğu bulunmuştur.[17]

2.2 Nöbet Tipi ve Aleksitimi Düzeyi

Fokal nöbet geçiren hastalarda aleksitimi düzeylerinin, jeneralize nöbet geçirenlere kıyasla daha yüksek olduğu bulunmuştur. Bu farkın, duygusal işlemleme ile ilgili beyin bölgelerinin lokal etkilenmesinden kaynaklandığı düşünülmektedir.[18]

3. Epilepsi, Psikopatoloji ve Aleksitimi

Epilepsi hastalarında depresyon, anksiyete ve sosyal geri çekilme gibi psikolojik belirtiler aleksitimi ile ilişkili bulunmuştur.[19] Aleksitimi düzeyi yüksek bireylerin, duygularını tanıyamadıkları ve ifade edemedikleri için stresle başa çıkmada zorlandıkları, bu durumun da psikolojik bozuklukları tetiklediği ileri sürülmektedir.

Epilepsili bireylerde yapılan çalışmalar, yüksek aleksitimi düzeylerinin yaşam kalitesi üzerinde olumsuz etkiler yarattığını göstermektedir. Özellikle duygusal farkındalık ve dışavurum becerileri zayıf olan bireylerin, sosyal ilişkilerde güçlük yaşadıkları, hastalıkla baş etmede zorlandıkları ve genel yaşam memnuniyetlerinin düştüğü bildirilmiştir. Ayrıca, aleksitiminin hem fiziksel hem de duygusal yaşam alanlarında belirgin etkileri olduğu saptanmıştır.[19] Epilepsi hastalarının çoğu, nöbetlerin yarattığı belirsizlik ve toplumsal damgalama gibi nedenlerle hali hazırda psikolojik baskı altındadır. Eğer bu bireylerde aleksitimi mevcutsa, bu baskılarla başa çıkmak daha da zor hale gelir. Yapılan bazı çalışmalar, aleksitimi düzeyi yüksek epilepsi hastalarının daha fazla sosyal izolasyon yaşadığını ve öz-bakım davranışlarında azalma gözlendiğini ortaya koymuştur.[2,18]

4. Klinik Önemi ve Tedavi

Aleksitimi kavramı, başlarda psikosomatik hastalardaki semptomları tanımlayabilmek için ortaya atılmış olsa da günümüzde sadece bu hastalarda değil, ruhsal ve fiziksel diğer hastalıklarda da sıklıkla karşılaşılan bir durum olduğu belirtilmektedir.[20-22] Klinik çalışmalar incelendiğinde; hipertansiyon, osteoartrit, fibromiyalji, astım, sistemik lupus eritematozus tanısı konan pek çok kronik hastalıklı bireylerle yapılmış çalışmaların mevcut olduğu görülmektedir. Ve bu çalışmalar aleksitimik özelliklerin normal popülasyona göre kronik hastalığı olan bireylerde de yüksek olduğunu göstermektedir.[10,20,21] Epilepsi tedavisinde aleksitimi kritik sonuçlar açısından önemli bir değişken olmasına rağmen çoğu zaman göz ardı edilen bir durumdur. Yüksek aleksitimi düzeyine sahip epilepsi hastaları, genellikle duygusal belirtilerini yeterince tanımlayamadıkları için depresyon, anksiyete gibi durumlar gözden kaçabilir. Bu da yaşam kalitesinin daha da bozulmasına neden olur. Bu nedenle, klinik uygulamalarda aleksitiminin erken tanılanması, bireysel psikoeğitim ve duygusal beceri kazandırma müdahaleleriyle yaşam kalitesinin artırılması mümkündür.[23] Duygusal farkındalığı artırmaya yönelik psikoeğitim, duygu odaklı terapi (emotion-focused therapy) ve mindfulness temelli terapilerin epilepsi hastalarında aleksitimi düzeylerini azaltmada etkili olabileceği öne sürülmektedir.[23,24] Aleksitimik hastaların uyku kalitesinin daha kötü düzeyde olduğu da bildirilmiştir.[15] Yapılmış farklı bir çalışmada epilepsili bireylerdeki aleksitiminin stigma ile ilişkili olduğu da ifade edilmiştir.[25] Epilepsili bireylerde algılanan damgalama seviyelerinin oldukça yüksek olması aleksitimik özelliklerin daha da yaygın görülmesine neden olabilir.

Aleksitiminin tedavi edilmesi doğrudan kolay olmasa da, psikoeğitim, duygusal farkındalık eğitimi ve bazı psikoterapi yöntemlerinin (özellikle duygu odaklı terapi) aleksitimi düzeyini azaltabileceği düşünülmektedir.[26]

5. Sonuç

Aleksitimi, epilepsi hastalarında sık rastlanan ve hastalığın psikososyal yükünü artıran önemli bir faktördür. Özellikle temporal lob epilepsisi olan bireylerde yüksek aleksitimi düzeyleri dikkat çekmektedir. Bu bulgular, epilepsi yönetiminde yalnızca nöbet kontrolüne değil, duygusal işlevselliğin de değerlendirilmesine ihtiyaç duyulduğunu göstermektedir.

Duygusal tanıma ve ifade becerilerindeki eksiklik, bireyin hastalıkla başa çıkmasını zorlaştırmakta ve sosyal ilişkilerden genel sağlığa kadar birçok alanı olumsuz etkilemektedir. Gelecekte yapılacak çalışmaların, aleksitiminin epilepsi üzerindeki etkilerini daha iyi anlamamıza ve kişiselleştirilmiş tedavi protokollerinin geliştirilmesine katkı sağlayacağı öngörülmektedir. Aleksitimi sabit ve değiştirilemez bir özellik değildir. Bireyin duygusal farkındalığını artırmaya yönelik yapılandırılmış psikoterapiler, yaratıcı terapi yöntemleri ve farkındalık çalışmaları ile anlamlı gelişmeler sağlanabilir. Uygun terapi ile birey, hem kendisiyle hem de çevresiyle daha sağlıklı bir ilişki kurabilir.

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RETROSPECTIVE INVESTIGATION OF COMPLICATIONS ENCOUNTERED IN THE USE OF A DRUG CALLED ANTITHYMOCYTE GLOBULIN (ATG) USED IN STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS

ABSTRACT

Objective: Various adverse drug reactions that may develop due to Antithymocyte Globulin (ATG) use can lead to severe clinical consequences, especially in pediatric patients. This situation reveals the necessity of effective pharmacovigilance practices to ensure drug safety. The study was planned to retrospectively examine the patient follow-up forms of patients who have taken the drug ATG, determine the complications observed during use, and provide data that can guide health professionals in the clinical follow-up and management processes.

Materials and Methods: The patient care plans (n:55) of child patients hospitalized in a university hospital's pediatric stem cell transplantation unit between December 01.12.2017-December 01.12.2019 and received ATG medication for their treatment were formed as a study sample. The complications seen by the researcher were determined by conducting an archive scan. The Chi-square test was used to compare the data. The work started after receiving the necessary ethics committee permits, institution trace, and informed consent forms.

Results: In this study, the gender, age group, diagnosis status, and observed complications of 55 participants were examined. 58.2% of the participants were male, 41.8% were female, and it was noted that the 0-6 age group accounted for the highest proportion (47.3%) in the age group distribution. In the diagnosis distribution, 61.8% of the participants had a non-malignant diagnosis, while 38.2% had a malignant diagnosis. Among the most common complications, hyperthermia (98.2%) and tachycardia (83.6%) came to the fore, while complications such as increased infection and bleeding were observed at lower rates. In addition, the increase in infection and the change in diarrhea conditions according to the periods were significant according to the Pearson Chi-Square test.

Conclusion: The most common side effects observed due to drug use were hyperthermia (98.2%), tachycardia (83.6%), chills (67.3%), and chills/chills (61.8%). It has been found that the majority of side effects occur on the first day of starting drug use. The findings obtained make the process safer and more systematic and improve the quality of care by providing important information for health professionals to strengthen patient monitoring and intervene early on possible side effects.

Keywords: ATG, drug side effect, pediatrics.

ÇOCUK HASTALARDA KÖK HÜCRE NAKLİNDE KULLANILAN ANTİTİMOSİT GLOBULİN (ATG) İSİMLİ İLACIN KULLANIMINDA KARŞILAŞILAN KOMPLİKASYONLARIN RETROSPEKTİF İNCELENMESİ

ÖZET

Amaç: Antitimosit Globulin **(**ATG) kullanımına bağlı olarak gelişebilen çeşitli advers ilaç reaksiyonları, özellikle çocuk hastalarda ciddi klinik sonuçlara yol açabilmektedir. Çalışma, ATG isimli ilacı almış olan çocuk hastaların hasta izlem formlarının geriye dönük incelenmesi ve kullanım sırasında görülen komplikasyonların belirlenip sağlık profesyonellerine klinik izlem ve yönetim süreçlerinde yol gösterici olabilecek veriler sunmak amacıyla planlanmıştır.

Materyal ve Yöntem: Araştırmanın örneklemini bir üniversite hastanesinde 01.12.2017-01.12.2019 tarihleri arasında pediatrik kök hücre transplantasyon ünitesinde yatan ve tedavisinde ATG ilacını alan çocuk hastaların hasta kayıtları (n:55) oluşturmuştur. Veriler araştırmacılar tarafından arşiv taraması yapılarak görülen komplikasyonlar belirlenmiştir. Verilerin analizinde Ki-kare Testi kullanılmıştır. Gerekli etik kurul izinleri, kurum izini ve bilgilendirilmiş onam formları alındıktan sonra çalışmaya başlanmıştır.

