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EDITORIAL

Değerli Medical Research Reports Dergisi Okuyucuları,

Medical Research Reports Dergisinin 2025 yılı birinci sayısını sizlerle paylaşıyoruz. Bu sayıda dört araştırma makalesi, üç derleme olmak üzere çok değerli yedi bilimsel araştırma bulunmaktadır. Literatüre kazandırılan bu çalışmaların ilgi ile okunacağını ve başka araştırmalara referans oluşturacağını umuyoruz.

Hedefimiz ve çalışmalarımız; okunurluğu ve erişilebilirliği yüksek, uluslararası standartlara uygun bilimsel bir yayın olmak yönündedir. Yeni yılla birlikte daha fazla indekste yer almaya çalışacağız. Mevcut standartlarımız ve yayın süreçlerimiz buna uygun şekilde yapılandırılmıştır.

Meslektaşlarımızı çalışmalarını Medical Research Reports aracılığı ile bilim dünyasıyla paylaşmaya davet eder, saygılarımızı sunarız.

Doç. Dr. Egemen Ünal
Baş Editör

Doç. Dr. Tayyib KADAK
Doç. Dr. Mehmet Enes GÖKLER
Editörler

Dear Readers of the Journal of Medical Research Reports,

We share with you the first issue of the Medical Research Reports Journal for 2025. There are seven scientific articles in this issue, including four original studies and three review. We hope that these studies brought to the literature will be read with interest and will serve as a reference for other studies.

Our goal and work; It aims to be a scientific publication with high readability and accessibility, in line with international standards. We will try to be included in more indexes with the new year. Our current standards and publication processes are structured accordingly.

We invite our colleagues to share their work with the scientific world through Medical Research Reports, and we present our respects.

Associate Professor Egemen Unal
Chief Editor

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Editors

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ORIGINAL ARTICLE

Maternal Exposure to Endocrine Disruptors, Lifestyle Factors, and Developmental Enamel Defects: A Pilot Study

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ABSTRACT

Aim: The aim of this study is to evaluate the relationship between endocrine disruptor chemicals using in the daily routine during breastfeeding and pregnancy period and the developmental enamel defects (DDE) and Molar Incisor Hypomineralization (MIH) presence. **Method:** 313 (n=313) parents and their child who aged between 8 and 11, along with their parents, were enrolled in the study for routine dental check-ups at the pediatric dentistry clinic was included to this current study. This is a descriptional and cross-sectional study. Prior to participant enrolment, this study was approved by the Hamidiye Scientific Ethical Research Committee, University of Health Sciences (22-591). After consent forms were completed, the surveys' questions were scanned via QR codes on patients' phones for them to answer. The dental examination of the child was conducted, and the condition of the teeth was documented based on enamel defects. The relationship between categorical variables obtained from oral findings was examined through chi-square analysis, with analyses conducted using SPSS 20.0 software at a 95% confidence interval. **Results:** MIH prevalence was 36 % (n=114) and DDE prevalence was 3% (n=10). 4% (n=15) of the population have defects on lower incisor teeth. There is a significant relationship between the consumption of packaged foods during the breastfeeding period and the MIH group ($p < 0.05$). Also, it was observed that there is a statistically significant association between drug usage during pregnancy and the occurrence of MIH and DDE. **Conclusion:** The likelihood of developmental enamel defects and Molar-Incisor Hypomineralization (MIH) has been associated with the consumption of packaged foods during pregnancy and lactation. Further comprehensive studies are needed regarding the use of endocrine-disrupting chemicals.

Keywords: Developmental defects of enamel, Endocrine disruptors, Molar hypomineralization

ÖZET

Amaç: Bu çalışmanın amacı, gebelik ve emzirme dönemlerinde günlük yaşamda kullanılan endokrin bozucu kimyasallar ile gelişimsel mine defektleri (GMD) ve Molar İnsizör Hipomineralizasyon (MIH) varlığı arasındaki ilişkiyi değerlendirmektir.**Yöntem:** Bu tanımlayıcı ve kesitsel çalışmaya, pedodonti kliniğinde rutin diş muayenesi için başvuran, yaşları 8 ile 11 arasında değişen toplam 313 (n=313) çocuk ve ebeveynleri dahil edilmiştir. Katılımcıların dahil edilmesinden önce çalışma, Sağlık Bilimleri Üniversitesi Hamidiye Bilimsel Etik Araştırma Komitesi tarafından onaylanmıştır (22-591). Onam formlarının doldurulmasının ardından, katılımcılar anket sorularını QR kodlar aracılığıyla kendi telefonlarından yanıtlamıştır. Çocukların dental muayeneleri gerçekleştirilmiş ve dişlerin durumu mine defektleri açısından belgelenmiştir. Ağız içi bulgulardan elde edilen kategorik değişkenler arasındaki ilişkiler ki-kare analizi ile incelenmiş olup analizler, %95 güven aralığında SPSS 20.0 yazılımı kullanılarak gerçekleştirilmiştir.**Bulgular:** MIH prevalansı %36 (n=114) ve GMD prevalansı %3 (n=10) olarak tespit edilmiştir. Popülasyonun %4'ünde (n=15) alt kesici dişlerde defektler gözlenmiştir. Emzirme döneminde paketlenmiş gıda tüketimi ile MIH arasında anlamlı bir ilişki bulunmuştur ($p < 0,05$). Ayrıca, gebelik sırasında ilaç kullanımının MIH ve GMD görülme sıklığı ile istatistiksel olarak anlamlı bir ilişki gösterdiği saptanmıştır.**Sonuç:** Gebelik ve emzirme döneminde paketlenmiş gıda tüketimi, gelişimsel mine defektleri ve Molar-İnsizör Hipomineralizasyon (MIH) olasılığı ile ilişkilendirilmiştir. Endokrin bozucu kimyasalların etkileri üzerine daha kapsamlı çalışmalara ihtiyaç duyulmaktadır.

Anahtar kelimeler: Gelişimsel mine defektleri, Endokrin bozucular, Molar hipomineralizasyon

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INTRODUCTION

Developmental enamel defects (DDE) arise due to biological imbalances that affect the cells responsible for enamel formation and maturation (1). Enamel is the most hard biomineralized tissue, the formation process of this unique structure is sequential, intricate, and highly detailed. It follows a series involving stages such as ameloblast proliferation, differentiation, maturation, and eventual death. Briefly, after stem cell commitment in the cervical loop, secretory-stage ameloblasts secrete enamel matrix proteins (EMPs) that determine enamel thickness, and maturation-stage ameloblasts secrete proteases, and control pH and ion transports, allowing apatite crystal assembly and complete enamel mineralization. Ameloblasts disappear during tooth eruption. Thus, any disruption of ameloblast activity leads to irreparable enamel defects that may be used for recording ameloblast stressors.

Molar-incisor hypomineralization (MIH) is a global health issue and a challenging dental problem to manage. Developmental defects in tooth enamel are observed quite commonly (with a prevalence rate of 12.9% - 15%) exhibiting notable variations among different countries (2, 3). Prevalence of MIH can range between 2.8 to 40.2% (4) can manifest during both the prenatal and postnatal periods as well as in newborns. The etiological mechanism behind MIH remains unclear. These developmental anomalies can be associated with over 100 environmental and genetic factors (5). Several potential causes have been proposed in the literature, such as respiratory tract infections, perinatal complications, dioxins, hypoxia, low birth weight, disruptions in calcium and phosphate metabolism, recurrent childhood illnesses, antibiotic usage, and prolonged breastfeeding. Furthermore, certain studies suggest the involvement of genetic factors in the onset of MIH, implying that genetic variations might interact with systemic factors, ultimately contributing to the development of MIH (6, 7).

The literature focused on developmental disturbances of enamel formation resulting from long-term exposure to chemicals. Endocrine-disrupting chemicals (EDCs) are a group of exogenous chemicals known to mimic hormones, and they are increasingly becoming a subject of extensive research. Bisphenol A (BPA) stands out as one of the most well-known endocrine disruptors. It was declared a "toxic substance" by the

Canadian government in 2010 (Canadian Environmental Protection Act, 2010) and most recently in 2017, it was identified as a "substance of very high concern" by the European Union (European Chemicals Agency, 2017). Despite concerns about its harmful effects, it remains a chemical with a high production volume globally, with an annual production exceeding 7 million tons(8). These chemicals can not only directly affect individuals but also can pass through the placental barrier, potentially exposing fetuses during gestation and subsequently being transferred to offspring after birth through breast milk (9, 10). Studying the impact of environmental toxic substances on human enamel development is challenging due to odontogenesis commencing during the embryonic period and further occurring within the confines of bone. Morphogenesis of deciduous teeth initiates around the sixth week of gestation. However, the effects of toxic substances' exposure can only be observed post the eruption of teeth into the oral cavity(11).

The quality and integrity of enamel are crucial concerning general health, quality of life, and sociability. They can be influenced by hereditary genetic traits, environmental factors, and lifestyle. Determining the effects of pollutants and contaminants on health is challenging as they are often found in low doses and are metabolized (12). The oral cavity serves as a primary route for contamination by molecules that can seep from various sources such as food, beverages, the air, and dental materials used in dentistry, leading to continuous exposure of oral tissues to such molecules. This study demonstrates how di- (2-ethylhexyl) phthalate (DEHP) / mono-ethylhexyl phthalate (MEHP), which persists in our environment despite limitations, affects tooth development in mice and could cause defects that might alter the quality of life if occurring in humans. Dental defects are highly prevalent and contribute to increased financial burdens, exacerbating social inequalities; hence, understanding and actively preventing these issues is essential. Furthermore, the precise characterization of acquired enamel defects will facilitate their use as early indicators of exposure to such molecules (13).
Studies in the literature suggest a potential association between DDEs and EDCs (14). Additionally, research indicates that DEDs may be influenced by various factors during pregnancy and lactation (7). However, no study has specifically investigated the relationship between exposure to different EDCs during pregnancy and lactation and the occurrence of DEDs. This study aims to evaluate the relationship between endocrine disruptor chemicals use in the daily routine during breastfeeding and pregnancy period and the presence of developmental enamel defects. The null hypothesis of this study is that there is no significant difference in the presence of DDE and MIH between individuals exposed and not exposed to endocrine-disrupting chemicals during pregnancy and breastfeeding.

MATERIAL AND METHODS

The power analysis for this study, conducted using the G*Power 3.1 program,

determined an effect size of 0.58 for the trimester of illness between the control and study groups. With an alpha error probability of 0.05 and a power value of 0.80, the sample size analysis indicated that a total of 322 participants (161 per group) would be required (15). The survey included 330 children who aged between 8 and 11, along with their parents, were enrolled in the study for routine dental check-ups at the pediatric dentistry clinic. 17 participants were excluded from the study due to incomplete survey responses. 313 (n=313) parents and their child was included to this current study.

This is a descriptional and cross-sectional study. Prior to participant enrolment, this study was approved by the Hamidiye Scientific Ethical Research Committee, University of Health Sciences (22-591).

After consent forms were completed, the surveys' questions were scanned via QR codes on patients' phones for them to answer. All questionnaires were completed voluntarily and anonymously.

Survey instrument

The survey questions were prepared based on relevant literature (16-19). The first section of the survey covers demographic information, while the second section focuses on systemic factors that might be related to developmental enamel defects during pregnancy and breastfeeding (such as smoking and alcohol consumption, systemic diseases, medication use, allergies, etc.). It includes questions about chemical exposure (use of cosmetic products, water consumption, plastic usage, etc.) as well as the level of stress during pregnancy and breastfeeding (Table 1 and 2).

The dental examination of the child was conducted, and the condition of the teeth was documented based on enamel defects. The classification system modified from Ghanim et al. (2015)(20), adapted from the European Academy of Pediatric Dentistry (EAPD) latest classification, was utilized. This classification encompasses both DDE and MIH information.

Table 1. Survey Questions

Mode of birth	**Ceserian**	**Normal**		
Duration of breast milk intake	0-6 m	6-12 m	12 m and more	
Number of ultrasound during pregnancy	0-3	3-10	10 and more	
Birth time	Early birth (36 week and before)	Normal timing birth (37-40 week)	Late birth (41 and more week)	
Childs birth weight	Low	Normal	More	
The material of the bottle used	Plastic	Polypropylene	Glass	Don’t know
Did you have filling during pregnancy?	Yes	No		

Type of water you consume?	Jug water	Plastic bottle	Purified water	Tap water	Glass bottle
Usage of cigarettes during pregnancy	No	1-10 per day	10-20 per day	1-2 pocket cigarettes	
Your stress level during pregnancy, number between 1-10					
Your stress level during breastfeeding, number between 1-10					
Folic acid usage in pregnancy	Yes	No	Don't know		
Alcohol usage in pregnancy	Yes	No	Don't know		
Medicament usage in pregnancy	Yes	No	Don't know		
Antibiotic usage in pregnancy	Yes	No	Don't know		
Any disease with fever in pregnancy	Yes	No	Don't know		
Neonatal jaundice	Yes	No	Don't know		
Any allergy	Yes	No	Don't know		
Any allergy of child	Yes	No	Don't know		
D vitamin deficiency	Yes	No	Don't know		
D vitamin deficiency of children	Yes	No	Don't know		
Fever disease to 1 year	Yes	No	Don't know		
Antibiotic usage to 1 year	Yes	No	Don't know		
Asthma of children	Yes	No	Don't know		

Table 2. Survey Questions Continued - About Habits During Pregnancy and Breastfeeding Habits During Pregnancy and Breastfeeding

Use of stretch film in meals
Plastic containers heating food
Plastic containers storing food
Perfume usage
Sprey cosmetic products usage
Nail polish usage
Lipstick usage
Shampoo usage
Deodorant usage

Cosmetic products in pregnancy/breastfeeding
Having an x ray in pregnancy/breastfeeding
Convience food
Pet bottle usage

Statistical Analysis

The relationship between categorical variables obtained from oral findings was examined through chi-square analysis, with analyses conducted using SPSS 20.0 software at a 95% confidence interval.

RESULTS

The mean age of the population was 9.2 ± 1.7. MIH. 38.3% of girls have MIH whereas 35% of boys have MIH. 5.8% of girls have DDE, while in males, the percentage is 0.6%. MIH prevalence was 36 % (n=114) and DDE prevalence was 3% (n=10) (Table 3).

Table 3. Demographic information and MIH, DDE status of the participants

		MIH+		MIH-DDE+		MIH-DDE-		p
		n	%	n	%	n	%	
Gender	Girl	59	38,3	9	5,8	86	55,8	**0,021**
	Boy	55	35,0	1	0,6	101	64,3	
Education level (mother)	Primary school	61	36,3	7	4,2	100	59,5	0,315
	High school	42	41,2	1	1,0	59	57,8	
	University or high	10	26,3	2	5,3	26	68,4	
Working status of mother	Yes	9	26,5	1	2,9	24	70,6	0,410
	No	105	37,9	9	3,2	163	58,8	
Income level	0-5000	28	45,2	4	6,5	30	48,4	0,155
	5000-10000	50	36,2	2	1,4	86	62,3	
	10000-20000	24	30,4	4	5,1	51	64,6	
	20000 and more	6	28,6	0	0,0	15	71,4	

MIH: Molar-incisor hypomineralization, **DDE**: Developmental enamel defects

4% (n=15) of the population have defects on lower incisor teeth 6% (n=19) of the population have atypical caries due to hypoplasia. There is no significant relationship between educational status, employment and household income level ($p > 0.05$) and MIH. There is no significant relationship between MIH status and mode of delivery, duration of breastfeeding, number of prenatal ultrasound scans gestational week at birth and birth weight of the child ($p >0.05$). When examining the relationship between the status of having twins and the MIH group, it was found that MIH was present in 69.2% of those with twins and 35% of those without twins. There is a significant relationship between the status of being twins and MIH ($p < 0.05$). There is a significant relationship between the consumption of packaged foods during the breastfeeding period and the MIH group ($p<0.05$). MIH was present in 32.5% of those didn't consume packaged foods during breastfeeding, while it was found in 45.5% of those who consume packaged foods. Also, it was observed that there is a statistically significant association between drug usage during pregnancy and the occurrence of MIH and DDE ($p<0.05$). The rate of MIH occurrence in pregnant women using drugs is 42.9%, while the rate of DDE occurrence is 6%. The rate of MIH occurrence among those with no symptoms is 51.2%. Among non-users of drugs, the rate of MIH occurrence is 34.2%, and the rate of DDE occurrence is 1.8%. There is no statistically significant relationship between using cosmetic products and plastics in the kitchen during pregnancy, lactation and MIH ($p > 0.05$).

DISCUSSION

The prevalence of DDE and MIH varies from 2.8% to 40.2% in numerous studies, presenting a significant range (2). In the current study, MIH prevalence was 36 % and DDE prevalence was 11%. Over the years, it has emerged as a growing issue with increasing prevalence. The etiology of this condition has been associated with numerous factors, yet a conclusive determination remains elusive. Ongoing research is being conducted to further explore this matter. The etiology of DDE is often multifactorial and complex, influenced by various factors such as geographical location, genetic predisposition, and environmental elements(6, 7).

The onset of the amelogenesis stage for deciduous teeth begins at the 15th week of gestation, completing its growth by one year after birth (with the eruption of the second primary molars). In developed countries, 10-49% of healthy children exhibit DDE in their primary teeth, and studies report that 9-63% of these children also have DDE in their permanent teeth(15, 21). Perinatal and postnatal problems, antibiotic usage in the first 3 years of life, and injuries of infected primary teeth are also factors affecting the DDE rate (19).

Recent genetic studies have indicated that MIH is a multifactorial disorder. The enamel maturation period, commonly affected by MIH, corresponds to the last trimester of pregnancy through the child's third year of life, suggesting possible interaction between genetic diversity and environmental factors. The hypothesis leans towards genetic diversity in ENAM, and AMELX genes may cause

localized enamel hypomineralization. Genetic factors solely affecting enamel may contribute to enamel defects, or a more generalized systemic syndrome may be responsible (21, 22).

In the current literature, maternal diseases, psychological stress, cesarean delivery, birth complications, respiratory tract infections, fever, and childhood illnesses are significantly associated with MIH (19). However, it has been reported that these findings should be interpreted with caution due to serious limitations such as selection of bias, uncertainty, and inconsistency in the studies from which the evidence is gathered (19). In this study, however, no significant association was found between type of birth, maternal, and child illnesses between MIH. However, in this study, it was observed that medication use during pregnancy increased the MIH prevalence.

Some recent studies have focused on potential determinants such as hypoxia in ameloblasts, dioxin in breast milk, respiratory tract infections, medication or antibiotic usage in children, and exposure to environmental pollution during the early stages of life, particularly prenatal, perinatal, and postnatal medical issues (23, 24). In this study, it was found that the likelihood of MIH occurrence is higher among those consuming packaged foods during the lactation period. Fully exploring the etiology of MIH is crucial for its prevention, necessitating field studies with large sample sizes.

Furthermore, recent genetic studies (6, 22) have reported that MIH is a multifactorial disorder. The maturation period of the enamel, which is widely affected by MIH, coincides with the last three months of pregnancy to the child's third year of life, during which enamel maturation is possible. Factors wherein genetic diversity may interact with environmental factors are conceivable. There is a hypothesis suggesting that genetic variations in ENAM and AMELX genes may lead to localized enamel hypomineralization. Genetic factors affecting only enamel may play a role in enamel defects or a more general systemic syndrome may cause them (6, 22).