Bulgular: Bu çalışmada, 55 katılımcının cinsiyet, yaş grubu, tanı durumu ve gözlemlenen komplikasyonları incelenmiştir. Katılımcıların %58,2'si erkek, %41,8'i kadın olup, yaş grubu dağılımında 0-6 yaş grubunun en yüksek oranı (%47,3) oluşturduğuna dikkat çekilmiştir. Tanı dağılımında ise katılımcıların %61,8'i non-malign bir tanıya sahipken, %38,2'si malign tanıya sahiptir. En yaygın komplikasyonlar arasında hipertermi (%98,2) ve taşikardi (%83,6) ön plana çıkarken, enfeksiyon artışı ve kanama gibi komplikasyonlar daha düşük oranlarda gözlemlenmiştir. Ayrıca, enfeksiyon artışı ve diyare durumlarının zaman dilimlerine göre değişimi, yapılan Pearson Ki-Kare testine göre anlamlı bulunmuştur.

Sonuç: İlaç kullanımına bağlı olarak en sık gözlenen yan etkiler hipertermi (%98,2), taşikardi (%83,6), titreme (%67,3) ve üşüme/ürperme (%61,8) olarak belirlenmiştir. Yan etkilerin çoğunluğunun ilaç kullanımına başlanan ilk gün ortaya çıktığı saptanmıştır. Elde edilen bulgular sağlık profesyonellerinin hastaların izlemini güçlendirmesi ve olası yan etkilere yönelik erken müdahalede bulunabilmesi açısından önemli bilgiler sağlayarak sürecin daha güvenli ve sistematik hale getireceği ve bakım kalitesini artıracağı düşünülmektedir.

Anahtar Kelimeler: ATG, ilaç yan etkisi, pediatri.

GİRİŞ

Kök hücre nakli, hematolojik hastalıkların tedavisinde, özellikle çocuk hasta grubunda hayati bir tedavi seçeneği olarak öne çıkmaktadır. Bu süreçte graft reddi, greft versus host hastalığı (GVHH) ve benzeri immünolojik komplikasyonları önlemek amacıyla immünosupresif ajanların kullanımı yaygındır. Antitimosit Globulin (ATG), T lenfositlere karşı geliştirilmiş bir immünoglobulin olup, allojenik kök hücre nakli öncesi kondüsyon rejimlerinde sıklıkla tercih edilmektedir.[1] Tavşan kökenli bir poliklonal antikor olan ATG Fresenius S, bağışıklık sistemini baskılayarak graft reddini önlemeyi ve transplant sonrası komplikasyonları azaltmayı hedefler.[2] Ancak ATG'nin immünosupresif etkisi, beraberinde önemli advers reaksiyonları da getirebilmektedir. Özellikle infüzyon sırasında ya da hemen sonrasında gelişen ateş, titreme, ürtiker, hipotansiyon, baş ağrısı ve gastrointestinal şikayetler gibi yan etkiler sıklıkla bildirilmiştir.[3,4] Bununla birlikte, anafilaksi, sitokin salınım sendromu, trombositopeni, lökopeni, akut böbrek yetmezliği ve ciddi viral enfeksiyonlar gibi hayatı tehdit edici komplikasyonlar da literatürde yer almaktadır.[5,6] Bu yan etkiler, özellikle bağışıklık sistemi henüz tam gelişmemiş olan çocuk hastalarda daha ciddi sonuçlar doğurabileceğinden, ATG uygulamaları sırasında dikkatli izlem ve yan etki yönetimi büyük önem taşımaktadır.[7] Tüm bu nedenlerle, ATG gibi yüksek riskli immünosupresif ilaçların kullanıldığı tedavi protokollerinde, advers ilaç reaksiyonlarının sistematik olarak incelenmesi, ilaç güvenliği açısından temel bir gerekliliktir.

İlaç güvenliğini sağlamada farmakovijilans uygulamaları hayati önem taşımaktadır. Dünya Sağlık Örgütü (2022)[8] ilaç reaksiyonlarını, normal dozda kullanılan ilaçlara karşı gelişen, zararlı ve istenmeyen tepkiler olarak tanımlamaktadır. Ancak Türkiye'de advers ilaç reaksiyonlarının bildirilme oranları oldukça düşüktür.[9] Bu da özellikle yüksek riskli ilaçların kullanımı sırasında oluşabilecek komplikasyonların sistematik şekilde kayıt altına alınmasını ve önleyici tedbirlerin geliştirilmesini zorlaştırmaktadır.

Bu çalışma, çocuk hastalarda kök hücre nakli sürecinde kullanılan ATG Fresenius S adlı ilacın kullanımına bağlı olarak gelişen advers etkilerin ve komplikasyonların retrospektif olarak incelenmesini amaçlamaktadır. Elde edilecek bulgular, bu hasta grubunda ilaç güvenliğini artırmaya yönelik farmakovijilans stratejilerinin geliştirilmesine katkı sağlayacağı düşünülmektedir.

GELİŞME

Gereç ve Yöntem

Araştırmanın Tipi

Bu çalışma, hasta kayıtlarının retrospektif olarak incelenmesiyle gerçekleştirilmiştir.

Araştırmanın Evren ve Örneklemi

Araştırmanın evreni, 01.12.2017-01.12.2019 tarihleri arasında bir üniversite hastanesinin pediatrik kök hücre transplantasyonu ünitesinde yatan tüm çocuk hastaların hasta kayıtlarıdır (n=86). Araştırmanın örneklemi ise, aynı dönemde kök hücre transplantasyonu geçiren, tedavi protokolünde Antitimosit Globulin (ATG) kullanılan, ebeveynlerinin çalışmaya onam verdiği ve hasta kayıtlarında günlük gözlem formlarının eksiksiz yer aldığı 55 çocuk hastadan oluşmaktadır.

Veri Toplama Süreci

Veri toplama sürecinde, araştırmacılar retrospektif bir arşiv taraması yaparak çocuk hastalarda görülen komplikasyonları belirlemiş ve bu veriler, araştırmacı tarafından oluşturulan veri toplama formuna kaydedilmiştir. Veri toplama formu, iki ana bölümden oluşmaktadır. İlk bölümde hastaların sosyodemografik bilgileri (yaş, cinsiyet vb.) yer almakta, ikinci bölümde ise ATG ilacının kullanım süresi, yan etkilerin gelişip gelişmediği, yan etkilerin hangi günlerde görüldüğü ve hangi yan etkilerin ortaya çıktığı gibi bilgiler toplanmıştır.

Çalışmanın verileri, 2017-2019 yılları arasında kök hücre transplantasyonu yapılan hastaların hasta kayıtları incelenerek toplanmıştır. İlgili klinikten alınan hasta kayıtları, Microsoft Excel dosyasında tek tek incelenmiş ve bu veriler ve araştırmacılar tarafından oluşturulan veri toplama formuna aktarılmıştır. Toplamda 86 hasta kaydı incelenmiş, bunlardan 55'inin tedavi sürecinde Antitimosit Globulin (ATG) kullandığı belirlenmiştir. Çalışmanın gerçekleştirilmesi için ilgili sağlık kurumundan 19.02.2020 tarihli ve Karar No: 20-2.1T/9 olan yazılı izin alınmıştır. Hastane yönetiminden gerekli izin alınmış ve çalışmanın etik gereklilikleri doğrultusunda veri toplama süreci başlatılmıştır.

Verilerin Analizi

Toplanan verilerin analizi için SPSS 24 istatistiksel paket programı kullanılmıştır. Sosyodemografik özelliklerin değerlendirilmesi için tanımlayıcı istatistikler hesaplanmış, farklılıkların incelenmesi için ise ki-kare testi uygulanmıştır. İstatistiksel anlamlılık düzeyi $p<0.05$ olarak belirlenmiştir.

Bulgular

Tablo 1. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastaların Cinsiyet, Yaş Grupları ve Tanılarına Göre Dağılımı

Sosyo-demografik Özellik		Sayı	Yüzde
Yaş Grubu	0-6 yaş grubu	26	47.3
	7-12 yaş grubu	13	23.6
	13 yaş ve üzeri	16	29.1
Cinsiyet	Kadın	23	41.8
	Erkek	32	58.2
Tanı	Non-malign	34	61.8
	Malign	21	38.2
TOPLAM		55	100.0

Antitimosit Globulin (ATG) ilacını kullanan çocuk hastaların%58.2'si erkektir**,** %29,1'i 13 ve üzeri yaş grubundadır, %47,3'ü 0-6 yaş grubundadır, %61,8'i non-malign bir tıbbi tanıya sahiptir (Tablo 1).

Tablo 2. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastalarda Gelişen Komplikasyonların Dağılımı

Komplikasyonlar	Gelişen		Gelişmeyen	
	Sayı	Yüzde	Sayı	Yüzde
Hipertermi	54	98.2	1	1,8
Taşikardi	46	83.6	9	16.4
Titreme	37	67.3	18	32.7
Üşüme/Ürperme	34	61.8	21	38.2
Bulantı	24	43.6	31	56.4
Kusma	22	40.0	33	60.0
Hipotansiyon	16	29.1	39	70.9
Kızarıklık	16	29.1	39	70.9
Diyare	15	27.3	40	72.7
Ciltte döküntü	14	25.5	41	74.5
Hipertansiyon	13	23.6	42	76.4
Ağrı	13	23.6	42	76.4
Kaşıntı	10	18.2	45	81.8
Lökositoz / enfeksiyon	8	14.5	47	85.5
Kanama	1	1.8	54	98.2
TOPLAM (n=55)				

Antitimosit Globulin (ATG) ilacını kullanan çocuk hastaların %98.2'sinde hipertermi, %83.6'sında taşikardi, %67.3'ünde titreme, %61.8' inde üşüme/ürperme, %43.6'sında bulantı, %40'ında kusma, %29.1'inde hipotansiyon ve kızarıklık, %27.3'ünde diyare, %25.5'inde ciltte döküntü, %23.6'sında hipertansiyon ve ağrı, %18.2'sinde kaşıntı, %14.5'inde Lökositoz/ enfeksiyon ve %1.8'inde kanama gelişmiştir (Tablo 2).