The limitations of this study include the fact that pregnancy and lactation are influenced by numerous variables, making it difficult to assess their effects accurately. Additionally, the identification of endocrine-disrupting chemicals is challenging. Furthermore, the lack of a severity-based classification in the evaluation of MIH is another limitation of the study. In investigating the etiology of enamel defects, a variety of methods have been employed, including the use of surveys accompanied by questions about individuals' lifestyle habits or the collection of their medical histories (25, 26). Developing a scale is may be necessary to investigate enamel defects during the pregnancy and lactation periods, which involve numerous variables. Particularly, there is a need for advancements in endocrine-disrupting chemicals.

CONCLUSION

The potential association between the consumption of packaged foods during pregnancy and lactation and the likelihood of developmental enamel defects, including Molar-Incisor Hypomineralization (MIH), warrants further investigation. Comprehensive studies are needed to better understand the role of endocrine-disrupting chemicals in this context.

Financial support: There is no funding to declare.

Conflict of interest: The authors have no conflicts of interest to declare.

Ethics approval: Informed consent Informed consent was obtained from all subjects involved in the study. This study was approved by the Hamidiye Scientific Ethical Research Committee, University of Health Sciences (22-591), in accordance with the Declaration of Helsinki . All of the participants completed consent forms. There is no acknowledgements. There was no funding.

Data availability: The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

List of abbreviations

Developmental enamel defects (DDE)

Molar-incisor hypomineralization (MIH)

Endocrine-disrupting chemicals (EDCs)

References

1. Seow WK. Developmental defects of enamel and dentine: challenges for basic science research and clinical management. Aust Dent J. 2014;59 Suppl 1:143-54.
2. Jalevik B. Prevalence and Diagnosis of Molar-Incisor- Hypomineralisation (MIH): A systematic review. Eur Arch Paediatr Dent. 2010;11(2):59-64.
3. Guerra BMDS Jorge RC, Reis PPGD, Machado GF, Fidalgo TKDS, Soviero VM. Prevalence of molar incisor hypomineralization and demands for treatment according to the severity of its clinical manifestation. Clin Oral Investig 2025 24(1):82.
4. Ghanim A, Silva MJ, Elfrink MEC, Lygidakis NA, Marino RJ, Weerheijm KL,et al.Molar incisor hypomineralisation (MIH) training manual for clinical field surveys and practice. Eur Arch Paediatr Dent. 2017;18(4):225-42.
5. Collignon AM, Vergnes JN, Germa A, Azogui S, Breinig S, Hollande C, et al. Factors and Mechanisms Involved in Acquired Developmental Defects of Enamel: A Scoping Review. Front Pediatr. 2022;10:836708.
6. Jeremias F, Koruyucu M, Kuchler EC, Bayram M, Tuna EB, Deeley K, et al. Genes expressed in dental enamel development are associated with molar-incisor hypomineralization. Arch Oral Biol. 2013;58(10):1434-42.
7. Teixeira R, Andrade NS, Queiroz LCC, Mendes FM, Moura MS, Moura L, et al. Exploring the association between genetic and environmental factors and molar incisor hypomineralization: evidence from a twin study. Int J Paediatr Dent. 2018;28(2):198-206.
8. Research GV. Bisphenol A (BPA) Market Analysis By Application (Polycarbonates, Epoxy resins) and segmentforecasts to2020;2015.Availablefrom:http://www.grandviewresearch.com/industryanalysis/bisphenol-a-bpa-market[Accessed 2nd December.2024].

9. Balakrishnan B, Thorstensen E, Ponnampalam A, Mitchell MD. Passage of 4-nonylphenol across the human placenta. Placenta. 2011;32(10):788-92.
10. Wan Y, Choi K, Kim S, Ji K, Chang H, Wiseman S, et al. Hydroxylated polybrominated diphenyl ethers and bisphenol A in pregnant women and their matching fetuses: placental transfer and potential risks. Environ Sci Technol. 2010;44(13):5233-9.
11. Logan WG, Kronfeld R. Development of the human jaws and surrounding structures from birth to the age of fifteen years. J Am Dent Assoc. 1933;20:379–427.
12. Lacruz RS, Habelitz S, Wright JT, Paine ML. Dental Enamel Formation and Implications for Oral Health and Disease. Physiol Rev. 2017;97(3):939-93.
13. Kawano S, Morotomi T, Toyono T, Nakamura N, Uchida T, Ohishi M, et al. Establishment of dental epithelial cell line (HAT-7) and the cell differentiation dependent on Notch signaling pathway. Connect Tissue Res. 2002;43(2-3):409-12.
14. Bui AT, Houari S., Loiodice S., Bazin D., Sadoine J., Roubier N., et al. Use of Dental Defects Associated with Low-Dose di(2-Ethylhexyl) Phthalate as an Early Marker of Exposure to Environmental Toxicants. EHP. 2022 Jun 1;130(6).
15. Ghanim A, Marino R, Morgan M, Bailey D, Manton D. An in vivo investigation of salivary properties, enamel hypomineralisation, and carious lesion severity in a group of Iraqi schoolchildren. Int J Paediatr Dent. 2013;23(1):2-12.
16. Costa FS, Silveira ER, Pinto GS, Nascimento GG, Thomson WM, Demarco FF. Developmental defects of enamel and dental caries in the primary dentition: A systematic review and meta-analysis. J Dent. 2017;60:1-7.
17. Bagattoni S, Carli E, Gatto MR, Gasperoni I, Piana G, Lardani L. Predisposing factors involved in the aetiology of Molar Incisor Hypomineralization: a case-control study. Eur J Paediatr Dent. 2022;23(2):116-20.
18. Philips EM, Jaddoe VWV, Asimakopoulos AG, Kannan K, Steegers EAP, Santos S, et al. Bisphenol and phthalate concentrations and its determinants among pregnant women in a population-based cohort in the Netherlands, 2004-5. Environ Res. 2018;161:562-72.
19. Fatturi AL, Wambier LM, Chibinski AC, Assuncao L, Brancher JA, Reis A, et al. A systematic review and meta-analysis of systemic exposure associated with molar incisor hypomineralization. Community Dent Oral Epidemiol. 2019;47(5):407-15.
20. Ghanim A., Elfrink M., Weerheijm K., Mariño R., Manton D. A practical method for use in epidemiological studies on enamel hypomineralisation. Eur Arch Paediatr Dent. 2015;16(3):235-46
21. Salanitri S, Seow WK. Developmental enamel defects in the primary dentition: aetiology and clinical management. Aust Dent J. 2013;58(2):133-40; quiz 266.
22. Jeremias F, Pierri RA, Souza JF, Fragelli CM, Restrepo M, Finoti LS, et al. Family-Based Genetic Association for Molar-Incisor Hypomineralization. Caries Res. 2016;50(3):310-8.
23. Kuscu OO, Caglar E, Aslan S, Durmusoglu E, Karademir A, Sandalli N. The prevalence of molar incisor hypomineralization (MIH) in a group of children in a highly polluted urban region and a windfarm-green energy island. Int J Paediatr Dent. 2009;19(3):176-85.
24. Oyedele TA, Folayan MO, Adekoya-Sofowora CA, Oziegbe EO, Esan TA. Prevalence, pattern and severity of molar incisor hypomineralisation in 8- to 10-year-old school children in Ile-Ife, Nigeria. Eur Arch Paediatr Dent. 2015;16(3):277-82.
25. Noor Mohamed R., Basha S., Virupaxi SG, Idawara Eregowda N., Parameshwarappa P. Hypomineralized Primary Teeth in Preterm Low Birth Weight Children and Its Association with Molar Incisor Hypomineralization A 3-Year-Prospective Study. Children. 2021;8(12): 1111.
26. Hernandez M, Boj J., Espasa E., Planells P., Peretz B. Molar-Incisor Hypomineralization: Positive Correlation with Atopic Dermatitis and Food Allergies. J Clin Pediatr Dent. 2018;42(5):344-48.

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ORIGINAL ARTICLE

The Relationship Between Blood Eosinophil Levels and COVID-19 Mortality

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ABSTRACT

Aim: COVID-19 is a global pandemic caused by severe acute respiratory syndrome (SARS-COV-2). The objective of this study is to determine the relationship between blood eosinophil levels and the severity and mortality of COVID-19. **Methods:** The data of 678 patients were retrospectively collected from the electronic database of a hospital by researchers between March 2020 and December 2021. This is a descriptive study, and no specific sampling method was employed. The data were evaluated based on three groups of patients (moderate, severe, and chronic). Eosinophil values within the first 24 hours following hospital admission were obtained. The data was analyzed through IBM SPSS Statistics (20.0) software. Parametric tests were used for the statistical evaluations when the normality assumptions were met. Mann-Whitney U was used for two independent groups and multivariate logistic regression analysis was used to identify the relations. p-value < 0.05 was considered statistically significant. **Results:** In our study, it was found that eosinophil levels did not have an effect on disease severity (p=0.941). The COVID-19 related mortality rate was 14.6%, and the rate of severe/critical disease progression was 27.3%. Upon examining hematological parameters, it was observed that critical cases had significantly higher NEU values (p=0.001) and PCT values (p=0.024). LYM (p=0.007), HGB (p=0.029), PLT (p=0.023), HCT (p=0.005), MCV (p=0.039), MCH (p=0.048), MCHC (p=0.001), and RDW (p=0.023) were significantly lower in the severe group. It was determined that age, HCT, MCV, MCHC, urea, uric acid, sodium and potassium parameters were not significant risk factors for mortality (p>0.05). A reduction in MCHC (OR: 0.996; p=0.007) and sodium (p=0.031) demonstrated a mitigating effect on disease severity. The predictive effect of other parameters was found to be statistically insignificant. **Conclusion:** The effect of eosinophil levels on the severity and mortality of COVID-19 has not been found, whereas a decrease in MCHC and sodium levels showed a mitigating effect on disease severity. Further research is needed to investigate the clinical significance of these indicators in COVID-19 patients.

Keywords: COVID-19, Disease Severity, Eosinophils, Mortality

ÖZET

Amaç: COVID-19, şiddetli akut solunum yolu sendromu SARS-COV-2'nin neden olduğu küresel bir pandemidir. Bu çalışmanın amacı, kan eozinofil düzeyleri ile COVID-19'un şiddeti ve mortalitesi arasındaki ilişkiyi belirlemektir. **Yöntem:** 678 hastanın verileri, Mart 2020 ile Aralık 2021 tarihleri arasında araştırmacılar tarafından bir hastanenin elektronik veri tabanından geriye dönük olarak toplandı. Bu tanımlayıcı bir çalışmadır ve özel bir örnekleme yöntemi kullanılmamıştır. Veriler, hastaların üç grubuna (orta, şiddetli ve kronik) dayanarak değerlendirildi. Hastaneye yatışı takip eden ilk 24 saat içinde alınan eozinofil değerleri elde edildi. Veriler, IBM SPSS Statistics (20.0) yazılımı kullanılarak analiz edildi. Normal dağılım varsayımlarının karşılandığı durumlarda parametrik testler kullanıldı. İki bağımsız grup için Mann-Whitney U testi ve ilişkileri belirlemek için çok değişkenli lojistik regresyon analizi kullanıldı. p değeri <0,05 istatistiksel olarak anlamlı kabul edildi. **Bulgular:** Çalışmamızda eozinofil düzeylerinin hastalık şiddetinde etkili olmadığı bulunmuştur (p=0,941). COVID-19'a bağlı ölüm oranı %14,6, şiddetli/kritik hastalık seyri oranı ise %27,3 olarak bulunmuştur. Hematolojik parametreler incelendiğinde, kritik vakaların anlamlı derecede daha yüksek NEU değerlerine (p=0,001) ve PCT değerlerine (p=0,024) sahip olduğu gözlenmiştir.

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LYM (p=0,007), HGB (p=0,029), PLT (p=0,023), HCT (p=0,005), MCV (p=0,039), MCH (p=0,048), MCHC (p=0,001) ve RDW (p=0,023) parametreleri şiddetli grupta anlamlı derecede düşüktür. Yaş, HCT, MCV, MCHC, üre, ürik asit, sodyum ve potasyum parametrelerinin mortalite için anlamlı risk faktörleri olmadığı belirlenmştir (p>0,05). MCHC'de azalma (OR: 0,996; p=0,007) ve sodyumda azalma (p=0,031) hastalık şiddeti üzerinde hafifletici bir etki göstermiştir. Diğer parametrelerin etkisi istatistiksel olarak anlamlı bulunmamıştır. **Sonuç:** Eozinofil düzeyinin COVID-19'un şiddeti ve mortalitesi üzerine etkisi bulunmamış olup, MCHC'de azalma ve sodyumda azalma hastalık şiddeti üzerinde hafifletici bir etki göstermiştir. Bu göstergelerin COVID-19 hastalarındaki klinik önemini araştırmak için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: COVID-19, Hastalık Şiddeti, Eozinofiller, Mortalite

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INTRODUCTION

COVID-19 is a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1). As the number of individuals infected with COVID-19 continues to rise globally and its effects on healthcare systems are observed, it is evident that clinical laboratories will play a crucial role in screening, diagnosis, monitoring, and contributing to treatments.

In this pandemic, the fundamental role of clinical laboratories extends beyond the etiological diagnosis of COVID-19. Monitoring COVID-19 patients biochemically through in vitro diagnostic tests is crucial not only for assessing disease diagnosis, severity, and progression but also for monitoring therapeutic interventions. One of the most significant contributions of laboratory findings encompasses the staging, prognosis, and therapeutic monitoring of COVID-19. Many laboratory tests can be highly beneficial in determining disease severity and assessing the risk of developing acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), and multiple organ failure (2).

Eosinophils are granulocytes that have strong pro-inflammatory effects and have been shown to participate in inflammation, immunoregulation, and host defense against various diseases, including viral infections. Eosinopenia is defined as a decrease in the circulating eosinophil count in peripheral blood. Eosinopenia has been observed during infection with SARS-CoV-2, the causative agent of COVID-19. Some studies have reported an association between eosinopenia and worsening respiratory symptoms (3). Recently, the role of eosinopenia as a diagnostic and prognostic indicator for COVID-19 has garnered interest. The role of eosinopenia becomes highly crucial as an early diagnostic indicator for COVID-19 infection, especially during pandemics when

resources are limited, and early decisions about patient triage and isolation are deemed extremely beneficial until nucleic acid confirmation is performed (4,5,6).

Regarding laboratory findings, in patients with severe illness, in addition to increased levels of inflammatory markers such as C-reactive protein (CRP), D-Dimer, and procalcitonin, other typical indicators include an increase in neutrophil counts and a decrease in lymphocyte levels. The aforementioned laboratory findings are shared with SARS-CoV-2 and MERS-CoV. A distinctive feature associated with SARS-CoV-2 infection is a decrease in eosinophil levels (eosinopenia). However, the results of previous studies on the relationship between eosinopenia and disease severity have been inconsistent (7,8,9). Since COVID-19 can lead to high mortality, studies have been conducted to investigate the relationship between eosinopenia and COVID-19 mortality, as well as to identify clinical conditions that may potentially lead to mortality. Identifying laboratory tests that contribute to the diagnosis and monitoring of COVID-19 is crucial not only for the diagnosis stage but also for distinguishing between severe and non-severe cases, as well as identifying those at low or high risk of mortality (10).

During a severe infection such as COVID-19, the levels of almost all markers can change, correlating with the severity of the disease and survival. However, until a biomarker is proven to have a significant impact, it cannot be translated into clinical practice for treatment guidance. Various studies have documented the relationship between the severity of COVID-19 and circulating levels of CRP and interleukin-6, evaluating the accuracy of CRP levels in predicting treatment responses. Promising findings related to prothrombin and D-Dimer have also been reported. However, the clinical utility of these biomarkers in COVID-19 is far from being proven (11). The surge in data generation during this pandemic has led to the publication of numerous studies with many significant disadvantages, weakening the strength of the findings.

The aim of this study is to determine the relationship between blood eosinophil levels and COVID-19 mortality.

MATERIAL AND METHODS

Patients

The data for the study were retrospectively collected by researchers between March 2020 and December 2021 from Izmir Menemen State Hospital. The study includes demographic information, clinical symptoms, comorbidities, laboratory data, and radiological materials of 678 confirmed COVID-19 patients who presented to the hospital. This is a descriptive study, and no specific sampling method was employed.

Clinical Classifications

Cases with a confirmed diagnosis of COVID-19 were included, consisting of individuals with SARS-CoV-2 infection confirmed through molecular methods, as well as patients with typical COVID-19 findings on CT scans. Patients currently hospitalized, those

discharged without medical advice, individuals undergoing steroid treatment, and patients presenting with eosinophilia were excluded from the study.

Data collection

According to the guidelines of the World Health Organization, patients with a positive result in the nucleic acid test for SARS-CoV-2 using real-time reverse transcription polymerase chain reaction (RT-PCR) were considered confirmed COVID-19 cases. Patients classified as moderate, severe, and critical cases during the assessment at the time of admission were included in the study. The collected data were evaluated based on these three groups of patients. Disease severity levels were classified according to the guidelines of the World Health Organization and the United States: Moderate disease: Presence of symptoms and signs of respiratory infection, but oxygen saturation is 94% or higher. Severe disease: Respiratory rate exceeding 30/minute, oxygen saturation below 94%, PaO2/FiO2 value less than 300 mmHg, or infiltration affecting more than 50% of the lungs. Critical disease: Defined by respiratory failure, septic shock, and/or multiple organ failure (12). In our hospital, an eosinophil count below 0.8% in mm^3 is defined as eosinopenia (reference range: 0.8-6). Eosinophil values within the first 24 hours following admission were collected for the patients included in the study. Patient information was kept confidential, consisting of demographic details, laboratory findings, accompanying illnesses, medical histories, clinical symptoms, chest CT images, and clinical details. The inclusion of other laboratory parameters may provide a better predictive model for disease outcomes in COVID-19 patients.

Statistical analysis

The data was analysed through IBM SPSS Statistics (20.0) software. Categoric variables were presented by number and percentages and continuous variables were given via descriptive statistics. Parametric tests were used for the statistical evaluations when the normality assumptions were met. Mann-Whitney U for was used for two independent groups, and multivariate logistic regression analysis were used to identify the relations. p value less than 0.05 was considered statistically significant.

Study approval

This protocol was approved by the Ethics Committee of Katip Çelebi University Non Interventional Clinic Studies (no. 57; date of approval: February 24, 2022), and was performed in accordance with the Declaration of Helsinki. Informed consent was not obtained as this is a retrospective study.

RESULTS

In our study, there were 307 (45.3%) female and 371 (54.7%) male patients. Patients under the age of 40 constituted 85 (12.5%), those between the ages of 40-64 accounted for 287 (42.3%), and patients aged 74 and above were 149 (22.0%). Disease severity was categorized into 67 (9.9%) severe cases and

118 (17.4%) critical cases, combined to form a total of 185 (27.3%) severe/critical cases, which were compared with 493 (72.7%) moderate cases. The fatality rate in our study was 14.6%, and the rate of severe/critical disease progression was 27.3%.