Tablo 3. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastalarda Diyare Gelişme Günlerine Göre Dağılımı

Diyare/Gün	Gelişen		Gelişmeyen		TOPLAM	
	Sayı	Yüzde	Sayı	Yüzde	Sayı	Yüzde
1.gün	3	11.5	23	88.5	26	100.0
2. gün	9	39.1	14	60.2	23	100.0
3. gün	3	50.0	3	50.0	6	100.0
Toplam	15	27.3	40	72.7	55	100.0
X^2=17.689; p=0.00; p<0.001						

Antitimosit Globulin (ATG) ilacını kullanan çocuk hastalarda diyare gelişme oranının gelişen ve gelişmeyen durumlar arasında zamanla bir fark olduğunu gösteren bu tabloda, Özellikle 1. günde gelişenlerin oranı çok düşükken (sadece %11.5), 2. gün bu oran önemli ölçüde artmış (%39.1) ve 3. gün ise gelişenlerin oranı %50'ye çıkmıştır ve bu farkın istatistiksel olarak anlamlı olduğu belirlenmiştir (X^2=17.689; p=0.00; p<0.001) (Tablo 3).

Tablo 4. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastalarda Lökositoz / Enfeksiyon Gelişme Günlerine Göre Dağılımı

Lökositoz-Enfeksiyon/Gün	Gelişen		Gelişmeyen		TOPLAM	
	Sayı	Yüzde	Sayı	Yüzde	Sayı	Yüzde
1.gün	0		26		26	100.0
2. gün	4		19		23	100.0
3. gün	4		2		6	100.0
Toplam	8		47		55	100.0
X^2=6,438; p=0.04; p<0.05						

Antitimosit Globulin (ATG) ilacını kullanan çocuk hastalarda lökositoz/enfeksiyon gelişme oranının ilerleyen günlerde giderek arttığı ve bu farkın istatistiksel olarak anlamlı olduğu belirlenmiştir (X^2=6,438; p=0.04; p<0.05)(Tablo 4).

Tablo 5. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastaların Yaş Gruplarına Göre Bazı Komplikasyonların Gelişme Oranlarının Dağılımı

Komplikasyonlar / Yaş Grubu	Gelişen		Gelişmeyen		TOPLAM	
	Sayı	Yüzde	Sayı	Yüzde	Sayı	Yüzde
Hipertermi						
0-6 yaş	26	100	0	0	26	100.0
7-12 yaş grubu	12	92,3	1	7,7	13	100.0
13 yaş ve üzeri	16	0	0	0	16	100.0
Toplam	54	98.2	1	1,8	55	100.0
X^2=5,984[a] ; S.D. : 4 p=0,200; p< 0.05						
Taşikardi						
0-6 yaş grubu	25	96,1	1	3,9	26	100.0
7-12 yaş grubu	11	84,6	2	15,4	13	100.0
13 yaş ve üzeri	10	62,5	6	37,5	16	100.0
Toplam	46	83,6	9	16,4	55	100.0
X^2=8,663[a]; S.D.: 4 p=0.070; p<0.05						
Titreme						
0-6 yaş grubu	18	69,2	8	30,8	26	100.0
7-12 yaş grubu	12	92,3	1	7,7	13	100.0
13 yaş ve üzeri	7	43,7	9	56,3	16	100.0
Toplam	37	67,2	18	32,8	55	100.0
X^2=8,393[a]; S.D.: 4 p=0.078; p<0.05						
Üşüme/Ürperme						
0-6 yaş grubu	15	57,6	11	42,3	26	100.0
7-12 yaş grubu	11	84,6	2	15,4	13	100.0
13 yaş ve üzeri	8	50	8	50	16	100.0
Toplam	34	61,8	21	38,2	55	100.0
X^2=6,641[a]; S.D.:4 p=0,156; p<0,05						
Bulantı						
0-6 yaş grubu	11	42,3	15	57,7	26	
7-12 yaş grubu	6	46,1	7	53,9	13	
13 yaş ve üzeri	7	43,7	9	56,3	16	
Toplam	24	43,6	31	56,4	55	100.0
X^2=4,639[a] ; S.D.:4 p=0.326; p<0.05						

Çalışmada yer alan 55 hastanın yaş gruplarına göre gelişen komplikasyonlar incelenmiştir. Komplikasyonlar, 0-6 yaş, 7-12 yaş ve 13 yaş ve üzeri olmak üzere üç ana yaş grubuna göre değerlendirilmiş ve her bir komplikasyon için yaş gruplarındaki dağılımlar istatistiksel olarak analiz edilmiştir. Hipertermi (ateş) komplikasyonu, 0-6 yaş grubunda %100, 7-12 yaş grubunda ise %92,3 oranında görülmektedir. Ancak, 13 yaş ve üzeri grupta hiç hipertermi gelişmemiştir. Taşikardi en yüksek oranda, 0-6 yaş grubunda (%96,1) gözlemlenmişken, 13 yaş ve üzeri grupta bu oran %62,5'e düşmektedir. Titreme, 7-12 yaş grubunda %92,3 oranla sık görülürken, 13 yaş ve üzeri grupta bu oran %43,7'ye düşmüştür. Üşüme/ürperme ve bulantı komplikasyonları, yaş gruplarına göre farklılıklar göstermekle birlikte, genel olarak tüm yaş gruplarında belirgin şekilde görülmüştür. Üşüme/ürperme oranı %61,8, bulantı oranı ise %43,6'dır.

Bu çalışmada yer alan komplikasyonların yaş gruplarına göre dağılımı incelendiğinde, her bir komplikasyon için yaş grupları arasında belirgin bir fark gözlemlenmemiştir. Hipertermi, taşikardi, titreme, üşüme/ürperme ve bulantı gibi komplikasyonların çoğu, tüm yaş gruplarında benzer oranlarla görülmüştür. Bununla birlikte, 13 yaş ve üzeri grupta bazı komplikasyonların daha düşük oranlarda görüldüğü fark edilmiştir, özellikle hipertermi ve titreme bu grupta belirgin şekilde daha düşük seviyelerdedir. Ancak, istatistiksel analizler (ki-kare testi) tüm komplikasyonlar için yaş grupları arasında anlamlı bir fark bulunmadığını göstermiştir.

Tablo 6. Antitimosit Globulin (ATG) İlacını Kullanan Çocuk Hastaların Cinsiyetlerine Göre Bazı Komplikasyonların Gelişme Oranlarının Dağılımı

Komplikasyonlar	Gelişen		Gelişmeyen		TOPLAM	
Cinsiyet	Sayı	Yüzde	Sayı	Yüzde	Sayı	Yüzde
Hipertermi						
Kadın	23	100	0	0	23	100.0
Erkek	31	96,8	1	3,2	32	100.0
Toplam	54	98,2	1	1,8	55	100.0
X^2=0,732[a]; S.D.: 1 p=0,392; p>0.05						
Taşikardi						
Kadın	16	69,5	7	30,5	23	
Erkek	30	93,8	2	6,2	32	
Toplam	46	83,6	9	16,4	55	100.0
X^2=5,719[a]; S.D.:1 p=0,017; p<0.05						
Titreme						
Kadın	12	52,1	11	47,9	23	
Erkek	25	78,1	7	21,9	32	
Toplam	37	67,2	18	32,8	55	100.0
X^2=4,093[a]; S.D.:1 p=0,043; p<0.05						
Üşüme/Ürperme						
Kadın	12	52,1	11	47,9	23	
Erkek	22	68,8	10	31,2	32	
Toplam	34	61,8	21	38,2	55	100.0
X^2=1,558[a]; S.D.:1 p=0,212; p>0.05						
Bulantı						
Kadın	9	39,1	14	60,9	23	
Erkek	15	46,8	17	53,2	32	
Toplam	24	43,6	31	56,4	55	100.0
X^2=0,326[a]; S.D.:1 p=0,568; p>0.05						

Antitimosit globulin (ATG) ilacını kullanan çocuk hastaların cinsiyet gruplarına göre bazı komplikasyonların gelişme oranlarının verildiği bu tabloya bakıldığında; Hipertermi açısından cinsiyetler arasında anlamlı bir fark bulunmamıştır (p=0,392). Hem kadınlar hem de erkeklerde yüksek oranda hipertermi gözlemlenmiştir. Taşikardi gelişimi, erkeklerde kadınlara göre anlamlı şekilde daha yüksektir (p=0,017). Erkeklerde taşikardi oranı %93,8 iken, kadınlarda %69,5'dir.Titreme komplikasyonu da erkeklerde daha yaygın olarak görülmektedir ve bu fark istatistiksel olarak anlamlıdır (p=0,043). Erkeklerde titreme oranı %78,1 iken, kadınlarda %52,1'dir.Üşüme/ürperme ve bulantı açısından cinsiyetler arasında anlamlı bir fark bulunmamıştır (p>0,05). Erkeklerde üşüme/ürperme oranı (%68,8) kadınlardan (%52,1) daha yüksek olmasına rağmen, bu fark istatistiksel olarak anlamlı değildir.