The severity of the disease did not show a significant difference according to gender (p=0.398). The rate of critical cases was significantly lower in individuals under 40 years old, and significantly higher in individuals over 74 years old (p<0.001). There is a significant relationship between the severity of the disease and age groups (p<0.001). In individuals under 40 and those between 40-64 years old, the rate of severe/critical cases was lower compared to other age groups. The rate of severe/critical cases was higher in individuals hospitalized (p<0.001), and the majority of death cases were observed in severe/critical cases (p<0.001). The presence of typical COVID-19 symptoms was associated with a higher incidence of severe/critical cases (p<0.001). Severe/critical cases were more prevalent in patients with severe findings on COVID-19 CT and positive PCR results (p<0.001). The majority of cases discharged with recovery were moderate cases, while the majority of referred cases were severe/critical (p<0.001). The rate of hospital discharge in severe cases was significantly higher (p<0.001) (Table 1).

Table 1: Comparison of Clinical Findings in Case Groups

	Disease Severity		
	Moderate Case (n=493) n(%)	**Severe/Critical Case (n=185) n(%)**	**p**
Gender			
Female	225 (73.3)	82 (26.7)	0.759
Male	268 (72.2)	103 (27.8)	
Age			
Below 40 years	69 (81.2)	16 (18.8)	**<0.001**
40-64 years	220 (76.7)	67 (23.3)	
65-74 years	112 (71.3)	45 (28.7)	
74 years and older	92 (61.7)	57 (38.3)	
Presence of chronic illness			
Yes	338 (73.3)	123 (26.7)	0.606
No	155 (71.4)	62 (28.6)	
Hospitalization status			
Yes	461 (75.9)	146 (24.1)	**<0.001**
No	32 (45.1)	39 (54.9)	
Total death			
Yes	41 (41.4)	58 (58.6)	**<0.001**
No	452 (78.1)	127 (21.9)	

CT Findings			
No Ct finding /incompatible with COVID-19	162 (85.7)	27 (14.3)	**<0.001**
Typical COVID-19 finding	331 (67.7)	158 (32.3)	
COVID-CT			
Mild	69 (71.9)	27 (28.1)	
Moderate	212 (73.4)	77 (26.6)	**<0.001**
Severe	49 (47.6)	54 (52.4)	
PCR			
Negative	2 (18.2)	9 (81.8)	**<0.001**
Positive	223 (85.1)	39 (14.9)	
Discharge Status			
Transfer(same or more comprehensive)	93 (38.1)	151 (61.9)	
Discharge with recovery	388 (92.4)	32 (7.6)	**<0.001**
Death	10 (90.9)	1 (9.1)	
Other	2 (66.7)	1 (33.3)	
Outpatient Treatment Death			
None	462 (78.3)	128 (21.7)	**<0.001**
Exist	31 (35.2)	57 (64.8)	

Eosinophil levels were found not to be effective in disease severity (p=0.941). When examining other hemogram parameters, NEU (neutrophil) values (p=0.001) and PCT (procalcitonin) values (p=0.024) were significantly higher in critical cases. LYM (lymphocyte) (p=0.007), HGB (hemoglobin) (p=0.029), PLT (platelet) (p=0.023), HCT (hematocrit) (p=0.005), MCV (mean corpuscular volume) (p=0.039), MCH (p=0.048), MCHC (mean corpuscular hemoglobin concentration) (p=0.001) and RDW (red cell distribution width) (p=0.023) parameters were observed to be significantly lower in the severe group (Table 2).

Table 2: Comparison of Hemogram Parameters According to the Severity of the Disease

	Disease Severity		**p**
	Moderate Case (n=493) mean±SD	**Severe/Critical Case (n=185) mean±SD**	
NEU(×103/µl)	8.29±6.57	10.95±5.15	**0.001**†
WBC (×103/µl)	4.93±7.48	7.05±17.17	0.135†
RBC (×103/µl)	9.59±20.02	14.00±26.64	0.505†
LYM(×103/µl)	1.26±2.46	0.96±1.20	**0.007**†

Monocyte (×103/µl)	2.60±25.89	3.56±15.15	0.282†
Eosinophil(×103/µl)	0.16±0.11	0.14±0.05	0.941†
Basophil	0.37±1.32	3.04±4.03	0.244†
HGB	7.75±8.22	6.89±12.35	**0.029**†
PLT	310.02±134.77	257.68±115.36	**0.023**†
HCT	30.50±15.43	21.28±18.82	**0.005**†
MCV	73.26±23.38	67.27±27.91	**0.039**†
MCH	22.13±11.76	20.04±13.87	**0.048**†
MCHC	20.43±15.87	13.44±15.58	**0.001**†
RDW	11.57±6.53	10.42±6.59	**0.023**†
MPV	8.75±37.06	3.92±5.05	0.070†
PDW	16.38±2.56	16.23±3.51	0.544†
PCT	9.21±12.89	14.58±14.44	**0.024**†

†Mann-Whitney U, p<0.05

Eosinophil levels were found not to be effective in disease severity (p=0.632). When examining other hemogram parameters, the NEU values of critical cases were found to be significantly elevated (p=0.046). Furthermore, in the severe group, the parameters of HGB (p=0.007), HCT (p=0.017), MCV (p<0.001), MCHC (p=0.002), and RDW (p=0.038) were significantly lower (Table 3).

Table 3: Comparison of Hemogram Parameters According to the Mortality

	Mortality		p
	Survived (n=579) mean±SD	**Deceased (n=99) mean±SD**	
NEU(×103/µl)	8.77±6.54	10.06±4.46	**0.046**†
WBC (×103/µl)	5.33±9.52	6.23±16.78	0.200†
RBC (×103/µl)	9.70±20.17	16.25±29.48	0.174†
LYM(×103/µl)	1.22±2.36	0.97±0.79	0.251†
Monocyte (×103/µl	2.89±25.27	0.72±0.70	0.739†
Eosinophil(×103/µl)	0.16±0.11	0.13±0.05	0.632†
Basophil	0.80±2.15	0.10±0.00	0.394†
HGB	7.89±9.63	5.31±7.53	**0.007**†
PLT	306.20±135.12	244.89±89.74	0.066†
HCT	29.52±16.11	19.35±18.65	**0.017**†

MCV	73.36±23.65	61.52±28.74	**0.000**†
MCH	21.44±11.49	22.74±16.87	0.848†
MCHC	20.06±15.92	10.84±14.70	**0.002**†
RDW	11.46±6.56	10.18±6.48	**0.038**†
MPV	8.23±34.68	3.18±4.01	0.075†
PDW	16.46±2.54	15.22±4.39	0.284†
PCT	10.08±13.43	13.73±13.19	0.365†

†Mann-Whitney U, p<0.05

In this study; when biochemical tests were evaluated according to mortality, D-Dimer (p=0.049), HDL (p=0.022), albumin (p=0.031), fasting glucose level (p=0.040), urea (p=0.014), uric acid (p=0.002), creatinine (p<0.001), and potassium (p=0.016) levels were found to be significantly higher in the deceased group. Sodium (p<0.001) was significantly lower in the deceased group.

When biochemical tests were evaluated among case groups, in the Critical Case group, D-Dimer (p=0.003), albumin (p=0.004), fasting glucose (p=0.005), urea (p<0.001), uric acid (p<0.001), creatinine (p<0.001), sodium (p=0.025), and potassium (p<0.001) parameters were observed to be significantly elevated, while ALT (p=0.042), AST (p=0.020), and fibrinogen (p=0.016) parameters were significantly lower (Table 4).

Tablo 4: Comparison of Biochemical Parameters According to Disease Severity

	Disease Severity		**p**
	Moderate Case (n=493) mean±SD	**Severe/Critical Case (n=185) mean±SD**	
CRP (mg/L)	35.00±23.03	41.86±28.98	0.156†
LDH (mg/dL)	103.17±133.24	73.80±81.44	0.196†
D-Dimer (mg/L)	4.14±18.26	7.80±21.79	**0.003**†
HDL	137.28±5.87	136.72±5.67	0.376†
Ferritin	286.42±239.36	325.93±262.15	0.339†
Albumin	8.92±8.15	14.45±9.71	**0.004**†
Troponin	51.22±309.57	7.64±22.46	0.472†
Prothrombin Time	13.25±18.29	13.62±19.93	0.497†
Fasting Glucose	135.52±63.83	178.69±75.80	**0.005**†
Urea	46.30±29.61	78.83±49.13	**<0.001**†
Uric Acid	11.80±27.52	35.43±69.08	**<0.001**†
Creatinine	10.15±29.08	20.63±41.33	**<0.001**†

ALT	45.03±40.99	37.96±33.52	**0.042**†
AST	38.14±27.24	31.32±19.73	**0.020**†
Na	135.99±5.34	125.11±30.82	**0.025**†
K	18.81±14.11	24.74±12.54	**<0.001**†
Respiratory Rate	17.47±9.01	19.13±8.88	0.560†
Saturation	91.59±7.06	88.49±9.12	0.061†
Alkaline Phosphate	90.75±46.55	86.19±43.67	0.633†
CK_MB_Mass	59.76±45.83	56.56±37.27	0.875†
Initial Hem	5.99±3.80	6.34±4.29	0.647†
Fibrinogen	205.70±163.30	153.59±131.53	**0.016**†

†Mann-Whitney U, p<0.05

In this study; the mortality status did not show significant gender differences (p=0.635). Mortality rate was significantly lower in individuals under 40 years old and significantly higher in those aged 74 and above (p<0.001). Hospitalized individuals had a higher mortality rate (p<0.001). The presence of typical COVID-19 symptoms indicated an increased mortality rate (p=0.001). Mortality rate was higher in severe COVID-19 CT cases (p<0.001) and in cases with positive PCR results (p=0.009).

Age, HCT, MCV, MCHC, urea, uric acid, sodium and potassium parameters were not identified as significant risk factors for mortality (p>0.05) (Table 5).

In this study a decrease in MCHC (OR: 0.996; p=0.007) and a decrease in sodium (p=0.031) were observed to have a mitigating effect on disease severity. The predictive effect of other parameters is not statistically significant.

Table 5: Multivariate Logistic Regression Analysis for Mortality Risk Factors

	OR	%95 GA	p
Age	1.053	(0.970-1.142)	0.218
HCT	1.028	(0.855-1.237)	0.768
MCV	0.974	(0.815-1.165)	0.773
MCHC	0.699	(0.222-2.202)	0.540
Urea	1.002	(0.964-1.041)	0.932
Uric acid	1.428	(0.911-2.237)	0.120
Na	0.868	(0.646-1.166)	0.347
K	0.594	(0.109-3.227)	0.547

DISCUSSION

In our study, which examined 678 patients diagnosed with COVID-19, we initially investigated factors influencing both the severity of the disease and mortality, particularly focusing on eosinophils. The fatality rate in our study was 14.6%, and the rate of severe/critical disease progression was 27.3%. An article evaluating fatality rates in hospitalized patients from different regions worldwide reported a fatality rate of 18.8% (13). Age has consistently been identified as one of the most important demographic factors affecting the severity of the disease course and fatality (14). A large-scale meta-analysis showed that the fatality rate was 2,32 times higher in individuals aged 70 and older (15). In Italy, one of the countries with the highest reported fatality rates in Europe, where a quarter of the population is aged 65 and over, an analysis found a crude fatality rate of 7.2%, with the fatality rate rising to approximately 20% in cases over 80 years old (16). In our study, a significant relationship was found between disease severity and age groups, with a notably higher rate of critical cases in individuals aged 74 and above. Elderly patients have numerous risk factors that predispose them to infection, and weakened immune function is one of them (17). Most of the cases hospitalized, referred, and deceased in our study were in this age group. However, referred patients are those referred from our hospital due to the need for intensive care, which may explain the higher rates of death and severe/critical cases in this group. Cases discharged with recovery mostly belonged to the moderate clinical cases. The out-of-hospital mortality rate is also high in severe cases, which is related to the advanced age group of patients admitted to the intensive care unit. Aging poses a significant risk in both getting sick and the severe progression of the disease. Especially in the elderly, the accurate identification of patients who need intensive care monitoring is crucial, and defining risk factors decisive for severe progression and intensive care follow-up is crucial, especially during periods of increased patient load. Identifying high-risk patients is essential for the effective use of healthcare resources in the face of an increasing patient burden.

In our study, when hematological parameters were examined according to disease severity, eosinophils were not identified as a parameter indicating disease severity. NEU and PCT values of critical cases are significantly higher. LYM, HGB, PLT, HCT, MCV, MCH, MCHC, and RDW parameters are significantly lower in the severe group. In a study by Yan et al., a progressive decrease in eosinophil levels, after controlling for confounding factors, was associated with the mortality rate in COVID-19 patients (18). Lymphopenia has been reported as a widespread anomaly in COVID-19 patients. They stated that coronaviruses, especially, affect T lymphocytes by reducing their numbers. This result is consistent with our study (19, 20). In the study by Li et al., the HGB level was found to be low, similar to our

results. This may be due to chronic disease anemia in elderly patients (21). Although low Hb levels are considered one of the poor prognosis criteria, more comprehensive studies are needed to explain this. Gu et al. mentioned an association between an increase in RDW and the severity of COVID-19, but our study did not show such a result (22). An increase in RDW may occur in systemic inflammations, but we may not have been able to demonstrate this increase due to the intensification of the patients' need for intensive care and their referral.

In our study, when hematological parameters were examined based on mortality, NEU values of critical cases were significantly higher. HGB, HCT, MCV, MCHC, and RDW parameters were significantly lower in the severe group. Hematological parameters were found in a similar way according to the severity of the disease. While lymphocytes were significantly lower in disease severity, they were not found to be effective in mortality. Lymphopenia is a prominent feature in critical patients with SARS-CoV-2 infection. Targeted invasion of SARS-CoV-2 viral particles damages the cytoplasmic component of lymphocytes, leading to their destruction (22). In patients who died from COVID-19, a significantly low lymphocyte count was determined compared to survivors (23). In a study, it was shown that the eosinophil counts of non-survivors were significantly lower compared to survivors (18). This result could not be supported by our study. However, eosinopenia may serve as a prognostic indicator for more severe COVID-19. COVID-19-associated eosinopenia is likely a secondary outcome and does not directly contribute to the course of the disease (24). The complete blood count (CBC) test, which is easily accessible in outpatient settings, is practical and cost-effective (25).

In our investigation, scrutiny of biochemical parameters in relation to the severity of the disease revealed that in the critical/severe case group, D-Dimer, albumin, fasting glucose, urea, uric acid, creatinine, and potassium parameters were elevated. Conversely, ALT, AST, and fibrinogen showed a significant decrease according to the severity of the disease. In the early studies, it was reported that AST and ALT values were elevated in more than one-third of patients, and this was associated with prolonged hospital stays (26). Gao et al. found that D-Dimer levels were statistically significantly higher in severe cases, establishing it as the most studied and robust prognostic marker (21). There are studies indicating that COVID-19 could exacerbate existing cardiovascular diseases or lead to cardiovascular complications by increasing risk factors (27). Particularly, elevated levels of acute cardiac injury and coagulation biomarkers are known to be associated with a worse prognosis (28). Among these markers, D-Dimer is frequently employed in predicting the prognosis of COVID-19, while serum potassium levels are negatively correlated with the severity of COVID-19 (29). According to a study, hypokalemia was predominant in COVID-19 patients, and the correction of hypokalemia was challenging due to continuous renal K+

loss caused by ACE2 disruption. In a prospective cohort study involving COVID-19 patients, the incidence of acute kidney injury and death during hospitalization was found to be significantly higher in patients with initially high serum creatinine levels compared to those with normal initial values (29). In a study, it was observed that the levels of serum aspartate aminotransferase significantly increased in patients with severe disease compared to those with moderate disease, indicating liver damage. Additionally, in critical cases, serum aspartate aminotransferase levels were further increased, suggesting worsening liver damage in critical cases (18). In advanced analyses in our study, a decrease in mean corpuscular hemoglobin concentration (MCHC) and a decrease in sodium were observed to have a mitigating effect on the severity of the disease. The predictive effect of other parameters was not statistically significant.

In our study, when biochemical parameters were examined based on mortality, it was observed that D-Dimer, HDL, albumin, fasting glucose level, urea, uric acid, creatinine, and potassium levels were significantly higher in the deceased group. In advanced analyses in our study, age, HCT, MCV, MCHC, urea, uric acid, sodium, and potassium parameters were not identified as significant risk factors for mortality. Some of these results did not align with other studies (27). The practical clinical utility of a specific biomarker is not proven until it assists clinicians in managing patients and making treatment decisions. A biomarker pipeline often involves many steps that can result in failure; therefore, the evaluation and validation of a specific molecule require rigorous studies with flawless methods and homogeneous characteristics. From this perspective, studies on the utility of biomarkers in COVID-19 have not proven an impact on treatment decisions, and they have been affected by various limitations, including differences in methods used and weaknesses in study design.

Some limitations in our study have influenced the results. It is a retrospective study, providing a lower level of evidence compared to prospective and interventional studies. Therefore, there is insufficient data to prove the usefulness of a biomarker in guiding treatment and appropriate patient management. The selected assay methods, cutoff points, and measurement times vary in our study. The collection of study subjects in a single center can affect the repeatability and robustness of the results and may lead to selection bias. The influence of unmeasured confounding factors should not be overlooked. Particularly noteworthy is the significant data gap in eosinophil counts, a parameter commonly used in current clinical practice.

CONCLUSIONS

It was found that eosinophil levels do not have an effect on the severity of the disease. Parameters such as age, HCT, MCV, MCHC, urea, uric acid, sodium, and potassium were not identified as significant risk factors for mortality. A reduction in MCHC and sodium was observed to have a mitigating effect on the severity of the disease. The

predictive effects of other parameters were statistically insignificant. Despite the identification of significant relationships, further research is needed to explore the clinical significance of these indicators in patients with COVID-19. Predicting risk, particularly in countries with limited financial resources, will aid in reducing mortality rates through monitoring and early, appropriate treatment, and will contribute to the optimal use of resources.

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Ethics approval: This protocol was approved by the Ethics Committee of Katip Çelebi University Non-Interventional Clinic Studies (no. 54; date of approval: February 24, 2022) and was performed in accordance with the Declaration of Helsinki. Informed consent was not obtained as this is a retrospective study.

Data availability statement: The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to ethical restrictions.

Author contributions: Conceptualization - GY, GŞ; Data Collection - GY, GŞ; Study Design - GY, GŞ; Supervision - GY, ET; Data Collection, Analysis, Interpretation - GY, GŞ; Literature Review - GY; Writing - GY; Critical Review - ET. All authors provided comments on the drafts and have read and approved the final manuscript.

References

1. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. Int J Antimicrob Agents. 2020 Mar;55(3):105924. doi: 10.1016/j.ijantimicag.2020.105924.

2. Memikoğlu O, Genç V. COVİD-19. E-Kitap. Ankara: Ankara Üniversitesi Basımevi; 2020. ISBN: 978-605-136-477-3.

3. Luecke E, Jeron A, Kroeger A, Bruder D, Stegemann-Koniszewski S, Jechorek D, Borucki K, Reinhold D, Reinhold A, Foellner S, Walles T, Hachenberg T, Schreiber J. Eosinophilic pulmonary vasculitis as a manifestation of the hyperinflammatory phase of COVID-19. J Allergy Clin Immunol. 2021 Jan;147(1):112-113. doi: 10.1016/j.jaci.2020.09.026.

4. Xia Z. Eosinopenia as an early diagnostic marker of COVID-19 at the time of the epidemic. EClinicalMedicine. 2020 Jun; 23:100398. doi:10.1016/j.eclinm.2020.100398

5. Tanni F, Akker E, Zaman MM, Figueroa N, Tharian B, Hupart KH. Eosinopenia and COVID-19. *J Am Osteopath Assoc*. Published online July 16, 2020. doi:10.7556/jaoa.2020.091

6. Zhao L, Zhang YP, Yang X, Liu X. Eosinopenia is associated with greater severity in patients with coronavirus disease 2019. *Allergy*. 2021;76(2):562-564. doi:10.1111/all.14455

7. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al.Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy. 2020 Jul;75(7):1730-1741. doi: 10.1111/all.14238.

8. Qian GQ, Yang NB, Ding F, Ma AHY, Wang ZY, Shen YF, et al. Epidemiologic and clinical characteristics of 91 hospitalized patients with COVID-19 in Zhejiang, China: a retrospective, multi-centre case series. QJM. 2020 Jul 1;113(7):474-481. doi: 10.1093/qjmed/hcaa089.

9. Zheng Y, Xu H, Yang M, Zeng Y, Chen H, Liu R, et al.Epidemiological characteristics and clinical features of 32 critical and 67 noncritical cases of COVID-19 in Chengdu. J Clin Virol. 2020 Jun;127:104366. doi: 10.1016/j.jcv.2020.104366.

10. Xuan W, Jiang X, Huang L, Pan S, Chen C, Zhang X, Zhu H, Zhang S, Yu W, Peng Z, Su D. Predictive Value of Eosinophil Count on COVID-19 Disease Progression and Outcomes, a Retrospective Study of Leishenshan Hospital in Wuhan, China. J Intensive Care Med. 2022 Mar;37(3):359-365. doi: 10.1177/08850666211037326.

11. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021 Nov; 41(6):540-548.

12. Sartini S, Massobrio L, Cutuli O, Campodonico P, Bernini C, Sartini M, et al. Role of SatO2, PaO2/FiO2 Ratio and PaO2 to Predict Adverse Outcome in COVID-19: A Retrospective, Cohort Study. International Journal of Environmental Research and Public Health. 2021; 18(21):11534. https://doi.org/10.3390/ijerph182111534

13. Noor FM, Islam MM. Prevalence and associated risk factors of mortality among COVID-19 patients: a meta-analysis. J Community Health. 2020 Dec; 45(6):1270-82.

14. Karakoc ZC, Pinarbasi Simsek B, Asil R, Dodurgali R, Caliskaner F, Ozsari A, et al. First wave in COVID-19 pandemic: a single center experience. Klimik Derg. 2020 Dec; 33(3):223-9.

15. Khan MMA, Khan MN, Mustagir MG, Rana J, Islam MS, Kabir MI. Effects of underlying morbidities on the occurrence of deaths in COVID-19 patients: A systematic review and meta-analysis. J Glob Health. 2020 Dec;10(2):020503. doi: 10.7189/jogh.10.020503.

16. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020 Mar; 323(14):1335.

17. Boe DM, Boule LA, Kovacs EJ. Innate immune responses in the ageing lung. Clin Exp Immunol. 2017 Jan; 187(1):16-25.

18. Yan B, Yang J, Xie Y, Tang X. Relationship between blood eosinophil levels and COVID-19 mortality. World Allergy Organ J. 2021 Mar; 14(3):100521.

19. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with Coronavirus 2019 (COVID-19) in Wuhan, China. Clin Infect Dis. 2020 Aug; 71(15):762-8.

20. Li Q, Ding X, Xia G, Chen HG, Chen F, Geng Z, et al. Eosinopenia and elevated C-reactive protein facilitate triage of COVID-19 patients in fever clinic: A retrospective case-control study. EClinicalMedicine. 2020 May 3;23:100375. doi: 10.1016/j.eclinm.2020.100375.

21. Gu J, Gong E, Zhang B, Zheng J, Gao Z, Zhong Y, et al. Multiple organ infection and the pathogenesis of SARS. J Exp Med. 2005 Aug; 202:415-24.

22. Velavan TP, Meyer CG. Mild versus severe COVID-19: laboratory markers. Int J Infect Dis. 2020 Jun; 95:304-7.

23. Lindsley AW, Schwartz JT, Rothenberg ME. Eosinophil responses during COVID-19 infections and coronavirus vaccination. J Allergy Clin Immunol. 2020 Jul; 146(1):1-7.

24. Huang J, Zhang Z, Liu S, Gong C, Chen L, Ai G, et al. Absolute eosinophil count predicts intensive care unit transfer among elderly COVID-19 patients from general isolation wards. Front Med. 2020 Nov; 11. doi:10.3389/fmed.2020.585222.

25. Chen F, Chen W, Chen J, Xu D, Xie W, Wang X, et al. Clinical features and risk factors of COVID-19-associated liver injury and function: A retrospective analysis of 830 cases. Ann Hepatol. 2021 Mar-Apr;21:100267. doi: 10.1016/j.aohep.2020.09.011.

26. Samidurai A, Das A. Cardiovascular complications associated with COVID-19 and potential therapeutic strategies. Int J Mol Sci. 2020 Sep; 21(18):6785.

27. Chidambaram V, Tun NL, Haque WZ, Majella MG, Sivakumar RK, Kumar A, et al. Factors associated with disease severity and mortality among patients with COVID-19: a systematic review and meta-analysis. PLoS One. 2020 Nov; 15(11):e0241541.

28. Wang D, Li R, Wang J, Jiang Q, Gao C, Yang J, et al.. Correlation analysis between disease severity and clinical and biochemical characteristics of 143 cases of COVID-19 in Wuhan, China: a descriptive study. BMC Infect Dis. 2020 Jul 16;20(1):519. doi: 10.1186/s12879-020-05242-w.

29. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020 May;97(5):829-838. doi: 10.1016/j.kint.2020.03.005.

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ORIGINAL ARTICLE

Effect of Artificial Light Sources on DNA Damage in Human Mononuclear Lymphocyte Cells Under In Vitro Conditions

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ABSTRACT

Aim: This study aimed to evaluate the effects of commonly used artificial light sources on DNA damage and oxidative stress parameters in human mononuclear lymphocyte cells. The potential effects of different lighting sources on cellular DNA integrity and oxidative stress levels were comprehensively evaluated. **Methods:** Isolated human mononuclear lymphocyte cells were exposed to artificial light sources at varying intensities and durations. DNA damage was analyzed using the alkaline single-cell gel electrophoresis (comet assay) method. The oxidative status of the cells was assessed using Erel's method. **Results:** The highest DNA damage was observed with white and yellow compact fluorescent lamps, whereas the least damage occurred with yellow incandescent light sources. Additionally, 100-watt fluorescent lamps caused the most DNA damage, while the least damage was detected with 20-watt lamps. Oxidative stress index levels significantly increased with prolonged exposure. **Conclusion:** Our findings indicate that artificial light sources can induce DNA damage by increasing both direct and oxidative stress. Different light types and exposure durations significantly affect cellular genotoxicity and oxidative stress levels. These results provide an important insight into the potential biological risks associated with artificial lighting.

Keywords: Artificial Light Sources, Comet Assay, DNA Damage, Oxidative Stress

ÖZET

Amaç: Bu çalışmanın amacı, günlük yapay ışık kaynaklarının insan mononükleer lenfosit hücrelerinde DNA hasarı ve oksidatif stres parametreleri üzerindeki etkilerini araştırmaktır. Farklı aydınlatma kaynaklarının hücresel DNA bütünlüğü ve oksidatif stres düzeylerine yönelik potansiyel DNA hasarı etkileri kapsamlı bir şekilde değerlendirmektir. **Yöntem:** İzole edilmiş insan mononükleer lenfosit hücreleri çeşitli yoğunluklarda yapay ışık kaynaklarına maruz bırakılmıştır. DNA hasarının analizi için alkalin tek hücreli jel elektroforezi (comet assay) yöntemi kullanılmıştır. Hücrelerin oksidatif durumları ise Erel yöntemiyle değerlendirilmiştir. **Bulgular:** En fazla DNA hasarının, beyaz ve sarı kompakt floresan lambalarda saptanmıştır. En az DNA hasarının ise sarı akkor ışık kaynaklarında meydana geldiği belirlenmiştir. Ayrıca, 100 watt'lık floresan ışık kaynaklarının en fazla DNA hasarına neden olduğu saptanmıştır. En az hasar ise 20 watt'lık lambalarda gözlemlenmiştir. Işığa maruz kalma süresi arttıkça oksidatif stres indeksinin anlamlı derecede yükseldiği tespit edilmiştir. **Sonuç:** Çalışmamız, yapay ışık kaynaklarının hem direk hem de oksidatif stres düzeylerini artırarak DNA hasarına neden olabileceğini ortaya koymuştur. Bulgularımız, farklı yapay ışık kaynaklarının ve maruziyet sürelerinin hücresel genotoksisite ve oksidatif stres üzerinde belirgin etkiler yarattığını göstermektedir. Bu sonuçlar, yapay aydınlatmanın potansiyel biyolojik risklerini göstermektedir.

Anahtar Kelimeler: Yapay Işık Kaynakları, Comet Assay, DNA Hasarı, Oksidatif Stres

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INTRODUCTION

Deoxyribonucleic acid (DNA) is the foundation of genetic information and plays a pivotal role in maintaining cellular integrity (1). Permanent alterations in DNA, such as mutations, can be inherited and contribute to disease and cancer development (1,2). Cells within an organism are constantly exposed to various physical and chemical factors that can damage proteins, lipids, and nucleic acids, ultimately compromising cellular function and stability (2).

DNA damage can result from both external sources, such as ultraviolet (UV) radiation and chemical agents, and internal factors, including errors during DNA replication and recombination and metabolic by-products such as free radicals. These reactive molecules cause oxidative damage to DNA, proteins, and lipids, leading to an increased oxidative stress index (OSI) within cells (3).

Oxidative stress occurs when there is an imbalance between oxidant production and the system that neutralizes them. Excessive accumulation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which are part of normal cell metabolism, can cause significant molecular damage, especially to DNA.

Artificial light sources are an essential part of modern life. People are exposed to them for long periods due to extended indoor activities and changing lifestyles. These light sources include incandescent bulbs, fluorescent lamps, compact fluorescent lamps, halogen lamps, and high-pressure mercury vapor lamps. The light they emit can have various biological effects.

UV light, particularly UV-C radiation, is known for its strong DNA-damaging effects (4). UV-C can cause covalent bonds to form between adjacent pyrimidines, leading to pyrimidine dimers in DNA (4). These lesions can disrupt replication and transcription, increasing the risk of mutations and cancer. Studies have linked exposure to UV light, γ-radiation, and certain chemical agents with the etiology and pathogenesis of malignancies (5). High levels of oxidative stress play a role in aging, various diseases, and the onset and progression of cancer (6).

While the harmful effects of UV radiation are well-known, the biological impact of other artificial light sources remains unclear. In particular, their role in causing DNA damage and oxidative stress needs further investigations. Given the widespread use of artificial lighting, understanding these effects

is important for public health and safety.

This study aimed to evaluate the effects of artificial light sources, applied at varying intensities and durations, on DNA damage and oxidative stress parameters in vitro in human mononuclear lymphocyte cell cultures. This research will help identify potential biological risks associated with artificial lighting and contribute to safety guidelines for exposure. To the best of our knowledge, this is the first study investigating the relationship between DNA damage and oxidative stress caused by artificial light sources commonly used in daily life.

MATERIAL AND METHODS

Light Sources

This study used four types of artificial light sources: a white compact fluorescent lamp (WCFL), a yellow compact fluorescent lamp (YCFL), a fluorescent lamp, and a yellow incandescent lamp (YIL). These light sources were mounted 72° apart on the perimeter of a circular board (30×30 cm) to ensure uniform exposure. No other light sources were present in the environment where the study was conducted.

Sample Collection and Cell Preparation

Venous whole blood was collected from a healthy volunteer into heparinized tubes to prevent coagulation. Mononuclear cells were isolated using the Histopaque-1077 density gradient centrifugation method. Briefly, blood was layered over the Histopaque solution and centrifuged at 400 × g for 30 minutes at room temperature. The mononuclear cell layer was carefully aspirated, washed twice with phosphate-buffered saline, and resuspended in 20 mL of cell culture medium.

The leukocyte suspension was distributed into flasks containing 10 mL of Dulbecco's modified eagle's medium supplemented with 10% fetal bovine serum, 1% penicillin-streptomycin, and 1% L-glutamine. The flasks were incubated at 37°C in a humidified incubator with 5% CO_2 to maintain physiological conditions and cell viability.

Exposure to Artificial Light

Mononuclear cells were vertically exposed to light from each artificial light source at a standardized distance of 1 meter. The light sources were operated at five different intensities (20W, 40W, 60W, 80W, and 100W), and exposure durations were set at one, two, and three hours to assess time-dependent effects. The incubator was completely shielded from external light to ensure exclusive exposure to the experimental light sources. Each experiment was conducted in triplicate, and standard deviations were calculated. External factors that could potentially cause DNA damage were controlled to minimize confounding effects.

Experimental Controls

Negative and positive control samples were obtained from healthy individuals included in previous studies. Negative controls consisted of cell suspensions incubated in the culture medium without light exposure. No DNA damage was observed in these samples. Positive controls comprised cell suspensions

incubated with 30% hydrogen peroxide (H_2O_2) for 30 minutes to induce maximum DNA damage. After incubation, H_2O_2 was removed by centrifugation, and the cells were resuspended in fresh medium.

Comet Assay for DNA Damage Analysis

DNA damage was assessed using the single-cell gel electrophoresis assay, commonly known as the comet assay, with modifications described by Singh et al. (7). All procedures were performed under minimal illumination to prevent unintended DNA damage. Briefly, 50 µL of cell suspension (~10,000 cells) was mixed with 500 µL of 1% low-melting-point agarose at 37°C and spread onto microscope slides pre-coated with normal melting point agarose. The slides were immersed in a lysis solution (2.5 M NaCl, 100 mM EDTA, 10 mM Tris, pH 10, with 1% freshly added Triton X-100) at 4°C for one hour to lyse cells and remove proteins, leaving nucleoids containing supercoiled DNA.

Following lysis, the slides were placed in a horizontal electrophoresis tank containing fresh alkaline electrophoresis buffer (300 mM NaOH, 1 mM EDTA, pH >13) and left for 20 minutes to allow DNA unwinding and the expression of alkali-labile sites. Electrophoresis was performed at 25 V (0.86 V/cm) and 300 mA for 20 minutes. After electrophoresis, the slides were neutralized with three washes of neutralization buffer 0.4 M Tris (pH 7.5) and stained with ethidium bromide (2 µg/mL).

Fluorescence microscopy (Olympus BX51, Japan) at 200× magnification was used for analysis. DNA damage was visually classified based on tail formation in 100 cells per slide, categorized into five classes from 0 (no damage) to 4 (maximum damage) (Figure 1). An arbitrary unit system was used for quantification (8).

Assessment of Oxidative Status

Total oxidant status (TOS) and total antioxidant status (TAS) in the cell culture medium were determined using commercially available assay kits. These values were measured via colorimetric methods developed by Erel (9) on a fully automated analyzer (Architect CI16200; Abbott Laboratories, Abbott Park, IL, USA).

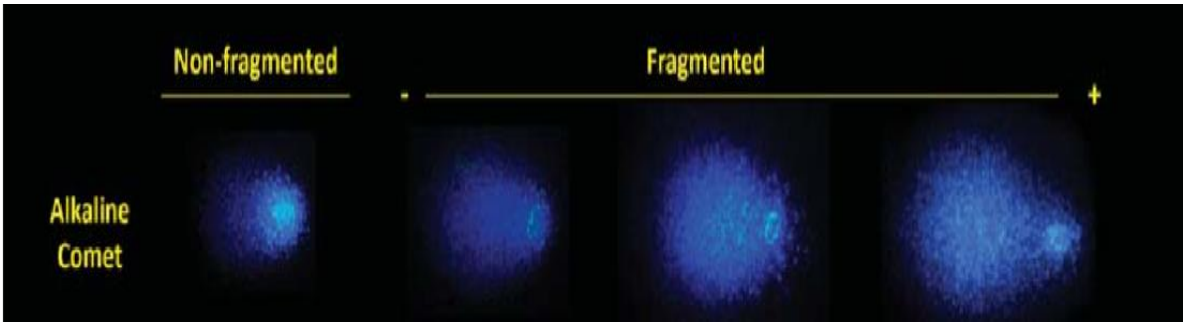

Figure 1. Non-fragmented and fragmented human mononuclear lymphocyte cells in the alkaline comet assays.

•TOS assay: This assay measures oxidation of ferrous ions to ferric ions in the presence of oxidants, forming a colored complex with xylenol orange in an acidic medium. The color intensity is proportional to the total oxidant content.

•TAS assay: This assay evaluates the antioxidative effect of the sample against a potent free radical reaction initiated by hydroxyl radical production. The absorbance change is inversely proportional to total antioxidant levels.

OSI was calculated as the percentage ratio of TOS to TAS (OSI = TOS/TAS) to quantify oxidative stress. TOS and TAS values were recorded at multiple time points during exposure.

Statistical Analysis

Data were analyzed using SPSS software (version 25.0; IBM Corp., Armonk, NY, USA). Results were presented as mean ± standard deviation or frequency (percentage). The association between DNA strand break values and malondialdehyde levels was evaluated using the Pearson correlation coefficient. Differences between groups were analyzed using one-way analysis of variance followed by Tukey's post hoc test. A p-value of <0.05 was considered statistically significant.

RESULTS

In experiments with the WCFL, the highest DNA damage was observed at 100 W after three hours, while the lowest DNA damage occurred at 20 W after one hour. A significant positive correlation was identified between light intensity and DNA damage, with higher intensities causing greater damage. DNA damage also increased proportionally with exposure, indicating a cumulative effect on DNA integrity. Specifically, DNA damage was significantly higher at three hours than that at two hours, and higher at two hours than at one hour (Table 1).

Table 1. DNA damage (arbitrary units) in relation to increasing light exposure duration in experiments with a white compact fluorescent lamp

	Hour 1	Hour 2	Hour 3	Positive control	Negative control	p
20 watt*	0 ± 0	2.66 ± 0.57[a]	9.33 ± 0.57[b.c]	80.33 ± 0.57	0 ± 0	<0.05
40 watt*	0.33 ± 0.57	5 ± 0[a]	10.66 ± 1[b.c]	77.33 ± 0.57	0 ± 0	<0.05
60 watt*	1.66 ± 1.52	7.66 ± 0.5773	15.33 ± 0.57[b.c]	77.33 ± 1.15	0 ± 0	<0.05
80 watt*	6.33 ± 1.15	10 ± 1[a]	21 ± 2[b.c]	81.67 ± 1.52	0 ± 0	<0.05
100 watt*	13.33 ± 1.52	17.66 ± 0.57	33.66 ± 3.51[b.c]	80.33 ± 2.51	0 ± 0	<0.05

[a,b,c]denote statistically significant differences between hours 1 and 2, hours 1 and 3, and hours 2 and 3, respectively. Note: Data presented as mean ± standard deviation

Similarly, in all experiments with the WCFL, OSI values increased significantly with longer exposure durations ($p<0.05$), indicating a direct relationship between exposure time and oxidative stress levels. These results suggest that prolonged exposure to WCFL exacerbates oxidative stress in mononuclear cells.