Sonuç olarak taşikardi ve titreme komplikasyonları cinsiyetler arasında anlamlı farklar göstermektedir. Erkeklerde her iki komplikasyon da kadınlara göre daha sık görülmüştür. Komplikasyonlar açısından cinsiyetle ilişkili olarak anlamlı farklar görülmemiştir.

Tartışma

Bu retrospektif çalışmada, kök hücre nakli sürecinde Antitimosit Globulin (ATG) tedavisi uygulanan çocuk hastalarda görülen komplikasyonlar yaş grupları ve cinsiyet açısından değerlendirilmiştir. Elde edilen bulgular, ATG tedavisiyle ilişkili çeşitli advers etkilerin çocuk hasta grubunda yüksek oranda görüldüğünü ortaya koymaktadır. Çalışma popülasyonunun %58,2'sini erkek hastalar oluştururken, en yüksek hasta oranı 0-6 yaş grubunda yer almaktadır (%47,3). Bu yaş grubunun hem immün sistem özellikleri hem de tedaviye yanıt biçimleri açısından farklılıklar göstermesi, komplikasyon gelişme oranlarının değerlendirilmesinde önem arz etmektedir.

Komplikasyonlar arasında en sık gözlemlenen bulgular hipertermi (%98,2), taşikardi (%83,6), titreme (%67,3) ve üşüme/ürperme (%61,8) olmuştur. Bu bulgular, ATG'nin infüzyon ilişkili etkilerinin çocuk hastalarda oldukça belirgin olduğunu göstermektedir. Literatürde de benzer şekilde, ATG uygulamaları sırasında sitokin salınımına bağlı olarak sistemik inflamatuar yanıtların sık görüldüğü belirtilmiştir.[10] Hipertermi, ATG tedavisi sırasında sık görülen bir yan etkidir. Ancak, yapılan istatistiksel değerlendirmeye göre, cinsiyetler arasında hipertermi gelişiminde anlamlı bir fark bulunmamıştır (p=0,392). Hem erkeklerde hem de kadınlarda yüksek oranlarda hipertermi gözlemlenmesi, ATG tedavisinin genel bir yan etkisi olarak kabul edilebilir. Bu bulgu, cinsiyetin bu spesifik yan etki üzerindeki etkisinin minimal olduğunu göstermektedir. Önceki çalışmalar, hiperterminin bir inflamatuar yanıt olarak, cinsiyetten bağımsız olarak ATG alan tüm hastalarda yaygın olduğunu öne sürmüştür.[4] Bu durum, ilaç tedavisinin vücutta oluşturduğu genel etki ile ilişkilendirilebilir.

Diyare ve lökositoz/enfeksiyon komplikasyonlarının tedavi günleri ilerledikçe anlamlı şekilde arttığı tespit edilmiştir. Diyare insidansının 1. günde düşük (%11,5), ancak 2. günde %39,1 ve 3. günde %50'ye yükselmesi (p<0.001), gastrointestinal yan etkilerin tedavi süresine bağlı olarak progresif geliştiğini göstermektedir. Benzer şekilde, lökositoz/enfeksiyon gelişme oranında da zamanla anlamlı bir artış gözlenmiştir (p<0.05). Bu bulgular, immünsüpresif tedavinin ilerleyen günlerinde ikincil enfeksiyon riskinin arttığını ve hasta takibinde dikkatli olunması gerektiğini vurgulamaktadır.[11]

Yaş gruplarına göre yapılan analizlerde, özellikle hipertermi ve taşikardi komplikasyonlarının daha küçük yaş gruplarında daha yüksek oranlarda görüldüğü, ancak

istatistiksel analizler sonucunda bu farkların anlamlı olmadığı belirlenmiştir. 13 yaş ve üzeri hastalarda hipertermi hiç görülmemiş olup, bu durum yaşla birlikte immün yanıtın değişebileceğine işaret etmektedir. Ancak genel olarak, yaş grupları arasında komplikasyon gelişme oranlarında istatistiksel anlamda anlamlı bir fark bulunmaması ($p>0.05$), ATG kaynaklı advers etkilerin yaşa bağlı olmaktan çok bireysel immün yanıt profili ile ilişkili olabileceğini düşündürmektedir.[12]

Cinsiyet açısından değerlendirildiğinde ise, taşikardi ve titreme komplikasyonlarının erkek hastalarda kadınlara göre anlamlı düzeyde daha sık görüldüğü tespit edilmiştir (sırasıyla $p=0.017$ ve $p=0.043$). Bu durum, erkek çocuklarda ATG'ye karşı daha belirgin fizyolojik veya immün yanıtların gelişebileceğine işaret edebilir. Taşikardi gelişimi, erkeklerde kadınlara göre anlamlı şekilde daha yaygın görülmüştür ($p=0,017$). Erkeklerde taşikardi oranı %93,8 iken, kadınlarda bu oran %69,5 olarak bulunmuştur. Bu bulgu, ATG tedavisinin cinsiyete bağlı olarak farklı kardiyovasküler yan etkiler üretebileceğini göstermektedir. Erkeklerin taşikardi gelişiminde daha yüksek bir oran sergilemesi, erkeklerin vücut yapısal özellikleri veya bağışıklık sistemlerinin ATG'ye farklı yanıt verme biçimleriyle açıklanabilir. Daha önce yapılan çalışmalarda, cinsiyetin kardiyovasküler yan etkiler üzerindeki etkisinin genellikle karmaşık olduğu ve hormonlar ile genetik faktörlerin bu tür reaksiyonları etkileyebileceği vurgulanmıştır.[2] Ayrıca, erkeklerin daha yüksek bağışıklık yanıtlarına sahip olması da bu tür yan etkilerin artmasına neden olabilir.[3]

Erkeklerde bu tür komplikasyonların daha sık görülmesi, ilaç tedavisinin cinsiyetle ilgili biyolojik faktörlerle etkileşimini gözler önüne sermektedir. Hipertermi, üşüme/ürperme ve bulantı gibi diğer komplikasyonlar açısından ise cinsiyetler arasında anlamlı bir fark saptanmamıştır. Literatürde çocuklarda cinsiyete bağlı immün yanıt farklılıkları üzerine sınırlı sayıda çalışma bulunduğundan, bu bulguların ileriye dönük araştırmalarla desteklenmesi gereklidir.[13,14]

Bu bulgular, cinsiyetin ATG tedavisinin yan etkileri üzerindeki etkisinin önemli bir faktör olabileceğini göstermektedir. Özellikle taşikardi ve titreme gibi kardiyovasküler ve nörolojik komplikasyonlar, erkeklerde daha sık görülmektedir. Bu durum, tedavi sürecinde erkek hastaların izlenmesinin daha dikkatli yapılmasını gerektirebilir. Cinsiyetler arasındaki bu farklılıklar, ATG'nin biyolojik etkilerinin daha fazla araştırılması gerektiğini ve tedavi sürecinde cinsiyete dayalı daha özelleştirilmiş yaklaşımlar geliştirilmesi gerektiğini ortaya koymaktadır.

ATG tedavisinin komplikasyonları hakkında daha fazla bilgi edinmek için gelecekteki çalışmalarda, daha geniş hasta grupları ile yapılan prospektif çalışmalara yer verilmesi önerilmektedir. Ayrıca, immünosupresif tedaviye verilen yanıtların cinsiyetler ve diğer demografik faktörlerle nasıl ilişkili olduğunun daha ayrıntılı incelenmesi, tedavi protokollerinin iyileştirilmesine katkı sağlayacaktır.

Sonuç ve Öneriler

Bu retrospektif çalışmada, Antitimosit Globulin (ATG) tedavisi uygulanan çocuk hastalarda en sık görülen komplikasyonlar hipertermi, taşikardi, titreme ve üşüme/ürperme olarak belirlenmiştir. Cinsiyet ve yaş faktörlerinin komplikasyonların görülme oranları üzerinde etkili olduğu, özellikle erkeklerde taşikardi ve titreme oranlarının daha yüksek olduğu tespit edilmiştir. Ayrıca, tedavi süresinin ilerleyen günlerinde diyare ve lökositoz/enfeksiyon oranlarının arttığı gözlemlenmiştir. Bu bulgular, ATG tedavisinin yan etkilerinin tedavi sürecinde dikkatle izlenmesi gerektiğini, ayrıca cinsiyet ve yaşa dayalı özelleştirilmiş

yaklaşımlar geliştirilmesi gerektiğini göstermektedir. Gelecekteki çalışmalarda, daha geniş hasta gruplarıyla yapılan prospektif araştırmalar ve immün yanıtların cinsiyet ve yaşla ilişkisi üzerine yapılacak derinlemesine analizler, tedavi protokollerinin iyileştirilmesine katkı sağlayabilir.

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EFFECT OF EDUCATION GIVEN TO NURSES ON PREVENTION OF MEDICAL DEVICE-RELATED PRESSURE INJURY ON THEIR KNOWLEDGE LEVEL

ABSTRACT

Aim: Medical device-related pressure injuries (TABBY) are a problem that develops during patient care worldwide. Nurses play a vital role in preventing these injuries, which is one indicator of quality of care, especially in intensive care units. This study was planned to examine the effectiveness of the training given to nurses on Medical Device-related Pressure Injuries.