Experiments with the YCFL demonstrated a similar trend, where DNA damage was positively correlated with light intensity. The highest DNA damage was observed at 100 W, with the order of damage by light intensity being 100 W > 80 W > 60 W > 40 W > 20 W ($p<0.05$, Table 2). Exposure duration also played a significant role in DNA damage, with damage at three hours being higher than at two hours and damage at two hours being higher than at one hour ($p<0.05$, Table 2). These findings highlight the additive effects of light intensity and exposure time on DNA damage.

Similar to WCFL, OSI values in YCFL experiments increased significantly with longer exposure times ($p<0.05$). This suggests that prolonged exposure to YCFL leads to increased oxidative stress, emphasizing the importance of understanding the long-term biological effects of these light sources.

Experiments with FL revealed significant DNA damage under all conditions. DNA damage levels were lower than in the positive control but higher than in the negative control in all experiments, confirming the genotoxic potential of FL. A significant increase in DNA damage was observed with increasing light intensity, with the highest damage recorded at 100 W. The order of DNA damage based on light intensity was 100 W > 80 W > 60 W > 40 W > 20 W ($p<0.05$, Table3). Similarly, OSI values increased significantly with longer exposure durations ($p<0.05$). This consistent increase indicates a cumulative effect of prolonged FL exposure on oxidative stress, further highlighting the potential risks of long-term exposure.

Table 2. DNA damage (arbitrary units) in relation to increasing light exposure duration in experiments with a yellow compact fluorescent lamp

	Hour 1	Hour 2	Hour 3	Positive control	Negative control	p
20 watt	0 ± 0	2.33 ± 1.15	7.66 ± 1.15[b]	83 ± 3	0 ± 0	<0.05
40 watt	0.66 ± 1.15	3.66 ± 0.57	9.33 ± 0.57[b.c]	82 ± 1	0 ± 0	<0.05
60 watt	2.33 ± 0.57	7 ± 0[a]	15.33 ± 0.57[b.c]	74.3 ± 2.51	0 ± 0	<0.05
80 watt	6 ± 1	9.66 ± 0.57	22.33 ± 0.57[b.c]	81.3 ± 1.52	0 ± 0	<0.05
100 watt	11.33 ± 0.57	15.66 ± 0.57[a]	31.33 ± 2.08[b.c]	79.67 ± 1.53	0 ± 0	<0.05

[a,b,c]denote statistically significant differences between hours 1 and 2, hours 1 and 3, and hours 2 and 3, respectively. Note: Data presented as mean ± standard deviation

Table 3. DNA damage (arbitrary units) in relation to increasing light exposure duration in experiments conducted with a fluorescent lamp

	Hour 1	Hour 1	Hour 3	Positive control	Negative control	p
20 watt	0 ± 0	2.33 ± 1.15[a]	7 ± 0[b.c]	83 ± 1	0 ± 0	<0.05
40 watt	0.33 ± 0.57	3 ± 0[a]	7.66 ± 1.15[b.c]	76.7 ± 1.53	0 ± 0	<0.05
60 watt	1.33 ± 0.57	5.66 ± 0.57	10 ± 1[b.c]	81 ± 2	0 ± 0	<0.05
80 watt	5.66 ± 0.57	7 ± 0[a]	15 ± 2.64[b.c]	82.67 ± 1.53	0 ± 0	<0.05
100 watt	8.33 ± 0.57	12.33 ± 0.57	25.66 ± 1.15[b.c]	81.3 ± 0.58	0 ± 0	<0.05

[a,b,c]denote statistically significant differences between hours 1 and 2, hours 1 and 3, and hours 2 and 3, respectively. Note: Data presented as mean ± standard deviation

In YIL experiments, DNA damage increased with light intensity, with the highest damage recorded at 100 W. The order of DNA damage by light intensity at the 2nd hours was 100 W > 80 W > 60 W = 40 W = 20 W. Although DNA damage was observed in all YIL experiments, it was consistently lower than in the positive control. The highest DNA damage occurred after three hours at 100 W, but this increase was not statistically significant across all conditions (Table 4).

Despite the generally lower DNA damage, OSI values increased significantly with longer exposure durations, indicating that even incandescent light, which is often considered less harmful, can induce oxidative stress with prolonged exposure.

Table 4. DNA damage (arbitrary units) in relation to increasing light exposure duration in experiments with an incandescent lamp

	Hour 1	Hour 2	Hour 3	Positive control	Negative control	p
20 watt*	0 ± 0	0 ± 0	0 ± 0	81.67 ± 1.53	0 ± 0	>0.05
40 watt*	0 ± 0	0 ± 0	0 ± 0	78 ± 1	0 ± 0	>0.05
60 watt*	0 ± 0	0 ± 0	0 ± 0	81.67 ± 1.15	0 ± 0	>0.05
80 watt*	0 ± 0	0.33 ± 0.57	0.66 ± 1.15	79.67 ± 1.53	0 ± 0	>0.05
100 watt*	0 ± 0	1.33 ± 0.57	2.33 ± 1.15	78.3 ± 2.3	0 ± 0	<0.05

[a,b,c]denote statistically significant differences between hours 1 and 2, hours 1 and 3, and hours 2 and 3, respectively. Note: Data presented as mean ± standard deviation

DISCUSSION

Previous studies have demonstrated that, in addition to UV radiation, both solar rays and artificial light sources can affect mutagenesis, carcinogenesis, and immune system functions (10).

Our study revealed that incandescent light sources induced DNA damage when mononuclear cells were exposed to high intensities for prolonged durations under in vitro conditions. In contrast, compact fluorescent and fluorescent light sources caused DNA damage at lower intensities and shorter durations. Furthermore, we observed a correlation between increased oxidative stress and DNA damage induced by these artificial light sources. However, our findings did not establish a significant correlation between the magnitude of DNA damage and OSI levels.

Previous research has identified multiple mechanisms by which light exposure can damage DNA (11). Pflaum et al. (12) reported that visible light inhibited antioxidants and induced oxidative DNA damage in mammalian cell cultures. Similarly, Kielbassa et al. (11) found that UV and visible light caused DNA damage via different mechanisms depending on the wavelength. Specifically, UV-B and UV-C (250–315 nm) induced direct DNA damage by forming pyrimidine dimers, whereas UV-A and visible light (320–740 nm) caused indirect DNA damage by generating oxidative radicals such as singlet oxygen, superoxide, and hydroxyl radicals. Additionally, Botta et al. (13) reported UV-A (320–400 nm) and visible light (400–800 nm) could trigger oxidative DNA damage by photoactivating polyaromatic hydrocarbons and benzopyrones.

Solar radiation causes both acute and chronic effects on human and animal skin cells (14). Chronic exposure leads to the development of benign and malignant skin tumors, particularly malignant melanoma. Animal studies have shown that UV-B (290–320 nm) is more mutagenic and carcinogenic than UV-A (320–400 nm) (15). Furthermore, epidemiological studies have demonstrated that UV radiation contributes to gene mutations and immunosuppression, increasing the risk of skin tumors. UV radiation has been reported to cause both direct and indirect DNA damage (16).

Since the skin is the primary organ exposed to light, skin cancers are among the most common malignancies in Western countries (17). Godley et al. reported that blue visible light (390–550 nm) increased free radical production and induced mitochondrial DNA damage in primary retinal epithelial cells (18). Consistent with these findings, our study also observed increased OSI levels and DNA damage in mononuclear cells following exposure to artificial light sources. However, it is important to note that our study was conducted in vivo using cell cultures. Further in vivo research involving living organisms is necessary to provide a better understanding of the biological relevance of these findings.

CONCLUSION

Our findings suggest that fluorescent and compact fluorescent lights induce greater DNA damage and oxidative stress than incandescent lights. A possible explanation is that incandescent lights primarily emit UV-A and visible light, which can indirectly cause DNA damage through oxidative radicals produced by photoreactions. In contrast, fluorescent and compact fluorescent lamps emit not only visible light but also UV-B and UV-C rays, which can directly damage DNA by forming thymine dimers.

This in vitro study indicates that artificial light sources commonly used in daily life are not entirely harmless and can cause significant DNA damage and oxidative stress when used at high intensities and for prolonged durations. Therefore, limiting light intensity and exposure time may help mitigate potential damage. Additionally, incandescent lights, which resulted in lower DNA damage, may be a safer alternative for reducing the risk of genotoxicity. However, given the in vitro nature of this study, further in vivo research is required to confirm these findings and assess their implications for human health.

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References

1. Carusillo A, Mussolino C. DNA Damage: FromThreattoTreatment. Cells. 2020 Jul; 9(7): 1665.
2. Sofińska K, Wilkosz N, Szymoński M, Lipiec E. Molecular Spectroscopic Markers of DNA Damage. Molecules. 2020 Jan 28;25(3):561.
3. Cadet J, Wagner JR. DNA base damage by reactive oxygen species, oxidizing agents, and UV radiation. Cold Spring Harb Perspect Biology. 2013 Feb 1;5(2):a012559.
4. Banaś AK, Zgłobicki P, Kowalska E, Bażant A, Dziga D, Strzałka W. All You Need Is Light. Photorepair of UV-Induced Pyrimidine Dimers. Genes (Basel). 2020 Nov 4;11(11):1304.
5. Basu AK. DNA Damage, Mutagenesis and Cancer. International Journal Molecular Science. 2018 Mar;19(4):970.
6. Sánchez-Rodríguez MA, Mendoza-Núñez VM. Oxidative Stress Indexes for Diagnosis of Health or Disease in Humans. Oxidative Medicine Cellular Longevity. 2019 Nov 25;2019:4128152.
7. Singh NP, McCoy MT, Tice RR, Schneider EL. A simple technique for quantitation of low levels of DNA damage in individual cells. Experimental Cell Research. 1988 Mar;175:184–191.
8. Dizdaroglu M. Oxidative damage to DNA in mammalian chromatin. Mutation Research. 1992 Sep; 275(3-6): 331-342.
9. Erel O. A new automated colorimetric method for measuring total oxidant status. Clinical Biochemistry. 2005 Dec;38(12):1103-11.
10. Robinson KS, Traynor NJ, Moseley H, Ferguson J, Woods JA.Cyclobutane pyrimidine dimers are photo sensitised by carprofen plus UVA in human HaCaTcells. Toxicology In Vitro. 2010 Jun; 24(4): 1126-1132.

11. Kielbassa C, Roza L, Epe B. Wavelength dependence of oxidative DNA damage induced by UV and visible light. Carcinogenesis. 1997 Apr; 18(4): 811-816.
12. Pflaum M, Kielbassa C, Garmyn M, Epe B. Oxidative DNA damage induced by visible light in mammaliancells: extent, inhibition by antioxidants and genotoxic effects. Mutation Research. 1998 Aug; 408(2): 137-146.
13. Botta C, Di Giorgio C, Sabatier AS, De Méo M. Effects of UVA and visible light on the photogenotoxicity of benzo[a]pyrene and pyrene. Environmental Toxicology. 2009 Oct;24(5):492-505.
14. Ichihashi M, Ueda M, Budiyanto A, Bito T, Oka M, Fukunaga M, et al. UV-induced skin damage. Toxicology. 2003 Jul 15;189(1-2):21-39.
15. Guerra KC, Zafar N, Crane JS. Skin Cancer Prevention. In: StatPearls [Internet] 2023 Aug 8. Treasure Island (FL): StatPearls Publishing; 2024 Jan–. PMID: 30137812. https://www.ncbi.nlm.nih.gov/books/NBK519527/?report=reader
16. Pfeifer GP. Mechanisms of UV-induced mutations and skin cancer. Genome Instability Disease. 2020 May;1(3):99-113.
17. Khan NH, Mir M, Qian L, Baloch M, Ali Khan MF, Rehman AU, et al. Skin cancer biology and barriers to treatment: Recent applications of polymeric micro/nanostructures. Journal of Advenced Research. 2021 Jun 16;36:223-247.
18. Godley, B. F., Shamsi, F. A., Liang, F. Q., Jarrett, S. G., Davies, S., & Boulton, M. Blue Light Induces Mitochondrial DNA Damage and Free Radical Production in Epithelial Cells: Journal of Biological Chemistry. 2005 Jun; 280(22):061 – 066.

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ORIGINAL ARTICLE

Investigation of Nosocomial Urinary Tract Infections in Patients with Urinary Catheters

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ABSTRACT

Aim: The most significant adverse outcome of urinary catheter use is the development of a urinary tract infection (UTI). This study evaluates the role of urinary catheterization in emergencies compared to elective conditions in wards, focusing on the development of catheter-associated urinary tract infections (CA-UTI). **Methods:** Our study is a single-center retrospective case-control study between August 1 and December 30, 2021. The case group consists of patients aged 18 years and older, who underwent urinary catheterization in the emergency department (ED) and were hospitalized for at least 48 hours. The control group consisted of patients who underwent elective urinary catheterization in the wards and continued to be hospitalized for at least 48 hours. Two groups were compared in terms of development, predisposing factors of CA-UTI and reasons of using urinary catheter. **Results**: The most reason for urinary catheterization in case and control groups, each of consisted of 106 patients, is for patients' unstable medical conditions with ratios of 82.1% and 77.4%, respectively. The duration of urinary catheterization in case and control groups was 8.4 and 11.17 days, respectively ($p<0.0001$). While majority of the urinary catheter insertions were performed by intern doctors in the ED; most of them were carried out by assistant doctors in the wards ($p=0.001$). The rate of development of CA-UTI in case and control groups, was 0.078 and 0.064 per 1000 catheter days, respectively, and although the case group was higher, there was no significant difference ($p>0.005$). **Conclusion**: The process of urinary catheterization in the emergency department has not been identified as an additional risk factor for the development of CA-UTI when compared to urinary catheterization in the ward. No difference was detected in terms of catheter practitioner. This may be related to the small total number of cases, the longer catheterization duration in the control group, and the low prevalence of CA-UTI in the study.

Keywords: Emergency Department, Prevention, Urinary Catheter, Urinary Tract Infection

ÖZET

Amaç: Üriner sonda kullanımının en önemli dezavantajı, idrar yolu enfeksiyonuna (İYE) zemin hazırlamasıdır. Bu çalışma, acil ve elektif koşullarda üriner sonda uygulamalarının karşılaştırılması ve bunun sonucunda kateter ilişkili idrar yolu enfeksiyonu (Kİ-İYE) gelişiminin değerlendirilmesi amaçlanmıştır. **Yöntem:** Çalışmamız, 1 Ağustos- 30 Aralık 2021 tarihleri arasında tek merkezli retrospektif bir vaka-kontrol çalışmasıdır. Vaka grubu, acil serviste (AS) üriner kateterizasyonu yapılan ve en az 48 saat hastanede yatan 18 yaş ve üzeri hastalardan oluşmaktadır. Kontrol grubu ise serviste elektif üriner kateterizasyonu yapılan ve en az 48 saat daha hastanede kalan hastalardan oluşmaktadır. İki grup, Kİ-İYE gelişimi, predispozan faktörler ve üriner kateter kullanma nedenleri açısından karşılaştırılmıştır. **Bulgular:** Hem vaka hem de kontrol gruplarında,106 hasta bulunmaktadır. En sık üriner kateterizasyon nedeni, sırasıyla %82.1ve %77.4 oranlarıyla genel durum bozukluğu olarak belirlenmiştir. Vaka ve kontrol gruplarında üriner kateterizasyon süresi sırasıyla 8,4 ve 11,17 gün olarak bulunmuştur ($p<0.0001$). Üriner kateter takma işlemi vaka grubunda daha çok intern doktorlar, kontrol grubunda ise asistan doktorlar tarafından yapılmıştı ($p=0.001$). Kİ-İYE gelişme oranı vaka ve kontrol gruplarında sırasıyla 1000 kateter günü başına 0.078 ve 0.064 idi ve vaka grubunda daha yüksek olmasına rağmen anlamlı bir fark yoktu ($p>0.005$). **Sonuç:** Acilde üriner kateter uygulanım süreci Kİ-İYE gelişimi açısından serviste üriner kateter uygulanımına göre ek bir risk faktörü olarak saptanmamıştır. Kateter uygulayıcısı açısından da farklılık saptanmamıştır. Toplam olgu sayısının azlığı, kontrol grubunda kateterizasyon süresinin daha uzun olması ve çalışmada Kİ-İYE prevalansının düşük olması ile ilişkili olabilir.

Anahtar Kelimeler: Acil Servis, Önleme, İdrar Kateteri, İdrar Yolu Enfeksiyonu

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INTRODUCTION

The most significant adverse outcome of urinary catheter use is the development of a urinary tract infection (UTI). Several risk factors contribute to catheter-associated urinary tract infections (CA-UTI), including age, female gender, diabetes, and prolonged catheterization time. Among these, the duration of catheterization is the most critical factor in the development of bacteriuria and UTI, with a daily risk of 3-7% for bacteriuria and 0.3% per catheter day for UTI (1, 2). One study found that physicians are often unaware (38% of the time) that their patients have indwelling urinary catheters, with unsuitable catheters being 'forgotten' more frequently than suitable ones (3).

Unnecessary urinary catheter placement is a significant issue in emergency departments. Often based on subjective judgment rather than objective criteria, many catheters are inserted without documented need. To prevent complications and reduce the risk of harm during hospitalization, it is crucial to avoid catheterization unless indicated. By strictly adhering to objective criteria for catheter placement, emergency departments can substantially decrease catheter usage. (4). When catheterization is necessary, sterile equipment and aseptic techniques should always be employed (5).

Existing knowledge on the prevention of urinary tract infections associated with urinary catheterization in the emergency department is limited. CA-UTI prevention programs have been developed with a focus on the entire hospital. Unlike programs that emphasize the continuous assessment of the necessity of the catheter and its early removal for CA-UTI prevention, in the emergency department, the focus has been on minimizing the use of urinary catheters and ensuring proper insertion techniques (13).

This study aims to evaluate the role of urinary catheterization in emergencies on the development of CA-UTI compared to the application of elective conditions in inpatient services.

MATERIAL AND METHOD

Our study is a single-center observational retrospective case-control study between August 1 and December 30, 2021, conducted in 1100-bed tertiary academic hospital.

The case group consists of patients aged 18 years and older, who underwent urinary catheterization in the ED and were hospitalized for at least 48 hours. The control group consisted of patients who underwent

elective urinary catheterization in the inpatient service and continued to be hospitalized for at least 48 hours. Patients followed in the intensive care unit have not been included. Both groups were evaluated for the development of CA-UTI until discharge or death. Hospital infection control committee follow-up data was used. CAUTIs were defined according to Centers for Disease Control and Prevention (CDC) criteria (6). The two groups were compared in terms of CA-UTI development, reasons of using urinary catheter and predisposing factors. Our study has received ethical approval from the Non-Invasive Research Ethics Committee of Eskişehir Osmangazi University Faculty of Medicine (Decision No: 2022/53, Date: 22/03/2022).

Statistical analysis

Statistical analyses were conducted using IBM SPSS 25. The Shapiro-Wilk test was utilized to assess the suitability of the data for normal distribution. Numerical values were analyzed using the Mann-Whitney U test, while categorical variables were examined through the Chi-Square test. Specifically, Fisher's Exact test was applied in 2x2 tables, and the Pearson Chi-Square test was used in other cases. The study, which included 212 patients had a power of 0.9, and a p-value of less than 0.05 was considered statistically significant. In the prior power analysis conducted to determine a significant difference between the patient and control groups, a power of 90%, a type I error of 0.05, and an effect size of 0.447 were used. The calculated sample size was a total of 212 (106 cases and 106 controls). The power analysis was performed using the G-Power 3.1.9.2 software.

RESULTS

The case and control group each consisted of 106 patients. The ratios of the reasons for using a urinary catheter in the case and control groups, respectively, are as follows; for urinary analyses (13.2% vs. 0%), for patients' unstable medical condition (82.1% vs. 77.4%) and for surgical preparation (4.7% vs. 22.6%) ($p<0.001$) (Table 1).

Table 1. Reasons for urinary catheter placement in case and control groups

Reason	Case group (n=106) %	Control group (n=106) %
Urinary analyses	13.2	0
Patients' unstable medical condition	82.1	77.4
Surgical preparation	4.7	22.6

Demographic characteristics and predisposing factors of the patients in the case and control groups were evaluated and there was no significant difference in terms of age, gender, and predisposing factors (stone, obstruction, prostatic disorders, malignity, incontinence, chronic disease) (Table 2).

The distribution of patients during the hospitalization period was as follows in the case and control groups, respectively; 32.1% and 23.6% in internal clinics, 34% and 44.3% in internal intensive care units, 13.2% and 11.3% in surgical clinics and 20.8% and 20.8% in surgical intensive care units (p=0.657).

The percentage of urinary analysis performed before urinary catheterization was 67.9% and 49.1% in the case and control groups, respectively (p=0.05). The rate of pyuria and nitrite positivity in the urine before urinary catheterization was 19.4% and 7%, respectively, in the case group, while it was 29.6% and 5.6%, respectively, in the control group. No statistically significant difference was found between the two groups in terms of pyuria and nitrite positivity (p=0.209 and p=1, respectively).

During the follow-up, urinary catheter changes were made in 7.5% of the case group, and 11.3% of the control group, and there was no statistical difference (p=0.384). There was no statistically significant difference between the groups in terms of catheter irrigation during the follow-up period (p=0.432) and it was 16% and 11.3% in the case and control groups, respectively. Interventions to the urinary catheter are shown in Table 3.

Table 2. Demographic characteristics and predisposing factors of case and control groups

	Case group	Control group	P
	n=106	n=106	
Age (Mean)/year	64.34	68.42	0.1*
Female/Male	52/54	47/59	0.165**
Stone	1	2	0.756***
Obstruction	2	3	0.931***
Prostatic disorders	4	0	0.26***
Malignity	7	16	0.188***
Incontinence	15	34	0.54***
Chronic Disease	47	58	0.784***

***** Mann-Whitney U test ****** Pearson Chi-Square ******* Fisher's Exact test

Table 3. Interventions to urinary catheter during the study period.

Interventions	Case group (n=106) %	Control group (n=106) %	P
Catheter replacement	7.5	11.3	0.384*
Catheter irrigation	16	11.3	0.432*

* Pearson Chi-Square

The length of stay of the urinary catheter in the case and control groups was 8.4 and 11.17 days, respectively, and there was a significant difference between the groups (p<0.0001).

Broad-spectrum antibiotic use was 64.6% and 69.5% in the case and control groups, respectively, and there was no statistically significant difference between the groups (p=0.551).

The causative agents of CA-UTI were similar in both groups, and the most common causative agent was Escherichia coli with a rate of 33% and 45% in the case and control groups, respectively. Other agents, in order of frequency, were Staphylococcus heamolyticus, Enterococcus feacalis, Acinetobacter baumanni, Candida glabrata, Enterococcus feacium and Klebsiella pneumoniae.

When the distribution of health workers who apply the urinary catheter is examined, 82% are intern doctors, 17% are assistant doctors and 1% are nurses in the ED.

In the wards, by contrast, 56% are assistant doctors and 44% are nurses. While majority of the urinary catheter insertions were performed by intern doctors in the ED; most of them were carried out by assistant doctors in the wards (p=0.001).

When the rate of development of CA-UTI is evaluated; 0.078 and 0.064 per 1000 urinary catheter days in the case and control groups, respectively. Although the case group was higher, there was no significant difference in the development of CA-UTI between the case and control groups (p>0.05).

DISCUSSION

Urinary catheters are used more frequently and with wider indications in ED. Despite the lack of comprehensive medical documentation for urinary catheters, this issue has been interpreted as inappropriate usage in several studies (7,17). A study reported that the rate of urinary catheterization in the emergency department for patients aged 65 and older was 73%. Of these, 4% were deemed inappropriate, and 8.7% developed CA-UTI. At the end of the study, it was recommended to create a list of acceptable indications for urinary catheter insertion in emergency departments (16). Fakih et al. (7) show that only 69.7% of patients undergo urinary catheterization in ED were

compliant with the institutional guidelines for catheterization. Gokula et al. (8) reported in their study that only 46% of catheter use was an appropriate indication. A study has demonstrated that educational programs for doctors and nurses, along with the mandatory implementation of a checklist containing acceptable indications, resulted in nearly an 80% reduction in catheter use in the emergency department. Additionally, the rate of 'appropriate catheter use' increased from 37% to 51% (p=0.06), while the proportion of physician order documentation rose from 43% to 63% (p<0.01) (18). A study based on long-term follow-up has shown that inpatients receiving routine monitoring of urinary catheter use, with a focus on re-evaluating indications and appropriateness during the hospitalization process and early discontinuation in the emergency department, demonstrated a trend toward a decrease in urinary catheter use across the hospital (20). In our study, in the ED, 13.2% of urinary catheters were applied only for urinary analysis. Even when inappropriately placed in the emergency department, urinary catheters are often transferred to the wards without removal. For this reason, the indication for urinary catheter application in ED should be carefully evaluated and the indication should be reviewed when the patient is transferred to the wards. Establishing an automated control or warning system can help clinicians in this regard.

The number of studies investigating the role of emergency and elective intervention in the development of CA-UTI is not high in the literature. While some studies have determined that urinary catheterization in the ED is a risk factor for bacterial colonization of catheters and CA-UTI (9, 10, 19), there is also a study in the literature that was not detected as a risk factor (11).Bhatia et al. (9) found that urinary catheter colonization and CA-UTI were more common in patients who underwent urinary catheterization in the ED, compared to patients with urinary catheterization in the wards. They attributed this to inadequate sterile precautions taken during catheter insertion in the ED, citing time constraints as a factor. Our study did not reveal a significant difference in CA-UTI rates between the case and control groups. This could be attributed to the small control group size, minimization of catheterization duration or the overall low CA-UTI prevalence.

Contamination of sterile catheters during urinary catheter insertion is unfortunately common. In a study where patients who had urinary catheters placed by nurses in the emergency department were prospectively observed for 6 months, a significant breach in aseptic technique was found in 59% of cases. The characteristics of the emergency department environment, where life-threatening conditions are prioritized, inconsistent or inappropriate placement of hand sanitizers, and limited space to create sterile moments, have been identified as contributing factors (15). The same study found no association between the catheter inserter or patient characteristics and variations in technique. In our study, urinary catheter insertion was more frequently performed by

intern doctors in the emergency clinic, while in the elective urinary catheter insertion group, it was performed by resident doctors. However, no difference was found in terms of CA-UTI development, and therefore, it was not defined as a risk factor.

The duration of catheterization is the most significant modifiable risk factor associated with the development of infection (14). Oumer et al. (12) stated that prolonged catheterization (7 days) is an independent risk factor for CA-UTIs. Conversely, Bhatia et al. (9) reported higher urinary catheter colonization and CA-UTI rates in ED patients despite shorter catheterization (4.3 days) compared to ward patients (6.2 days), attributing this to inadequate ED sterile precautions due to time constraints. Our case group exhibited shorter catheterization (8.4 days) than the control group (11.17 days, $p<0.0001$), possibly due to earlier catheter removal in the wards. However, despite this shorter duration, we observed no significant difference in CA-UTI rates between groups. This suggests that factors beyond catheterization time, such as inadequate ED sterile precautions, may contribute to CA-UTI development. Further research is needed to elucidate these factors.

A study has shown that obtaining a urine culture when urinary catheterization is performed in the emergency department helps reduce unnecessary tests and treatments in the subsequent process (7). Another study found that among cases where both urine analysis and culture were performed along with urinary catheter insertion in the emergency clinic, 26% exhibited evidence of UTI (10). In our study, urine analysis was performed prior to catheterization, and no significant difference was found in terms of CA-UTI development.

Limitations

There are some limitations in our study. The team applied the urinary catheter was not followed up. Therefore, data on inappropriate use of the urinary catheter could not be obtained. There are no medical records regarding the criteria for the clinical appropriateness of urinary catheters or the adherence to aseptic techniques. In addition, the small number of patients weakened our results.

CONCLUSIONS

Urinary catheterization in the emergency department was not found to be an additional risk factor for CA-UTI development compared to urinary catheterization in the inpatient setting. This may be related to the small total sample size, the longer catheterization duration in the control group, and the generally low prevalence of CA-UTI. No significant difference was found regarding urinary catheter practitioners in the emergency department. The fact that the study was conducted in a tertiary care hospital emergency department, where practitioners undergo regular and standardized training and aseptic techniques are monitored, may explain this finding. Further evaluation is warranted through large-scale studies with a larger sample size to provide more robust evidence.

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References

1. Nicolle LE. Catheter associated urinary tract infections. Antimicrob Resist Infect Control 2014; 3:23.
2. Chenoweth CE, Gould CV, Saint S. Diagnosis, management, and prevention of catheter-associated urinary tract infections. Infect Dis Clin North Am 2014; 28(1):105-19.
3. Saint S, Wiese J, Amory JK, Bernstein ML, Patel UD, Zemencuk JK, et al. Are physicians aware of which of their patients have indwelling urinary catheters? Am J Med 2000;109(6):476-80.
4. Fakih MG, Heavens M, Grotemeyer J, Szpunar SM, Groves C, Hendrich A. Avoiding potential harm by improving appropriateness of urinary catheter use in 18 emergency departments. Ann Emerg Med 2014;63(6):761-8 e1.
5. Shuman EK, Chenoweth CE. Recognition and prevention of healthcare-associated urinary tract infections in the intensive care unit. Crit Care Med 2010;38(8 Suppl): S373-9.
6. Hooton TM, Bradley SF, Cardenas DD, Colgan R, Geerlings SE, Rice JC, et al. Diagnosis, prevention, and treatment of catheter-associated urinary tract infection in adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America. Clin Infect Dis 2010;50(5):625-63.
7. Fakih MG, Shemes SP, Pena ME, Dyc N, Rey JE, Szpunar SM, et al. Urinary catheters in the emergency department: very elderly women are at high risk for unnecessary utilization. Am J Infect Control 2010;38(9):683-8.
8. Gokula RRM, Hickner JA, Smith MA. Inappropriate use of urinary catheters in elderly patients at a midwestern community teaching hospital. Am J Infect Control 2004;32(4):196-9.
9. Bhatia N, Daga MK, Garg S, Prakash S. Urinary catheterization in medical wards. J Glob Infect Dis 2010;2(2):83.
10. Burnett KP, Erickson D, Hunt A, Beaulieu L, Bobo P, Shute P. Strategies to prevent urinary tract infection from urinary catheter insertion in the emergency department. J Emerg Nurs 2010;36(6):546-50.
11. Nguyen-Van-Tam S, Nguyen-Van-Tam J, Myint S, Pearson J. Risk factors for hospital-acquired urinary tract infection in a large English teaching hospital: a case-control study. Infection 1999;27(3):192-7.
12. Oumer Y, Regasa Dadi B, Seid M, Biresaw G, Manilal A. Catheter-Associated Urinary Tract Infection: Incidence, Associated Factors and Drug Resistance Patterns of Bacterial Isolates in Southern Ethiopia. Infect Drug Resist 2021; 14:2883-94.

13. Carter EJ, Pallin DJ, Mandel L, Sinnette C, Schuur JD. Emergency Department Catheter-Associated Urinary Tract Infection Prevention: Multisite Qualitative Study of Perceived Risks and Implemented Strategies. Infect Control Hosp Epidemiol 2016;37(2):156-62.

14. Scruggs-Wodkowski E, Kidder I, Meddings J, Patel PK. Urinary Catheter-Associated Infections. Infect Dis Clin North Am 2024; 38:713-29.

15. Manojlovich M, Saint S, Meddings J, Ratz D, Havey R, Bickmann J, et al. Indwelling Urinary Catheter Insertion Practices in the Emergency Department: An Observational Study. Infect Control Hosp Epidemiol 2015;37(1):20-26.

16. Hazelett SE, Tsai M, Gareri M, Allen K. The association between indwelling urinary catheter use in the elderly and urinary tract infection in acute care. BMC Geriatr 2006; 6:15.

17. Liang SY, Theodoro DL, Schuur JD, Marschall J. Infection Prevention in the Emergency Department. Ann Emerg Med 2014;64(3):299-313.

18. Gokula RM, Smith MA, Hickner J. Emergency room staff education and use of a urinary catheter indication sheet improves appropriate use of foley catheters. Am J Infect Control 2007;35(9):589-93.

19. Markovic-Denic L, Mijovic B, Jankovic S. Risk factors for hospital-acquired urinary tract infection: a case–control study. Int Urol Nephrol 2011; 43:303-8.

20. Fakih MG, Rey JE, Pena ME, Szpunar S., Saravolatz LD. Sustained reductions in urinary catheter use over 5 years: Bedside nurses view themselves responsible for evaluation of catheter necessity. Am J Infect Control 2013;41(3):236-9.

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REVIEW

Hasta Başı Testlerin Birinci Basamak Sağlık Hizmetlerine Etkisi

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ÖZET

Bu derleme, hasta başı testlerin (HBT) birinci basamak sağlık hizmetleri üzerine mevcut ve potansiyel etkilerini ortaya koymayı amaçlamaktadır. HBT, hasta başında veya merkezi laboratuvarların dışında test yapma olanağı sağlayarak hızlı ve eyleme geçirilebilir tanısal bilgi sunmaktadır. Böylelikle teşhis sürecini kısaltmakta, özellikle acil sağlık hizmetleri veya kronik hastalık yönetiminde müdahalelerin doğru zamanlı olarak düzenlenmesine imkân tanımaktadır. HBT'lerin birinci basamak sağlık hizmetleri kapsamında kullanım alanı oldukça geniştir. Bulaşıcı hastalıklar (örneğin; HİV, sıtma ve tüberküloz) için hızlı testlerin, kaynakların kısıtlı olduğu bölgelerde erken teşhis ve tedaviye katkı sunduğu gösterilmiştir. Buna ek olarak, diyabet ve hipertansiyon gibi kronik hastalıkların kontrolünün sağlanmasında, hasta başında ölçülebilen kan şekeri veya HbA1c seviyeleri önemli rol oynamaktadır. Kardiyovasküler hastalıklarda troponin gibi biyobelirteçlerin hızlı tayini de özellikle acil durumlarda mortalite oranlarının azalması ile sonuçlanan zaman tasarrufu sağlamaktadır. HBT'nin sunduğu en önemli avantajlardan biri, test sonucuna hızlı erişimle hasta memnuniyetini artırması ve gereksiz sevkleri azaltmasıdır. Bu durum hem hasta hem de sağlık sistemi açısından maliyet etkili olmakta, sağlık hizmeti sunumunu hızlandırmakta ve ikinci basamak sağlık kuruluşlarının yükünü hafifletmektedir. Bununla birlikte, HBT'lerin klinik doğruluk, profesyonel eğitim ihtiyacı, altyapı eksikliği ve tedarik zinciri yönetimi gibi konularda bazı zorluklar barındırdığı da unutulmamalıdır. Bu zorlukları aşmak için kalite kontrol mekanizmalarının standardize edilmesi, teknolojik gelişmelerin desteklenmesi ve sağlık hizmeti sunucularının bu testleri uygulama konusunda sürekli mesleki eğitime tabii tutulması önem taşımaktadır. Sonuç olarak, HBT'ler; bulaşıcı hastalıklar, kronik hastalık yönetimi ve anne-çocuk sağlığı gibi pek çok alanda birinci basamak sağlık hizmetleri için kritik bir araçtır. Hem yüksek gelir düzeyine sahip hem de kaynakların kısıtlı olduğu ortamlarda uygulanabilirliği, test sonuçlarının dakikalar içinde alınabilmesi ve hasta merkezli bakıma uyum sağlaması, HBT'nin gelecekte sağlık sistemlerinde daha fazla benimsenebileceğini göstermektedir.

Anahtar Kelimeler: Birinci basamak sağlık hizmetleri, Hasta başı test, Halk sağlığı

ABSTRACT

This review aims to explore the current and potential impact of point-of-care testing (POCT) on primary healthcare. POCT provides rapid and actionable diagnostic information by enabling testing at the point of care or out of centralized laboratories. Thus, it shortens the diagnostic process and enables the timely organization of interventions, especially in emergency health services or chronic disease management. POCTs are widely used in primary healthcare. Rapid tests for infectious diseases (e.g. HIV, malaria and tuberculosis) have been shown to contribute to early diagnosis and treatment in resource-limited settings. In addition, blood glucose or HbA1c levels that can be measured at the point of care play an important role in managing chronic diseases such as diabetes and hypertension. Rapid measurement of biomarkers such as troponin in cardiovascular diseases also saves time, resulting in reduced mortality rates, especially in emergency situations. One of the most important advantages offered by POCT is the rapid access to test results, which increases patient satisfaction and reduces unnecessary referrals. This is cost-effective for both the patient and the healthcare system, accelerates healthcare delivery and relieves the burden on secondary healthcare organizations. However, it should be noted that POCTs have some challenges in terms of clinical accuracy, need for professional training, lack of infrastructure and supply chain management. To overcome these challenges, it is important to standardize quality control mechanisms, support technological advances, and provide continuous professional training for healthcare providers on the implementation of these tests. In conclusion, POCTs are a critical tool for primary healthcare in many areas such as infectious diseases, chronic disease management and maternal and infant health. Its applicability in both high-income and resource-limited settings, the ability to obtain test results within minutes, and its adaptability to patient-centered healthcare suggest that POCT may further be adopted in health systems in the future.

Keywords: Primary healthcare, Point-of-care testing, Public health

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GİRİŞ

Hasta başı test (HBT), tıbbi teşhis alanında hızla gelişen bir alandır ve testlerin hasta başında veya yakınında yapılması olarak tanımlanmaktadır. Bu yaklaşım, klinik karar verme süreçlerini ve hasta yönetimini önemli ölçüde etkileyebilecek anında sonuçlara olanak sağlamaktadır. HBT tanımı; acil servisler, poliklinikler ve hatta hastaların evleri de dahil olmak üzere konvansiyonel laboratuvar ortamlarının dışında gerçekleştirilmekte olan çok çeşitli tanısal testleri kapsamaktadır. HBT'nin birincil amacı, hasta sonuçlarının iyileştirilmesine ve daha verimli sağlık hizmeti sunumuna yol açabilecek zamanında ve eyleme geçirilebilir tanısal bilgiler sağlamaktır (1-3). HBT'nin temelinde, genellikle dakikalar içinde hızlı teşhis sonuçları sunma ve böylece anlık klinik kararları kolaylaştırma yetisi yatmaktadır. Bu, özellikle zaman hassasiyetine sahip müdahalelerin gerekli olduğu acil durumlarda çok önemlidir. Çalışmalar, HBT'nin kardiyak troponin gibi biyobelirteçlerin hızlı bir şekilde ölçümü sayesinde göğüs ağrısı ile başvuran hastaların hastanede kalış sürelerini kısaltabileceğini göstermektedir (4). Ayrıca, sonuçların aynı klinik başvuru sırasında alınabilmesinin rahatlığı hastalar tarafından takdir edildiğinden, HBT'lerin kullanımı hasta memnuniyetinin artmasıyla ilişkilendirilmektedir (5).