Method: The universe of this quasi-experimental study with a single group pre-test/post-test design (n=40) was formed by all nurses who had been working in the Ege University Hospital Chest Diseases 2nd and 3rd Level Intensive Care Unit for at least 3 months between February 2024 and December 1, 2024, and the sample consisted of a total of 31 nurses who were not on leave and agreed to participate in the study. A questionnaire form and face-to-face training were used in data collection. A questionnaire form and face-to-face training were used in data collection. The questionnaire form included a 7-question Introductory Characteristics Questionnaire and a 32-question Form For Determining The Knowledge Level on Preventing Medical Device-related Pressure Injuries developed by the researchers in line with the literature. A pre-test was administered to the nurses just before the training, a 60-minute training was given with PowerPoint, and a post-test was administered 15 days later. Written permission was obtained from the ethics committee and the institution where the study was conducted. Before the application, the purpose of the research and the necessary information were explained to the participants by the researcher, and written consent was obtained from the participants.

Results: The average age of the nurses participating in the study was 31±6.0; 85% were female, 92.5% had a bachelor's degree, and 55% had 1-5 years of experience working in an intensive care unit. The average score of the nurses after the training increased (28.47±2.08) compared to the average score of the nurses before the training (21.75±5.52). It was found that the duration of working in an intensive care unit and the age group of the nurses did not create a difference in the TABBY pre-test and post-test score averages.

Conclusion: The nurses' training on medical device-related pressure injuries was effective. New studies with a larger sample and clinical nurses should be conducted.

Keywords: Nursing; Pressure Ulcer; Equipment and Supplies; Critical Care; Nursing Care

TIBBİ ARAÇ İLİŞKİLİ BASINÇ YARASINI ÖNLEME İLE İLGİLİ HEMŞİRELERE VERİLEN EĞİTİMİN BİLGİ DÜZEYLERİNE ETKİSİ

ÖZET

Amaç: Tıbbi araca bağlı basınç yaralanmaları tüm dünyada hasta bakımı sırasında gelişen bir sorundur. Hemşireler özellikle yoğun bakım biriminde, bakım kalitesinin göstergelerinden biri olan tıbbi araca bağlı basınç yaralanmalarının önlenmesinde hayati bir rol oynarlar.

Hemşirelere tıbbi araca bağlı basınç yaralanmaları hakkında verilen eğitimin etkinliğini incelemek amacıyla planlanmıştır.

Materyal ve Yöntem: Tek grup ön test/ son test desenli yarı deneysel türdeki bu çalışmanın evrenini (n=40) Şubat 2024 ve 1 Aralık 2024 tarihleri arasında Ege Üniversitesi Hastanesi Göğüs Hastalıkları 2.ve 3. Basamak Yoğun Bakım Ünitesinde en az 3 aydır çalışan tüm hemşireler, örneklemini ise izinli olmayan ve çalışmaya katılmayı kabul eden toplam 31 hemşire oluşturmuştur. Veri toplamada anket formu ve yüzyüze eğitim kullanılmıştır. Anket formunda 7 sorudan oluşan Tanıtıcı Özellikler Soru Formu ve 32 sorudan oluşan literatür doğrultusunda araştırmacılar tarafından geliştirilen Tıbbi Araca Bağlı Basınç Yarasını Önlemeye İlişkin Bilgi Düzeyini Belirleme Formu yer almaktadır. Hemşirelere eğitimden hemen önce öntest uygulanmış, PowerPoint eşliğinde 60 dakikalık eğitim verilmiş ve 15 gün sonra son-test uygulanmıştır. Anket formunun yanıtlanması 12-15 dakika sürmüştür. Araştırmanın yürütülmesi için etik kuruldan ve çalışmanın yürütüldüğü kurumdan yazılı izin alınmıştır. Uygulama öncesi katılımcılara araştırmanın amacı ve gerekli bilgiler araştırmacı tarafından anlatılarak katılımcıların yazılı onamları alınmıştır.

Bulgular: Çalışmaya katılan hemşirelerin yaş ortalaması 31±6,0 yıl olup, %85'i kadın, %92,5'i lisans mezunudur, %55'inin 1-5 yıl yoğun bakım biriminde çalışma deneyimine sahiptir. Hemşirelerin eğitim öncesi puan ortalamasına (21,75±5.52) oranla, eğitim sonrası puan ortalaması (28,47±2.08) artmıştır. Yoğun bakımda çalışma süresinin ve hemşirelerin yaş grubunun TABBY ön test ve son test puan ortalamalarında bir farklılık yaratmadığı bulunmuştur.

Sonuç: Hemşirelere tıbbi araca bağlı basınç yaralanmaları (TABBY) verilen eğitimin etkin olduğu söylenebilir. Daha geniş bir örneklemde ve klinik hemşirelerinin da dahil edildiği yeni çalışmaların yapılması önerilmektedir.

Anahtar kelimeler: Bası yarası, ekipman ve sarf malzemeleri, yoğun bakım, hemşirelik bakımı

GİRİŞ

Tıbbi araca bağlı basınç yaralanmaları (TABBY), hastaya uygulanan tıbbi araçların sürekli basınç, sürtünme veya kesilme kuvveti oluşturması sonucu meydana gelen[1,2] tanısal veya terapötik amaçlar için kullanılan araçların kullanımından kaynaklanan,[3] tıbbi aracın şeklini yansıtan, ciltte ve/veya mukozada lokalize bir yaralanma[4] olarak tanımlanmaktadır. TABBY 'ler genellikle nazal kanül, nazogastrik tüp, alçı bandaj, atel, entübasyon tüpü, maske, boyunluk, nabız oksimetre probu, elektrokardiyogram elektrodu ve arteriovenöz kateter gibi tıbbi araçların cilde sürekli bası yapması sonucu gelişmektedir.[1,2,5]

Özellikle yoğun bakım üniteleri ile uzun süreli hastanede yatış gerektiren durumlarda yüksek prevalans gösteren[6] TABBY'ı iyileşmesi güç doku hasarlarına yol açar, enfeksiyon riskini artırır, hastanın iyileşme süresini ve hastanede kalış süresini uzatır, ciddi komplikasyonlara yol açar,[3,5,7] mortalite riskini artırır[8] ve sağlık sistemleri üzerindeki yük oluşturur.[1,9] Uluslararası basınç yarası prevalans çalışmalarında TAİBY oranlarının %10 ile %35 arasında değiştiği bildirilmiştir.[3,10] Yapılan bir çalışmada TABBY oranının %32.5 olduğu, bunların %29.2'sinin nazogastrik tüp, %18.5'inin endotrakeal tüp, %15.4'ünün CPAP maskesi nedeniyle geliştiği, %53.8'inin ise mukozal olduğu, %18.5'inin cilt bası zedelenmesinin 2. Aşamasında olduğu saptanmıştır. [11] Yapılan çalışmalarda TAİBY 'lerin %30 - %70'inin solunum ekipmanından kaynaklandığı görülmüştür. [6] Minnesota'nın zorunlu eyalet çapında yatan hasta verilerinin analizinde, tıbbi araçla ilgili basınç yaralanmalarının %63'ü için aracın temizlik veya deri muayenesi için düzenli aralıklarla çıkarılmasına ilişkin hiçbir belgenin bulunmadığını ve bu tür basınç yaralarının %74'ü, evre 3 veya daha fazla olana kadar keşfedilmediği bildirilmiştir.[12] Hanönü ve ark. (2016)[13] yapmış olduğu prospektif bir çalışmada, hastaların %40'ında TABBY olduğunu bulmuştur.[13] Barakat Johnson ve ark. (2017)[8] Avustralya'da üçüncü basamak bir hastanede yatan tüm hastalarda genel TAİBY insidansının %27,9 olduğunu bildirmiştir. Yoğun bakım üniteleri gibi uzun süreli araç kullanımının kaçınılmaz olduğu ortamlarda bu oran daha da yükselmektedir.[7,13]

Tıbbi araca bağlı basınç yaralanmaları, hemşirelik bakım kalitesinin göstergeleri arasındadır ve hemşireler bu yaraların önlenmesinde ve başlamasına yanıt vermede hayati bir rol oynamaktadırlar.[14] Bununla birlikte, mevcut basınç yaralanması risk değerlendirme araçlarından Norton ölçeği, Braden ölçeği ve Waterlow skoru[15] genellikle tıbbi yaralanma riskini tahmin etmede yetersiz olup bu risk değerlendirme araçları, araçların hareketliliğinden ziyade hastanın hareketsizliğine odaklandığından, hastalar arasında araçla ilişkili basınç yaralanması gelişimini değerlendirmede hemşireler yetersiz kalabilmektedir.[16] Bu nedenle, hemşireler ve diğer sağlık hizmeti sağlayıcıları, tıbbi araçla ilgili basınç yaralanmasını değerlendirmek için klinik muhakemeye ve cildin görsel incelemesine güvenir; bu da tıbbi araçla ilgili bazı basınç yaralanmalarının tanınmadığı veya kaydedilmediği anlamına gelmektedir.[17] Tıbbi araç ilişkili basınç yaralarının önlenmesi büyük ölçüde hemşirelerin bilgi, tutum ve uygulama becerilerine bağlıdır. Hemşireler, hastaların günlük izleminde, araçların yerleştirilmesi, sabitlenmesi ve cilt bütünlüğünün korunmasında kritik bir role sahiptirler.[12] Ancak yapılan çalışmalar, hemşirelerin TABBY konusunda bilgi düzeylerinin yeterli olmadığını ve standart koruyucu uygulamaları her zaman etkin bir şekilde uygulamadıklarını göstermektedir.[18,19] Erbay Dallı ve Kelebek Girgin'in (2022)[20] yaptığı çalışmada, yoğun bakım hemşirelerinin TABBY'yi önleme bilgi düzeylerinin orta düzeyde olduğu ve eğitim ihtiyacının açık bir şekilde bulunduğu vurgulanmıştır.

Literatürde, hemşirelere yönelik uygulamalı eğitim programlarının TABBY önleme konusundaki bilgi, tutum ve uygulama performanslarını önemli ölçüde artırdığı bildirilmiştir.[21] Söz konusu eğitimler, hemşirelerin TABBY gelişimini erken evrede fark etmesini, riskli araç yerleşimlerini değiştirmesini ve cilt koruyucu önlemleri sistematik şekilde uygulamasını desteklemektedir.[22,23] Hemşireler, günlük yara bakım protokollerinin tam olarak farkında olmayabilir ve kanıta dayalı uygulamalar konusunda yeterli bilgiye sahip olmayabilirler.[19] Çoğu zaman hemşirelerin uygulamaları bilgi temelli değil; kişisel deneyimlere veya alışkanlıklara dayalı olabilmektedir.[24] Oysa basınç yaralanmalarının önlenmesi için hemşirenin bilgi düzeyi, risk değerlendirmesi yapabilmesi, risk yönetimi ve önleyici yaklaşımları etkin bir şekilde uygulayabilmesi büyük önem taşımaktadır.[25] TABBY ile ilgili önceki araştırmalar, genellikle risk değerlendirme ölçeklerinin geliştirilmesi ve uygulanması üzerine yoğunlaşmıştır.[5,26] Bu durum, hemşirelerin TABBY konusunda bilgi edinmeleri, bu tür yaraları doğru bir şekilde değerlendirebilmeleri ve etkili önleme stratejileri geliştirebilmeleri için özel eğitim programlarına olan ihtiyacı ortaya koymaktadır. Bu nedenle, günümüzde hemşirelerin günlük yara bakım protokollerine hakim olmalarını ve kanıta dayalı uygulamalar hakkında yeterli bilgiye sahip olmalarını destekleyecek eğitimlerin geliştirilmesi büyük önem taşımaktadır.

Literatürde hemşirelerin TABBY hakkında bilgi düzeylerini arttırmada eğitim ihtiyacının kaçınılmaz bir gereklilik olarak vurgulandığı görülmektedir.[23,27,28] Sönmez ve ark. (2025) 'nın[29] çalışmasında, yoğun bakım hemşirelerinin TABBY konusundaki bilgi düzeyleri incelendiğinde doğru cevap oranlarının %56,5 olduğu bildirilmiştir. Benzer şekilde, Kim ve ark. (2019)[17] ile Zhang ve ark. (2021)[22] da klinik hemşirelerin TABBY önlenmesine yönelik bilgi, tutum ve uygulama düzeylerinin geliştirilmesi gerektiğini vurgulamışlardır.

Amaç: Bu çalışmada hemşirelere tıbbi araca bağlı basınç yarasını önlemeye yönelik verilen eğitimin etkisini incelemek amaçlanmıştır.

GELİŞME

Araştırma hipotezleri:

H1: Yoğun bakımda çalışan hemşirelere tıbbi araca bağlı basınç yarası hakkında verilen eğitim sonrası puan ortalamaları, eğitim öncesi aldıkları puan ortalamalarından daha yüksektir.

H2: Hemşirelerin yoğun bakımda çalışma süresi eğitim öncesi ve sonrası bilgi puan ortalamasını etkiler.

H3: Yoğun bakımda çalışan hemşirelerin yaş grubu eğitim öncesi ve sonrası bilgi puan ortalamasını etkiler

Değişkenler:

Hemşirelerin tıbbi araca bağlı basınç yarası hakkında verilen eğitim öncesi ve eğitim sonrası puan ortalamaları çalışmanın bağımlı değişkenlerini; Hemşirelerin yaşı ve çalışma süresi ise çalışmanın bağımsız değişkenlerini oluşturmuştur**.**

GEREÇ VE YÖNTEMLER

Araştırmanın Tipi, Yeri ve Zamanı

Araştırma 30 Ekim 2024 ve 30 Aralık 2024 tarihleri arasında Ege Üniversitesi Hastanesi Göğüs Hastalıkları 2.ve 3. Basamak Yoğun Bakım Ünitelerinde deney grubunun kontrol grubu ile aynı olduğu ön test/ son test desenli yarı deneysel bir çalışma olarak planlanmıştır.

Araştırmanın Evreni ve Örneklemi

Çalışmanın evrenini 30 Ekim 2024 ve 30 Aralık 2024 tarihleri arasında Ege Üniversitesi Hastanesi' Göğüs Hastalıkları 2. Ve 3. Basamak Yoğun Bakım Ünitelerinde çalışan (n:40) tüm hemşireler oluşturacaktır. Evrenin tamamına ulaşılması hedeflendiğinden örnekleme yoluna gidilmeyecektir.

Dâhil edilme kriterleri: Araştırmaya katılmaya gönüllü olması; yoğun bakım biriminde en az 3 aydır çalışıyor olması, araştırmanın yürütüldüğü tarihlerinde herhangi bir nedenle uzun süreli izinli olmamak veya görevli olarak kurum dışında bulunmamak.

Veri Toplama Araçları: Veriler anket formu ile toplanmıştır. Anket formu Tanıtıcı Özellikler Soru Formu ve Tıbbi Araçla İlgili Basınç Yaralanmaları Soru Formu'ndan oluşmuştur. Tanıtıcı Özellikler Soru Formunda hemşirelerin yaşı, cinsiyeti, eğitim durumu, hemşire olarak çalışma süresi, YBÜ'de çalışma süresi, TABBY'ye ilişkin eğitim alma durumu ve bu eğitimin yeterli ve güncel olduğunu düşünüp-düşünmeme gibi tanıtıcı özelliklerini irdeleyen 7 sorudan oluşmuştur. Tıbbi Araçla İlgili Basınç Yaralanmaları Soru Formu'nda çalışmanın veri toplama tarihinde konuya ilişkin Türkçe geçerli ve güvenilir bir ölçme aracına erişilemediğinden; hemşirelerin bilgi düzeyini ölçmek amacıyla araştırmacılar tarafından Klinik Uygulama Kılavuzu'nda (EPUAP, NPIAP, PPPIA, 2019) belirtilen BY'ler için olası araçların listesi dikkate alınarak bir form geliştirilmiştir. Geliştirilen formun kapsam geçerliliğinin değerlendirilmesi amacıyla Davis tekniği kullanılmış ve Hemşirelik Fakültesi'nde görev yapan 5 öğretim üyesi ile alanda uzman 6 hemşire olmak üzere toplam 11 uzmandan görüş alınmıştır. İçerik geçerliliği için uzmanlardan her soruyu anlaşılırlık, bilimsel içerik, ölçüm ve değerlendirme kriterleri açısından değerlendirmesi ve gerektiğinde yeni maddeler önermeleri istenmiştir. Uzmanlar, her bir maddeyi 4'lü Likert tipi bir ölçek kullanarak değerlendirmiştir. Uzman görüşlerinin değerlendirilmesinde İçerik Geçerlilik İndeksi (CVI) kullanılmıştır. İçerik geçerliliğinin sağlandığı belirlendikten sonra (CVI = 0,869) ölçüm aracının iç tutarlılığı değerlendirilmiş ve güvenilirlik analizi yapılmıştır. Formda, doğru ve yanlış ifadelerden oluşan, hem düz hem de ters ifadeleri kapsayan toplam 32 soru 5 alt boyutta ele alınmıştır: 1.Tanımlama (5 madde), 2.Risk değerlendirme (6 madde), 3.İzlem/Gözlem (7 madde), 4.Önleme ve tedavi (12 madde) ve 5.Sınıflama ve evreleme (2 madde). Formda yer alan bilgi sorularında, "doğru" yanıtlar 1 puan, "yanlış" yanıtlar ise 0 puan olarak değerlendirilmiş ve bireylerin toplam bilgi puanları bu şekilde hesaplanmıştır. Yüksek bir puan, TABBY'ler konusunda daha yüksek düzeyde bilgiyi göstermektedir.

Veri Toplama: Eğitim öncesi, hemşirelere anket formu (ön test) uygulanmıştır. Hemşirelere kurum yöneticilerinin belirlediği yer, tarih ve saatte PowerPoint eşliğinde görselliği de kapsayan 60 dakikalık eğitim verilmiştir. Eğitim, konu anlatımı ile katılımcıların sorularının yanıtlanması biçiminde yapılmıştır. Eğitimden 15 gün sonra formun ikinci bölümü (son test) tekrar uygulatılmıştır. İki bölümden oluşan veri toplama formunun uygulanma süresi yaklaşık 10-15 dakikadır.