HBT cihazları, kapsamlı laboratuvar eğitimi olmayanlar da dahil olmak üzere sağlık hizmeti sunucularının testleri yapmasına ve sonuçları yorumlamasına olanak tanıyacak şekilde kullanıcı dostu olarak tasarlanmıştır. Bu erişilebilirlik, konvansiyonel laboratuvar altyapısının eksik olabileceği, kaynakların sınırlı olduğu ortamlarda hayati önem taşımaktadır. Örneğin, HIV ve Covid-19 gibi bulaşıcı hastalıklar için HBT'ler, toplum sağlığı merkezlerinde hızlı sonuçlar sağlamak üzere geliştirilmiş olup, hastalık yönetimi ve kontrol çabalarını önemli ölçüde güçlendirmektedir (6,7).

Kırsal kliniklerden kentsel acil servislere kadar çeşitli ortamlarda test yapabilme yeteneği, HBT'nin modern sağlık hizmetleri içerisindeki çok yönlülüğünün ve öneminin altını çizmektedir (8).

Bu çalışmanın amacı, HBT'lerin birinci basamak sağlık hizmetleri kapsamında kullanımının sağlayabileceği klinik ve maliyet faydalarına dair literatürde yer alan güncel verilerin analiz edilmesi ve özetlenmesidir. Bulgular, sağlık hizmeti sunucuları aracılığı ile gerçekleştirilecek birinci basamak sağlık hizmeti sunumunun kalitesi ile klinik ve maliyet etkililiğinin artırılmasını sağlayacaktır.

Hasta Başı Testlerin Birinci Basamak Sağlık Hizmetleri Kapsamında Kullanım Alanları

HBT'ler, birinci basamak sağlık hizmetlerinde dönüştürücü bir unsur olarak ortaya çıkmış olup; teşhis verimliliğini, tedavi doğruluğunu ve hasta sonuçlarını önemli ölçüde etkilemektedir. HBT'nin birinci basamak sağlık hizmetlerine entegrasyonu, doğru zamanlı klinik kararlar için çok önemli olan hızlı tanı koyma olanaklarını mümkün kılmaktadır. HBT'lerin hasta numunesinin alınması ile sonucun elde edilmesi arasındaki süreyi yalnızca dakikalara indirgeyebilmesi ile sağlanan hızlı geri dönüş, özellikle tedavi planlarında yapılan doğru zamanlı müdahalelerin sağlık sonuçlarının iyileşmesine sebep olabileceği diyabet ve hipertansiyon gibi kronik hastalıkların yönetiminde faydalıdır (9,10). HBT'lerin kullanım alanları, bulaşıcı hastalıklar, kronik hastalık yönetimi ve acil sağlık hizmetleri de dahil olmak üzere çok çeşitli tıbbi durumları kapsamaktadır.

HBT'nin en önemli kullanım alanlarından biri bulaşıcı hastalıkların teşhisi ve yönetimidir. HIV, sıtma ve tüberküloz gibi hastalıklara yönelik hızlı testler, merkezi laboratuvar imkânlarının yetersiz olabileceği, kaynakların yetersiz olduğu koşullarda son derece önem arz eden, anlık sonuçlar verecek şekilde geliştirilmiştir.

HBT'ler, CYBE yönetiminde de giderek daha fazla kullanılmaktadır. Sifiliz ve hepatit de dahil olmak üzere CYBE'ler için hızlı testlerin geliştirilmesi, salgınların kontrol altına alınması ve daha fazla bulaşın önlenmesi için gerekli olan acil teşhis ve tedaviye olanak sağlamaktadır (11,12). CYBE'ler için HBT uygulamasının, yüksek riskli topluluklar için özellikle kaynakların kısıtlı olduğu ortamlarda tekrarlayan klinik başvurulara duyulan ihtiyacı ortadan kaldırması sayesinde test oranlarını artırdığı ve sağlık hizmetlerine erişimi iyileştirdiği gösterilmiştir (13).

Çalışmalar, HIV için hızlı antikor testleri gibi hasta başı testlerin dakikalar içinde sonuç verebildiğini, tedaviye zamanında başlanmasını sağladığını ve hasta takibindeki kayıpları azalttığını göstermiştir (6,14). Benzer şekilde, sıtma hastalığı için hızlı tanı testlerinin kullanılmaya başlanması, vaka yönetiminin iyileştirilmesinde ve hastalıkla ilişkili morbidite ve mortalitenin azaltılmasında etkili olmuştur (15). Bu testlerin hasta başında yapılabilmesi, erken teşhis ve tedaviyi kolaylaştırarak hasta sonuçlarını önemli ölçüde iyileştirmektedir (16).

Bulaşıcı hastalıklara ek olarak; HBT'ler, özellikle diyabet ve kardiyovasküler hastalıklar gibi kronik hastalıkların yönetiminde de kritik bir rol oynamaktadır. Diyabet yönetimi için; hasta başı kan şekeri ölçüm cihazları, hastaların kan şekeri seviyelerini rahatça izleyebilmelerini sağlayarak daha iyi bir glisemik kontrol sağlayarak komplikasyonların azaltılmasını mümkün kılmaktadır (17,18). Ayrıca, HbA1c düzeyleri için hasta başında yapılan testlerin hem hastalara hem de sağlık hizmeti sunucularına anında geri bildirim sağlayarak diyabet kontrolünü iyileştirdiği ve böylece tedavi planlarında doğru zamanlı düzenlemeler

yapılmasını kolaylaştırdığı gösterilmiştir (19). Kardiyovasküler açıdan, troponin gibi kardiyak biyobelirteçler için HBT, miyokard enfarktüsünün hızlı bir şekilde değerlendirilmesini sağlayarak hayat kurtarıcı olabilecek hızlı klinik karar süreçlerine olanak tanımaktadır (20,21).

HBT'lerin afet müdahale planlarına entegrasyonu, halk sağlığı açısından acil durumların yönetilmesinde çok önemli bir unsur olarak vurgulanmış ve sahada anında teşhis yapılmasına olanak sağlamıştır (22). Anne ve çocuk sağlığı bağlamında, HBT'ler doğum öncesi ve yenidoğan sağlık hizmetlerinin iyileştirilmesinde çok önemli bir rol oynamaktadır. Örneğin, hamile kadınlar için HIV'e yönelik hasta başı testler, uygun müdahalelerin vakit kaybetmeden başlatılmasını sağlayarak anneden çocuğa bulaş riskini önemli ölçüde azaltabilir (14,23). Aynı zamanda, gestasyonel diyabet gibi rahatsızlıklar için hızlı testlerin kullanılması, doğru zamanlı müdahaleye olanak tanıyarak maternal ve fetal sonuçları iyileştirmektedir (24).

Buna ek olarak, HBT'lerin birinci basamak sağlık hizmetlerinde kullanımının ekonomik faydaları da göz ardı edilmemelidir. Laboratuvar geri dönüş sürelerindeki azalma ve buna bağlı olarak hasta bekleme sürelerindeki düşüş, hasta memnuniyetinin artmasına ve daha verimli sağlık hizmeti sunumuna katkıda bulunmaktadır (5). Çalışmalar, HBT'lerin kullanımının gereksiz sevkleri ve hastane yatışlarını en aza indirerek maliyet tasarrufu sağlayabileceğini ve sonuçta hem sağlık sistemlerine hem de hastalara fayda sağlayabileceğini göstermektedir (24). Birinci basamak sağlık hizmetleri kapsamında hasta başı C reaktif protein (CRP) testinin kullanımının, klinik yönlendirmelerle birleştirildiğinde antibiyotik kullanımını önemli ölçüde azalttığını ve böylece küresel antimikrobiyal direnç tehdidini hafiflettiği ortaya konulmuştur (25). Bu sadece hasta yönetimini optimize etmekle kalmamakta, aynı zamanda ikinci basamak sağlık kuruluşlarının yükünü en aza indirerek sağlık sistemlerinin genel verimliliğini de artırmaktadır (26,27).

Kaynakların sınırlı olduğu ortamlarda HBT'ler, temel tıbbi tanı hizmetlerine erişimin genişletilmesinde kritik bir rol oynamaktadır. Örneğin, Gana'da sıtma ve anemi hastalıkları için HBT kullanımının hem uygun maliyetli hem de pratik olduğu kanıtlanmış ve sağlık hizmeti sunucularının kapsamlı bir laboratuvar altyapısına ihtiyaç duymadan doğru teşhisler koyabilmesine olanak sağlanmıştır (28,29). Bu tür test olanakları, merkezi laboratuvarlara erişimin sınırlı olduğu kırsal bölgelerde hayati önem taşımakta ve böylece hastaların doğru zamanlı ve uygun sağlık hizmeti almalarını sağlamaktadır (10,30).

Hasta Başı Testlerin Birinci Basamak Sağlık Hizmetlerine Entegrasyonu

HBT'lerin bir diğer kritik yönü de bu testlerin mevcut sağlık hizmeti iş akışlarına entegrasyonudur. Başarılı bir uygulama; sorunsuz iletişim ve veri yönetimi sağlamak adına sağlık hizmeti sunucuları, laboratuvar personeli ve bilgi teknolojisi sistemleri

arasında iş birliği gerektirmektedir (4,31). Ayrıca, test sonuçlarının bütünlüğünü korumak ve klinik karar verme süreçleri içerisinde uygun şekilde kullanılmalarını sağlamak için kalite kontrol ve güvence protokolleri oluşturulmalıdır (32,33). HBT için kılavuzların ve çerçevelerin geliştirilmesi, uygulamaların standartlaştırılmasına ve bu test yöntemleri aracılığıyla sunulan sağlık hizmeti sunum kalitesinin iyileştirilmesine yardımcı olabilir (34). HBT'lerin birinci basamak sağlık hizmeti ortamlarına entegrasyonu, özellikle kırsal ve yetersiz sağlık hizmeti sunulan topluluklarda coğrafi engellerin yol açtığı zorlukları da çözüme kavuşturmaktadır. HBT, sağlık hizmeti sunucularının yerinde tanı testleri yapabilmesini sağlayarak hastaların laboratuvar hizmetlerine erişmek için uzun mesafeler kat etme ihtiyacını azaltmakta ve böylece sağlık hizmetlerine erişilebilirliği artırmaktadır (35). Bu durum özellikle sağlık altyapısının kısıtlı olabileceği düşük ve orta gelirli ülkeler için anlamlıdır (15). HBT cihazlarıyla donatılmış birinci basamak sağlık hizmetleri sunucularının, bu ortamlarda sağlık hizmeti sunumunu geliştirdiği ve bu sayede çeşitli hastalıkların erken teşhis ve tedavisinin kolaylaştırıldığı gösterilmiştir (36).

Sayısız avantajına rağmen, birinci basamak sağlık hizmetleri kapsamında HBT'lerin başarılı bir şekilde kullanımı zorluklar içermektedir. Sağlık hizmeti sunucularının yetersiz eğitimi, altyapı eksikliği ve yetersiz tedarik zinciri yönetimi gibi engeller HBT'lerin etkili kullanımı konusunda engel oluşturabilmektedir (29,30). HBT'lerin sağlık hizmeti sunumunu iyileştirme potansiyeline tam olarak erişebilmek için bu zorlukların ele alınması şarttır. Ayrıca, HBT cihazlarının özgüllüğünü ve duyarlılığını artırmak ve birinci basamak sağlık hizmeti sunucularının klinik ihtiyaçlarını karşılamalarını sağlamak için bu alanda sürekli araştırma ve geliştirmeler yapılması gerekmektedir (26,37). Farklı HBT cihazlarının doğruluğu ve güvenilirliğindeki değişkenlik, bu konudaki mevcut endişe kaynaklarındandır. Birçok HBT, son derece hassas ve özgül olacak şekilde tasarlanmış olsa da; tüm HBT cihazları, klinik ortamlarda, özellikle de yanlış negatif sonuçların ciddi sıkıntılara yol açabileceği ikinci basamak sağlık hizmetleri kapsamında yeterli performans gösterememiştir (38,39). Bu nedenle, HBT teknolojilerinin yaygın olarak benimsenmeden önce geçerlilik ve güvenirlik için gerekli standartları karşıladığından emin olmak için sıkı klinik doğrulamalarının yapılması gerekmektedir (40).

Birinci Basamak Sağlık Hizmetlerinde Hasta Başı Testlerin Geleceği

Birinci basamak sağlık hizmetlerinde kullanılan HBT'lerin geleceği, teknolojik gelişmeler, zamanında teşhis ihtiyacı ve hasta merkezli bakıma giderek daha fazla öncelik veren gelişen sağlık hizmetleri ortamı nedeniyle önemli bir dönüşüme hazırlanmaktadır.

HBT alanındaki teknolojik gelişmeler ışığında; mikroçip görüntüleme sitometreleri ve otomatik tanı araçları gibi yenilikler, HBT

cihazlarını daha kolay taşınabilir, daha düşük maliyetli ve daha kullanıcı dostu hale getirmektedir (41).

Ayrıca; birinci basamak sağlık hizmetlerinde HBT'nin geleceği, hasta merkezli bakıma yapılan vurgunun artmasıyla şekillenecektir. Sağlık hizmeti sunucuları hastaları kendi sağlık süreçlerine daha aktif bir şekilde dahil etmeye çalıştıkça, HBT, anında geri bildirim ve sonuç sağlama imkanı sunarak sağlık yönetiminde işbirliğine dayalı bir yaklaşımı teşvik edecektir.

SONUÇ

HBT'ler, teşhis hızını ve doğruluğunu, aynı zamanda hasta memnuniyetini artırarak ve gereksiz sevkleri azaltarak birinci basamak sağlık hizmetlerini önemli ölçüde etkilemektedir. Uygulamada zorluklar devam etse de, HBT'nin doğru zamanlı ve etkili sağlık hizmeti sunumunu kolaylaştırmadaki faydaları, özellikle kaynakların sınırlı olduğu ortamlarda belirgindir. Birinci basamak sağlık hizmetleri kapsamında HBT'nin potansiyelini en üst düzeye çıkarmak için; eğitim, altyapı ve teknoloji geliştirme yatırımlarının devam etmesi büyük önem arz etmektedir.

Sonuç olarak; HBT'ler, bulaşıcı hastalıkların teşhisi, kronik hastalıkların yönetimi, acil sağlık hizmetleri, anne ve çocuk sağlığı ile CYBE'lerin yönetimini kapsayan uygulamalarıyla birinci basamak sağlık hizmetlerinin hayati bir bileşeni olarak kendini kanıtlamıştır.

Hasta başında hızlı, doğru ve erişilebilir tanısal bilgi sağlama kabiliyeti, hasta sonuçlarını iyileştirmekte ve özellikle kaynakların sınırlı olduğu ortamlarda sağlık hizmeti sunumunu ideal hâle getirmektedir.

HBT'lerin modern sağlık sistemleri içerisinde günden güne daha fazla fayda sağlayabilmesi adına, bu alanda gerçekleştirilecek daha fazla çalışmaya ve de özellikle kalite kontrol mekanizmalarının çerçevesinin belirlenmiş olduğu düzenlemelere ihtiyaç duyulmaktadır.

HBT'lerin koruyucu sağlık hizmetleri kapsamında erken tedbirlerin alınmasına ve halk sağlığının korunmasına katkıları yadsınamaz.

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Kaynaklar

1. Baba M., Vidergar N., Marcello A.. Virological Point-of-Care Testing for the Developing World. Future Virology 2014;9(6):595-603. https://doi.org/10.2217/fvl.14.33
2. Mooney C., Byrne M., Kapuya P., Pentony L., Cambridge T., Foley D. Point of Care Testing in General Haematology. British Journal of Haematology 2019;187(3):296-306. https://doi.org/10.1111/bjh.16208
3. Epner P. Achieving the Promise of Point-of-Care Testing. Point of Care the Journal of Near-Patient Testing & Technology 2014;13(3):112-113. https://doi.org/10.1097/poc.0000000000000022
4. Singer A., Ardise J., Gulla J., Cangro J.. Point-of-Care Testing Reduces Length of Stay in Emergency Department Chest Pain Patients. Annals of Emergency Medicine 2005;45(6):587-591. https://doi.org/10.1016/j.annemergmed.2004.11.020
5. Laurence C., Gialamas A., Bubner T., Yelland L., Willson K., Ryan P. et al.. Patient Satisfaction with Point-of-Care Testing in General Practice. British Journal of General Practice 2010;60(572):e98-e104. https://doi.org/10.3399/bjgp10x483508
6. Dalcin D., Bogoch I.. Point-of-care Testing for HIV. Canadian Medical Association Journal 2018;190(18):E569-E569. https://doi.org/10.1503/cmaj.180068
7. Gupta N., Rana S., Singh H.. Innovative Point-of-Care Molecular Diagnostic Test for Covid-19 in India. The Lancet Microbe 2020;1(7):e277. https://doi.org/10.1016/s2666-5247(20)30164-6
8. Drain P., Hyle E., Noubary F., Freedberg K., Wilson D., Bishai W. et al.. Diagnostic point-of-care tests in resource-limited settings. The Lancet Infectious Diseases 2014;14(3):239-249. https://doi.org/10.1016/s1473-3099(13)70250-0
9. Simwita Y., Helgheim B.. Application of Agile and Simulation Approaches for the Maximal Benefits of Reduced Turnaround Time from the Point of Care Testing. Tanzania Journal of Science 2023;49(2):468-478. https://doi.org/10.4314/tjs.v49i2.17
10. Heidt B., Siqueira W., Eersels K., Diliën H., Grinsven B., Fujiwara R. et al.. Point of Care Diagnostics in Resource-limited Settings: A Review of the Present and Future of POC in Its Most Needed Environment. Biosensors 2020;10(10):133. https://doi.org/10.3390/bios10100133
11. Tucker J., Bien C., Peeling R.. Point-of-Care Testing for Sexually Transmitted Infections. Current Opinion in Infectious Diseases 2013;26(1):73-79. https://doi.org/10.1097/qco.0b013e32835c21b0
12. Dzobo M., Dzinamarira T., Murewanhema G., Madziva R., Herrera H., Musuka G.. Limited Syphilis Testing for Key Populations in Zimbabwe: A Silent Public Health Threat. Southern African Journal of Infectious Diseases 2022;37(1). https://doi.org/10.4102/sajid.v37i1.385
13. Toskin I., Peeling R., Mabey D., Holmes K., Ballard R., Kiarie J. et al.. Point-of-Care Tests for STIs: the Way Forward. Sexually Transmitted Infections 2017;93(S4):S1-S2. https://doi.org/10.1136/sextrans-2016-053074
14. Sutcliffe C., Mutanga J., Moyo N., Agarwal A., Schue J., Hamahuwa M., et al.. Point-of-Care P24 Antigen Detection for Early Infant Diagnosis of HIV Infection: Cross-sectional and Longitudinal Studies in Zambia. BMC Infectious Diseases 2021;21(1). https://doi.org/10.1186/s12879-021-05808-2
15. Pai N., Vadnais C., Denkinger C., Engel N., Pai M.. Point-of-Care Testing for Infectious Diseases: Diversity, Complexity, and Barriers in Low- and Middle-Income Countries. Public Library of Science Medicine 2012;9(9):e1001306. https://doi.org/10.1371/journal.pmed.1001306
16. Dorward J., Drain P., Garrett N.. Point-of-Care Viral Load Testing and Differentiated HIV Care. The Lancet HIV 2018;5(1):e8-e9. https://doi.org/10.1016/s2352-3018(17)30211-4
17. Visser L. , Shahid S. , Mahmud A.. Point-of-care testing for diabetes patients: investigating diabetes management by older adults. In: Jones M, Palanque P. CHI '14 Extended Abstracts on Human Factors in Computing Systems. New York, USA: Association for Computing Machinery; 2014. P. 1645–1650. https://doi.org/10.1145/2559206.2581193
18. Macrury S., Srinivasan A., Mahoney J.. Performance of a New Meter Designed for Assisted Monitoring of Blood Glucose and Point-of-Care Testing. Journal of Diabetes Science and Technology 2013;7(2):389-398. https://doi.org/10.1177/193229681300700215