Verilerin Analizi: Veriler SPSS programında kodlanarak analiz edilmiştir. Bilgi sorularına verilen cevaplar ‘ doğru’ ve ‘ yanlış ‘ şeklinde olup “doğru” ya 1, “yanlış” a 0 verilerek toplam bilgi puanı hesaplanmıştır. Toplam puanlar eğitim öncesi ve sonrası hesaplanmış ve aralarındaki fark analiz edilmiştir. Verilerin iki eş arasındaki farkın önemlilik testi ve korelasyon kullanmıştır. Eğitim öncesi ve sonrası elde edilen toplam bilgi puanları karşılaştırılmış, iki ölçüm arasındaki farkın anlamlılığı için bağımlı örneklemler t testi kullanılmıştır. Ayrıca, değişkenler arasındaki ilişkiyi belirlemek amacıyla korelasyon analizi gerçekleştirilmiştir

Araştırmanın Etik Yönü: Bu çalışma Helsinki Deklarasyonu’nda belirtilen yönergelere uygun olarak yürütülmüştür. Araştırmanın yürütülmesi için Ege Üniversitesi’nin İnsan Araştırmaları Etik Kurulu'ndan etik onay (09.03.2023 ve karar numarası:23-3T/42) ve çalışmanın yürütüldüğü kurumdan yazılı izin (18.10.2024 ve sayı numarası 2106259) alınmıştır. Uygulama öncesi katılımcılara araştırmanın amacı ve gerekli bilgiler araştırmacılar tarafından anlatılarak katılımcıların yazılı onamları alınmıştır.

Araştırmanın Sınırlılıkları: Bu araştırma, 30 Ekim 2024 ve 30 Aralık 2024 tarihleri arasında Ege Üniversitesi Tıp Fakültesi Hastanesi Göğüs Hastalıkları 2. Ve 3. Basamak YBÜ’de çalışan hemşireler ile sınırlıdır, diğer kurumlarda çalışan hemşireler genellenemez.

BULGULAR

Çalışmaya katılan hemşirelerin yaş ortalaması 31±6,0 yıl olup, %85’i kadın, %92,5’i lisans mezunu, %45’nin 1-5 yıl hemşirelikte çalışma deneyimi var iken ;%55’inin 1-5 yıl yoğun bakım biriminde çalışma deneyimine sahip olduğu ve %77,5’inin TABBY’ye yönelik eğitim almadığı belirtilmiştir (Tablo 1).

Tablo 1. Hemşirelerin Tanıtıcı Özelliklerine Göre Dağılımı

Tanıtıcı Özellikler	**Sayı**	**Yüzde**
Yaş Grubu		
24-30	18	45.0
31-47	22	55.0
Yaş ortalaması: 31±6,0 yıl (min:24; max; 47)		
Cinsiyet		
Kadın	34	85.0
Erkek	6	15.0
Eğitim Düzeyi		
Lisans	37	92,5
Yüksek Lisans	3	7,5
Doktora	0	-
Hemşirelikte Çalışma Süresi		
1-5 yıl	18	45.0
6-10 yıl	11	27.5
11 yıl ve üzeri	11	27.5
Yoğun Bakımda Çalışma Süresi		
1-5 yıl	22	55.0
6 yıl ve üzeri	18	45.0
TABBY 'ye İlişkin Eğitim Alma		
Eğitim alan	9	22.5
Eğitim almayan	31	77.5

Tablo 2. Hemşirelerin Eğitim Öncesi Ve Eğitim Sonrası TABBY Bilgi Puan Ortalamalarının Karşılaştırılması

	n	Ort ± S.D	Paired sample t	p
Toplam ön test puanı	40	21,75 ± 5.52	- 6,539	0,000
Toplam son test puanı	40	28,47 ± 2.08		

Tablo 2'de görüldüğü gibi hemşirelerin eğitim öncesi puan ortalamasına oranla, eğitim sonrası puan ortalaması artmıştır (p<0,000).

Tablo 3. Hemşirelerin Yoğun Bakım Biriminde Çalışma Sürelerine Göre Eğitim Öncesi Ve Sonrası Bilgi Puanlarının Dağılımı

			n	Ort ± S.D	t	p
Yoğun Bakımda Çalışma Süresi	Toplam ön test puanı	1-5 yıl	22	22,00± 5,99	,313	,756
		6yıl ve üzeri	18	21,44±5,05		
	Toplam son test puanı	1-5 yıl	22	28,95±1,88	1,641	,109
		6yıl ve üzeri	18	27,88±2.21		

Değişik süre boyunca yoğun bakımda çalışan hemşirelerin ön test ve son test puan ortalamaları arasında bir farklılık bulunmamıştır (p>0,05) (Tablo 3).

Tablo 4. Hemşirelerin Yaş Gruplarına Göre Eğitim Öncesi Ve Sonrası Bilgi Puan Ortalamalarının Dağılımı

			n	Ort ± S.D	t	p
Yaş Grubu	Toplam ön test puanı	24-30 yaş	18	21,72±6,39	-,028	,978
		31-47 yaş	22	21,77±4,85		
	Toplam son test puanı	24-30 yaş	18	29,00±1,68	1,459	,153
		31-47 yaş	22	28,04±2,31		

Araştırma kapsamındaki hemşirelerin yaş gruplarına göre TABBY ön test ve son test puan ortalamaları arasında farklılık bulunmamıştır (p>0.05) (Tablo 4).

TARTIŞMA

Bu çalışmada, hemşirelerin TABBY konusundaki bilgi düzeylerinin artırılması amacıyla verilen eğitimin etkisi incelenmiştir. Bulgularımız, literatürdeki önceki çalışmalarla uyumlu olarak, eğitim programlarının hemşirelerin bilgi düzeylerini ve klinik uygulama becerilerini anlamlı şekilde geliştirdiğini göstermekte olup H_1 hipotezinin kabul edilmiştir.

Çalışmaya katılan hemşirelerin yaş ortalaması 31±6,0 yıl olup, büyük çoğunluğunu (%85) kadınlar oluşturmuştur. Katılımcıların %92,5'i lisans mezunu, %45'i 1-5 yıl genel hemşirelik deneyimine ve %55'i 1-5 yıl yoğun bakım deneyimine sahipti. Ayrıca hemşirelerin %77,5'inin TABBY'ye yönelik daha önce herhangi bir eğitim almadığı saptanmıştır. Bu durum, TABBY konusunda mesleki eğitimin yaygın olmadığını ve hemşirelerin bilgi düzeylerinin artırılmasına yönelik eğitim programlarına duyulan ihtiyacı göstermektedir. Çalışma bulgularına göre, yoğun bakımda farklı sürelerde çalışan hemşirelerin eğitim öncesi ve sonrası test puan ortalamaları arasında istatistiksel olarak anlamlı bir fark bulunmamıştır (p>0,05). Benzer şekilde, yaş gruplarına göre de TABBY ön test ve son test puanları arasında anlamlı bir farklılık olmadığı tespit edilmiştir (p>0,05). Bu sonuçlar, TABBY konusundaki bilgi düzeyinin yaş veya yoğun bakımda çalışma süresinden bağımsız olarak, doğrudan verilen eğitime bağlı olarak değişebileceğini göstermektedir. Bu bulgular literatürdeki bazı çalışmalarla hem paralellik hem de farklılık göstermektedir. Sönmez ve Bahar'ın (2022) **30** çalışmasında, hemşirelerin bilgi düzeylerinin cinsiyet, yoğun bakımda çalışma süresi, daha önce konu hakkında bilgi sahibi olma durumu ve TABBY ile karşılaşma sıklığı gibi bireysel faktörlerden etkilendiği belirtilmiştir. Ancak mevcut çalışmada yaş ve çalışma süresi gibi faktörlerin bilgi düzeyinde anlamlı bir farklılık oluşturmadığı görülmüştür. Bu durum, eğitim içeriğinin ve yönteminin, bireysel değişkenlerden bağımsız olarak hemşirelerin bilgi düzeyini geliştirmede etkili olabileceğini düşündürmektedir.

TABBY'yi önlemeye yönelik yapılan eğitimin hemşirelerin performansı ve hastaların klinik sonuçları üzerindeki etkisinin incelendiği bir çalışmada, 70 hemşire ve 60 erişkin hasta örnekleme alınmış ve eğitimden 3 hafta sonra hemşirelerin bilgi düzeyinin ve uygulama becerilerini arttığı saptanmıştır.[21] Dallı ve Girgin'in (2024)[31] benzer çalışmasında ise eğitim sonrası hemşirelerin TABBY bilgi puanlarında anlamlı bir artış olduğu (13.23 ± 1.43'ten 20.02 ± 1.30'a, p = 0.001) ve en büyük gelişimin evreleme ve önleme temalarında gerçekleştiği belirtilmiştir.[31] Bu bulgular, hemşirelerin eğitim öncesi ve sonrası bilgi düzeyinde artış (21,75± 5.52'ten 28,47 ± 2.08) trendi ile tutarlıdır (Tablo 2). Bu bulgu, yapılandırılmış eğitimlerin, hemşirelerin TABBY önleme konusundaki bilgi düzeylerini artırmada etkili olduğunu göstermektedir. Literatürde de benzer şekilde, eğitim müdahalelerinin hemşirelerin bilgi, tutum ve uygulama becerilerini artırdığı çeşitli çalışmalarda ortaya konmuştur.[2,19] Bu bulgular, eğitim programlarının hemşirelerin TABBY önleme performansını geliştirmede önemli bir araç olduğunu göstermektedir.

Yoğun bakım biriminde çalışma süresi: Yoğun bakım biriminde çalışma süresi ile bilgi düzeyi arasındaki ilişki incelendiğinde, 6 yıldan az deneyime sahip hemşirelerin eğitim öncesi bilgi düzeylerinin daha yüksek olduğu, ancak genel olarak deneyim süresinin bilgi düzeyi üzerinde anlamlı bir etkisinin bulunmadığı saptanmıştır (p>0,05). Bu sonuç, mesleki deneyimin tek başına bilgi düzeyini belirleyici bir faktör olmadığını, bilgi düzeyinin güncel klinik uygulamalar, hizmet içi eğitimler ve bireysel öğrenme motivasyonuyla daha yakından ilişkili olduğunu göstermektedir. Benzer şekilde, Erbay Dallı ve Kelebek Girgin'in (2022)[20] 142 yoğun bakım hemşiresi ile yürüttüğü çalışmada da hemşirelerin TABBY bilgi puan ortalamasının %68,4 olduğu, yaş ve çalışma yılı ile bilgi düzeyi arasında anlamlı bir ilişki bulunmadığı, bilgi düzeyinin daha çok eğitime erişimle ilişkili olduğu vurgulanmıştır.[20] Literatürde yer alan diğer çalışmalar da bu bulguları desteklemektedir. Örneğin Apold ve Rydrych (2012)[12] çalışma süresinden bağımsız olarak, düzenli eğitim programlarının hemşirelerin TABBY önleme konusundaki bilgi ve uygulamalarını geliştirdiğini bildirmiştir. Arnold-Long ve ark. (2017)[32] ise, uzun süreli akut bakım hastanelerinde, hemşirelerin deneyim süresine bakılmaksızın, tıbbi araç kaynaklı basınç yaralanmalarının önlenmesinde bilgi eksikliklerinin devam ettiğini belirtmiştir. Dang ve ark.'nın (2022)[33] çalışmasında deneyim süresi ile TABBY risk faktörleri bilgisi arasında zayıf bir korelasyon olduğu (r=0,13, p=0,084) bildirilmiştir. Yılmaz ve Gürlek Kısacık (2025)[34] mesleki deneyim süresinin bilgiye etkisinin sınırlı olduğu gösterilmiştir (β=0,11, p=0,07). Coyer ve arkadaşlarının (2014)[7] çalışmasında hem deneyimli hem de daha az deneyime sahip hemşirelerin TABBY farkındalığında benzer eksiklikler gösterdiği, güncel bilgi ve protokollere ulaşımın kritik bir etken olduğu ifade edilmiştir. Benzer şekilde, Barakat-Johnson ve arkadaşları (2017) [8] ile Black ve Kalowes (2016)[1] tarafından yapılan çalışmalarda da, deneyim yılı arttıkça bilgi düzeyinin otomatik olarak artmadığı, sürekli eğitimlerin gerekli olduğu vurgulanmıştır. Çalışma, bilgi düzeyinin deneyim süresi yerine eğitim ve farkındalık düzeyine bağlı olduğunu göstermiştir. Bu bulgu Zhang ve arkadaşlarının (2021)[22] Çin'de yaptığı çalışma sonucu ile paraleldir; burada da hemşirelerin TABBY'yi önleme konusundaki bilgi, tutum ve uygulamalarının geliştirilmesinde deneyimden çok eğitim programlarının etkili olduğu belirlenmiştir. Sonuç olarak, mevcut bulgular, hemşirelerin TABBY'yi önleme konusudnaki bilgi düzeylerinin artırılması için yalnızca klinik deneyime güvenmenin yetersiz olduğunu; düzenli hizmet içi eğitimlerin, güncel klinik rehberlere erişimin ve bireysel öğrenme motivasyonunun teşvik edilmesinin kritik olduğunu ortaya koymaktadır. Böylece hemşirelerin bilgi düzeyleri yükseltilerek, hasta güvenliği ve bakım kalitesi önemli ölçüde artırılabilir.

Yaş grupları: Yaş değişkeni açısından değerlendirildiğinde, 24-30 ve 31-47 yaş grupları arasında eğitim öncesi bilgi düzeylerinde istatistiksel olarak anlamlı bir fark bulunmamıştır ($p>0,05$). Ayrıca, yoğun bakımda çalışan hemşirelerin yoğun bakımda çalışma süresi ile eğitim öncesi ve sonrası bilgi puan ortalamaları arasında da anlamlı bir farklılık saptanmamıştır ($p>0,05$, Tablo 3). Bu nedenle, H_2 hipotezi reddedilmiştir. Bu bulgu, yaşın öğrenme kapasitesi üzerinde sınırlayıcı bir etkisinin bulunmadığını ve etkili bir eğitim programının farklı yaş gruplarındaki sağlık profesyonelleri üzerinde benzer düzeyde olumlu sonuçlar doğurabileceğini göstermektedir. Bu sonuçlar Zhang ve ark.'nın (2021)[22] çalışma sonuçları ile paralellik göstermektedir. Sun ve arkadaşları (2023)[23] ise yaşın bilgi düzeyi ile negatif yönde çok zayıf bir ilişki gösterdiğini ($r=-0,083$, $p>0,05$) ancak anlamlılık düzeyine ulaşmadığını bildirmiştir. Bu sonuçlar yaşın, tıbbi araç ilişkili basınç yaralanmalarının önlenmesine yönelik bilgi ve uygulamalarda belirleyici bir faktör olmadığını desteklemektedir.

Öte yandan benzer şekilde, Dalvand ve arkadaşlarının (2018)[19] sistematik derlemesinde de yaşın bilgi düzeyi üzerindeki etkisinin tutarsız olduğu ve çoğu çalışmada anlamlı bir ilişki bulunmadığı belirtilmiştir. Sonuç olarak, literatürdeki bulgular yaşın eğitim sonrası bilgi düzeyine etkisinin minimal olduğunu, etkili eğitim programlarının yaş bağımsız olarak tüm sağlık profesyonellerinde bilgi artışı sağladığını göstermektedir. Bu da, farklı yaş gruplarındaki hemşirelerin eğitim gereksinimlerinin karşılanabileceğini ve yaş faktörünün eğitim planlamasında sınırlayıcı bir unsur olarak değerlendirilmemesi gerektiğini ortaya koymaktadır.

Eğitim düzeyi: Bu çalışmada eğitim düzeyinin yüksek lisans derecesine sahip hemşirelerin bilgi düzeyleri ortalaması 25,3 olarak lisans derecesindeki hemşirelerden yüksek bulunmuş olup yine benzer bir sonuç 2023 yılında yoğun bakım ünitesi hemşirelerinin TABBY konusundaki bilgi, tutum ve uygulama yeteneğinin araştırıldığı bir çalışmada hemşirelerin bilgi ve tutumlarının Yüksek eğitim geçmişi, katılımda bulunulan eğitim, yüksek çalışma yılı ve yüksek mesleki unvan arasında bir ilişki olduğu bulunmuştur (Sun ve ark., 2023).[23]

Bu bulgu literatürdeki birçok çalışma ile uyumludur. Apold ve Rydrych'ın[12] çalışmasında, veri temelli iyileştirme süreçlerinde lisansüstü eğitim almış hemşirelerin TABBY önlenmesinde daha etkin olduğu rapor edilmiştir.[12] Öte yandan Zhang ve arkadaşlarının (2021)[22] Çin'de 1002 yoğun bakım hemşiresiyle gerçekleştirdiği çalışmada lisans ve üzeri eğitim düzeyine sahip hemşirelerin bilgi ve uygulama puanlarının diğer hemşirelere göre anlamlı derecede yüksek olduğunu ortaya koymuştur.[22]

SONUÇ

Bu çalışma, TABBY'nin önlenmesinde hemşirelerin eğitim düzeyinin önemli bir belirleyici olduğunu ortaya koymuştur. Toplam 40 hemşireyi kapsayan çalışmamızda, eğitimin TABBY hakkında bilgi düzeyine etkisi istatistiksel olarak anlamlı bulunmuştur. Hemşirelerin eğitim öncesi bilgi puan ortalamasının 21,75 olması, bu konudaki bilgi düzeylerinin orta seviyede olduğunu göstermektedir. Eğitim sonrasında bilgi düzeylerinde anlamlı bir artış gözlemlenmiş, bu da hemşirelerin TABBY konusunda farkındalıklarının ve bilgilenmelerinin eğitim yoluyla artırılabileceğini göstermiştir. Sonuç olarak, TABBY'lerin önlenmesinde hemşirelerin bilgi düzeyinin artırılması kritik öneme sahiptir. Hemşirelere yönelik düzenli, güncel ve kanıta dayalı eğitim programlarının planlanması ve sürdürülmesi; bilgi düzeyinin kalıcılığının sağlanması ve bu bilgilerin klinik uygulamalara etkin şekilde yansıtılması açısından gereklidir. Özellikle yoğun bakım hemşireleri için sürekli hizmet içi

eğitim programlarının oluşturulması ve bu programların düzenli aralıklarla güncellenmesi önerilmektedir.

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REKTÖRLÜK MAKAMINA

Üniversitemiz, İktisadi Kalkınma ve Sosyal Araştırmalar Enstitüsü iş birliğinde 15-19 Mayıs 2025 tarihleri arasında Dubai'de düzenlenecek olan Ispec 9.Uluslararası Tıp Ve Sağlık Bilimleri Kongresinde ***Kongre Başkanı*** olarak gerekli iş ve işlemleri düzenleyebilmek adına Fakültemiz akademik personelinden ***Doç. Dr. H. Turan AKKOYUN'un*** kurulda yer alması hususunu;

Olurlarınıza arz ederim.

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İlgi yazınız gereği alınan Rektörlük Makamı Oluru yazımız ekinde sunulmuştur.
Bilginize rica ederim.

Prof. Dr. Mehmet SAĞLAM
Dekan V.

Ek:Kongre Baskani Oluru (Doc. Dr. H. Turan AKKOYUN)

Bu belge, güvenli elektronik imza ile imzalanmıştır.

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