19. Kristensen T., Waldorff F., Nexøe J., Skovsgaard C., Olsen K.. Variation in Point-of-Care Testing of HbA1c in Diabetes Care in General Practice. International Journal of Environmental Research and Public Health 2017;14(11):1363. https://doi.org/10.3390/ijerph14111363
20. Kost G., Kost L., Suwanyangyuen A., Cheema S., Curtis C., Sumner S. et al.. Emergency Cardiac Biomarkers and Point-of-Care Testing. Point of Care: The Journal of Near-Patient Testing & Technology 2010;9(2):53-64. https://doi.org/10.1097/poc.0b013e3181d9d45c
21. Curtis C., Kost G., Louie R., Sonu R., Ammirati E., Sumner S.. Point-of-Care Hematology and Coagulation Testing in Primary, Rural Emergency, and Disaster Care Scenarios. Point of Care: The Journal of Near- Patient Testing & Technology 2012;11(2):140-145. https://doi.org/10.1097/poc.0b013e31825a9d3a
22. Tran N. , Godwin Z. , Bockhold J.. Point-of-Care Testing at the Disaster–Emergency–Critical Care Interface. Point of Care: The Journal of Near-Patient Testing & Technology 2012;11(4):180-183. https://doi.org/10.1097/poc.0b013e318265f7d9
23. Spooner E., Reddy T., Mchunu N., Reddy S., Daniels B., Ngomane N. et al.. Point-of-Care CD4 Testing: Differentiated Care for the Most Vulnerable. Journal of Global Health 2022;12. https://doi.org/10.7189/jogh.12.04004
24. Wong H., Marcu L., Bezak E., Parange N.. Review of Health Economics of Point-of-Care Testing Worldwide and Its Efficacy of Implementation in the Primary Health Care Setting in Remote Australia. Risk Management and Healthcare Policy 2020;13:379-386. https://doi.org/10.2147/rmhp.s247774
25. Cooke J., Llor C., Hopstaken R., Dryden M., Butler C.. Respiratory Tract Infections (RTIs) in Primary Care: Narrative Review of C Reactive Protein (CRP) Point-of-Care Testing (POCT) and Antibacterial Use in Patients Who Present with Symptoms of RTI. BMJ Open Respiratory Research 2020;7(1):e000624. https://doi.org/10.1136/bmjresp-2020-000624
26. Charman S., Okwose N., Maniatopoulos G., Graziadio S., Metzler T., Banks H. et al.. Opportunities and Challenges of a Novel Cardiac Output Response to Stress (CORS) Test to Enhance Diagnosis of Heart Failure in Primary Care: Qualitative Study. BMJ Open 2019;9(4):e028122. https://doi.org/10.1136/bmjopen- 2018-028122
27. Howick J., Cals J., Jones C., Price C., Plüddemann A., Heneghan C. et al.. Current and Future Use of Point-of-Care Tests in Primary Care: An International Survey in Australia, Belgium, the Netherlands, the UK and the USA. BMJ Open 2014;4(8):e005611. https://doi.org/10.1136/bmjopen-2014-005611
28. Palmer T., Aiyenigba A., Bates I., Okyere D., Tagbor H., Ampofo G.. Improving the Effectiveness of Point of Care Tests for Malaria and Anaemia: A Qualitative Study Across Three Ghanaian Antenatal Clinics. BMC Health Services Research 2020;20(1). https://doi.org/10.1186/s12913-020-05274-7
29. Ansu-Mensah M., Bawontuo V., Kuupiel D., Ginindza T.. Sustainable Solutions to Barriers of Point-of-Care Diagnostic Testing Services in Health Facilities without Laboratories in the Bono Region, Ghana: A Qualitative Study. BMC Primary Care 2024;25(1). https://doi.org/10.1186/s12875-024- 02406-4
30. Kuupiel D., Adu K., Bawontuo V., Adogboba D., Drain P., Moshabela M. et al.. Geographical Accessibility to Glucose-6-Phosphate Dioxygenase Deficiency Point-of-Care Testing for Antenatal Care in Ghana. Diagnostics 2020;10(4):229. https://doi.org/10.3390/diagnostics10040229
31. Johannis W., Bietenbeck A., Malchau G., Streichert T.. Point-of-Care Testing (POCT) and IT Security Concepts. Journal of Laboratory Medicine 2020;44(2):107-111. https://doi.org/10.1515/labmed-2019-0199
32. Rawlinson W., Escott R., Baleriola C., Morris A.. Quality Control and Quality Assurance for Point of Care (POC) Diagnostic Tests. Microbiology Australia 2006;27(2):58-60. https://doi.org/10.1071/MA06058
33. Lewandrowski K., Gregory K., MacMillan D.. Assuring Quality in Point-of-Care Testing: Evolution of Technologies, Informatics, and Program Management. Archives of Pathology & Laboratory Medicine 2011;135(11):1405-1414. https://doi.org/10.5858/arpa.2011-0157-ra
34. Briggs C., Guthrie D., Hyde K., Mackie I., Parker N., Popek M. et al.. Guidelines for Point-of- Care Testing: Haematology. British Journal of Haematology 2008;142(6):904-915. https://doi.org/10.1111/j.1365-2141.2008.07274.x
35. Licher Y., Visser J., Van G., Diehl J.. Formulating Design Recommendations for the Acceptance of the Use and Results of Point-of-Care Testing in Low- and Middle-Income Countries: A Literature Review. Proceedings of the Design Society: International Conference on Engineering Design 2019;1(1):2795-2804. https://doi.org/10.1017/dsi.2019.286

36. Ehui E., Jules B., Gisele K.. Cascade of Care for HIV Positive Patients in A Rural Health Region in the North-Central Region of Ivory Coast: A Follow-up Study. Journal of Microbiology and Infectious Diseases 2017:144-147. https://doi.org/10.5799/jmid.367556

37. Kip M., Hummel J., Eppink E., Koffijberg H., Hopstaken R., IJzerman M. et al.. Understanding the Adoption and Use of Point-of-Care Tests in Dutch General Practices Using Multi- criteria Decision Analysis. BMC Family Practice 2019;20(1). https://doi.org/10.1186/s12875-018-0893- 4

38. Brendish N., Poole S., Naidu V., Mansbridge C., Norton N., Wheeler H. et al.. Clinical Impact of Molecular Point-of-Care Testing for Suspected Covid-19 in Hospital (COV-19POC): A Prospective, Interventional, Non-randomised, Controlled Study. The Lancet Respiratory Medicine 2020;8(12):1192 1200. https://doi.org/10.1016/s2213-2600(20)30454-9

39. Micocci M., Gordon A., Seo M., Allen J., Davies K., Lasserson D. et al.. Is Point-of-Care Testing Feasible and Safe in Care Homes in England? An Exploratory Usability and Accuracy Evaluation of A Point-of-Care Polymerase Chain Reaction Test for SARS-COV-2. Age and Ageing 2021;50(5):1464- 1472. https://doi.org/10.1093/ageing/afab072

40. Chen H., Liu K., Zhao L., Wang P.. Point of Care Testing for Infectious Diseases. International Journal of Clinical Chemistry and Diagnostic Laboratory Medicine 2019;493:138-147. https://doi.org/10.1016/j.cca.2019.03.008

41. Yuan X., Darcie T., Wei Z., Aitchison J.. Microchip Imaging Cytometer: Making Healthcare Available, Accessible, and Affordable. Opto-Electronic Advances 2022;5(11):210130-210130. https://doi.org/10.29026/oea.2022.210130

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REVIEW

A Vitamini Eksikliğinin Anemi Üzerindeki Etki Mekanizmaları

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ÖZET

Bu çalışmada mevcut literatür yardımıyla A vitamini eksikliğinin (AVE) kan demir düzeyi ve anemi durumu üzerindeki potansiyel etki mekanizmalarının açıklanması amaçlanmıştır. Öncelikle A vitamini eksikliği ve anemi arasındaki ilişki, çeşitli mekanizmalar aracılığıyla gerçekleşmekte olup karmaşık bir yapıya sahiptir. Eritropoez modülasyonu, enfeksiyona karşı bağışıklık fonksiyonu ve demir metabolizması bu etkileşimlerin anahtar noktalarıdır. Epidemiyolojik çalışmalar, özellikle çocuk ve hamile kadın popülasyonlarında AVE ve anemi arasında güçlü bir ilişki olduğunu göstermektedir. A vitamini, eritropoietin (EPO) geninin transkripsiyonunu aktive ederek eritropoezi etkileyebilir ve enfeksiyon anemisini azaltabilir. Bununla birlikte, AVE sırasında demirin hapsedilmesi ve serbest bırakılmaması, anemi ve demir indekslerinin anormalleşmesine neden olabilir. Yapılan araştırmalarda, A vitamini takviyelerinin kan demir düzeyi ve anemi durumu üzerindeki etkisi hakkında çelişkili bulgular mevcuttur. Bazı çalışmalarda A vitamini takviyesinin kan demir düzeyini ve anemi durumunu iyileştirebileceği rapor edilirken, bazı çalışmalarda ise bu konuda anlamlı bir etki tespit edilmemiştir. Sonuç olarak, A vitamini eksikliğinin anemi üzerinde olumsuz etkileri olabilir ve A vitamini takviyeleri AVE ve anemi gibi sorunların önlenmesi ve tedavisi için önemli bir yöntem olabilir.
Anahtar kelimeler: A Vitamini, A Vitamini Eksikliği, Anemi, Demir

ABSTRACT

In this study, it is aimed to explain the potential mechanisms of vitamin A deficiency (VAD) on blood iron levels and anemia status with the help of the existing literature. First of all, the relationship between vitamin A deficiency and anemia is mediated through various mechanisms and has a complex structure. Modulation of erythropoiesis, immune function against infection and iron metabolism are key points of these interactions. Epidemiological studies show a strong association between VAD and anemia, especially in populations of children and pregnant women. Vitamin A may affect erythropoiesis by activating transcription of the erythropoietin (EPO) gene and reduce infection anemia. However, the trapping and non-release of iron during VAD can lead to anemia and abnormalization of iron indices. There are conflicting findings in research on the effect of vitamin A supplements on blood iron levels and anemia status. While some studies have reported that vitamin A supplementation can improve blood iron levels and anemia, some studies have found no significant effect. In conclusion, vitamin A deficiency may have adverse effects on anemia and vitamin A supplements may be an important method for the prevention and treatment of problems such as VAD and anemia.
Keywords: Vitamin A, Vitamin A Deficiency, Anemia, Iron

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GİRİŞ

A vitamininin anemi üzerindeki etkisi çeşitli çalışmalarda araştırılmış olup, bazı çalışmalar A vitamini takviyesinin vücudun kırmızı kan hücreleri de dahil olmak üzere kan hücreleri üretme sürecini (hematopoezi) iyileştirebileceğini göstermektedir (1, 2). Bununla birlikte, A vitamininin hematopoez üzerindeki etkisini Meksikalı çocuklar üzerinde araştıran bir çalışma sonucunda ise hem demir eksikliği hem de A vitamini eksikliği durumlarında düşük hemoglobin seviyeleri görüldüğü rapor edilmiştir. Bu durum birden fazla mikro besin eksikliğinin anemiye katkıda bulunabileceğini göstermektedir (3). Özellikle çocuklarda demir eksikliği anemisinin tedavisinde kullanılan demir takviyesinin etkinliğini artırmada A vitamininin rolünü destekleyen çalışmalar mevcuttur (1, 2).

Bu derlemenin amacı A vitamini eksikliğinin anemi üzerindeki etki mekanizmalarını araştırmaktır. Ayrıca çalışmada A vitamini takviyesinin demir metabolizması ve anemi üzerindeki potansiyel etkilerine de değinilmiştir.

A Vitamini Eksikliği Anemisinin Epidemiyolojisi

Anemi ve A vitamini eksikliği (AVE) arasındaki yakın ilişki, başta çocuk ve hamile kadınlar olmak üzere çeşitli epidemiyolojik çalışmalarda gözlemlenmiştir. Ayrıca araştırmalar tarafından bu popülasyonlarda AVE ve anemi prevalansının sıklıkla yüksek olduğu rapor edilmiştir. Örneğin; Nepal'de gebe kadınlar arasında AVE prevalansı % 20 iken, anemi oranı % 79'dur (4). Dreyfuss ve arkadaşları, Nepalli hamile kadınların % 54'ünün serum retinol düzeylerinin <1,05 µmol/l olduğunu ve % 73'ünde anemi olduğunu rapor etmiştir (5). Yapılan bir başka çalışmada ise Malavi'de serum retinol düzeyi <1,05 µmol/l (% 89) olan HIV pozitif gebe kadın yüzdesinin, Nepal'e kıyasla daha yüksek olduğu saptanmıştır. Bunun yanı sıra bu iki coğrafik bölgedeki anemik kadın yüzdesinin benzer olduğu tespit edilmiştir (6). Diğer yandan Honduras'ta, 1 ila 5 yaş arası çocukların % 15,5'inde hem AVE'nin hem de aneminin mevcut olduğu belirlenmiştir. Ayrıca bu çalışmada çocukların büyük bir bölümünde hem AVE'yi hem de anemiyi tedavi etmek için uygulanacak olan beslenme tedavilerinin bu iki rahatsızlığı aynı anda giderecek şekilde düzenlenmesi tavsiye edilmiştir (7).

Bunların yanı sıra hemoglobin (Hb) ve plazma veya serum retinol konsantrasyonları arasında pozitif bir korelasyon olduğu ifade edilmiştir. Gelişmekte olan sekiz ülkeden toplanan verilerin analizinde Hodges ve arkadaşları 15-45 yaşlarındaki gebe olmayan kadınlar arasında 0,77 ($p<0,05$) düzeyinde ve pozitif yönde yüksek bir korelasyon saptamışlardır (8). Endonezyalı bebekler ve anneler arasında A vitamini düzeyinin düşük olmasının demir eksikliği anemisi riskini 2,4 kat arttırdığı belirlenmiştir (9). Benzer şekilde, Hb düzeyi <9,0 g/dl olan gebelerin kontrol

grubuna kıyasla A vitamini eksikliği riskinin 2,2 kat daha fazla olduğu tespit edilmiştir (10).

Potansiyel Mekanizmalar

A vitamininin, demir metabolizması üzerinde etkili olduğuna dair çeşitli olası mekanizmalar öne sürülmüştür. Bu mekanizmalar şu şekilde kategorize edilebilir: 1) Eritropoez modülasyonu 2) Enfeksiyona ve enfeksiyon anemisine karşı bağışıklık modülasyonu ve 3) Demir metabolizmasının modülasyonu (11-15).

Eritropoez ve Eritropoietinin Transkripsiyonu

Eritropoez, kırmızı kan hücrelerinin üretildiği bir süreçtir. Kırmızı kan hücresi olgunlaşması sürecinde kök hücreler eritroid patlama oluşturan birimler, eritroid koloni oluşturma birimleri, proeritroblastlar, ortokromik eritroblastlar, retikülositler ve son olarak olgun eritrositler şeklinde bir dizi farklılaşmaya uğrar. EPO içeren bir geri bildirim döngüsü eritroid progenitör hücrelerin proeritroblastları ayırt etmek, retikülositler ve olgun eritrositlere dönüşmek için indüklenmesiyle eritropoez sürecini düzenlemeye yardımcı olur. Hb sentezi eritroid koloni oluşturan birimlerin eritrosit öncüleri olarak ayrılması sırasında ortaya çıkar ve retikülositlerin eritrositlere olgunlaşmasına kadar devam eder. Ek olarak, retinoidler eritropoetik progenitör hücrelerde apoptozisi düzenler. Hem RAR'ların hem de RXR'lerin, eritroid progenitör hücrelerin retinoik asit (RA) aracılı apoptozisinde rol oynadığı belirtilmiştir(16).

RA'nın eritropoez üzerine etkileri karmaşıktır ve hücre olgunlaşma aşamasına bağlıdır. RA, embriyonal karsinom hücrelerinde EPO geninin transkripsiyonel aktivasyonu yoluyla EPO üretiminin bir indükleyicisi olarak tanımlanmıştır (17). A vitamini tüketen sıçanlar trans-RA ile beslendiğinde, serum EPO konsantrasyonları artmıştır (18). Benzer şekilde A vitamini, böbreklerde ve insan hepatoma hücre çizgilerinde perfüze izole edilmiş EPO sentezini artırmıştır (19, 20).

A vitamini takviyesinin EPO konsantrasyonlarını etkileyip etkilemeyeceği yapılan bazı çalışmalarla araştırılmıştır. Malavi'de Semba ve arkadaşları, gebe kadınların günlük A vitamini takviyesinin (3 mg RE) plazma EPO konsantrasyonlarını artırmadığını bulmuşlardır (21). EPO konsantrasyonları hamilelik sırasında dalgalanma göstermiş olabilir, bu nedenle araştırmacıların sonuçları karıştırmış olabileceği düşünülmektedir. Ağır anemik Zanzibarlı okul öncesi çocuklarda tek bir yüksek doz A vitamini takviyesi, serum EPO konsantrasyonlarını ve ferritin düzeylerini azaltmış, ancak retikülosit üretim indeksini artırmıştır (22). Fas'ta yapılan başka bir klinik çalışma ise sıtma bulunmayan bir bölgede A vitamini ve demir düzeyleri zayıf olan okul çağındaki çocuklar üzerinde gerçekleştirilmiştir. Çalışma sonucunda A vitamini takviyesinin (200.000 IU) dolaşımdaki EPO konsantrasyonlarını artırdığı tespit edilmiştir (23).

Anti-Enfektif

A vitamininin anemiyi, enfeksiyon anemisini azaltarak etkilediği düşünülmektedir (24). Bu konuda olası bir açıklama ise hem demir hem de A vitamininin sırasıyla negatif akut faz proteinleri, transferrin ve retinol bağlayıcı protein (RBP) ile taşınmasıdır. Enfeksiyon veya inflamasyon sırasında transferrin ve RBP sentezi, karaciğerde, dalakta demir ve A vitamini tutulumunun azalmasına neden olmaktadır. A vitamini ile enfeksiyonun baskılanması, tüberküloz ve RBP sentezinin yeniden başlamasına yol açar. Bu nedenle tutulan demir ve A vitamini serbest bırakılmaktadır (25).

Demir Metabolizması

AVE durumunda demirin karaciğer ve dalakta hapsedildiği ve etkin bir şekilde serbest bırakılmadığı, bunun yanı sıra anemi ve anormal demir indekslerinin gelişmesine neden olan eritropoez için kullanıldığı öne sürülmektedir. A vitamini eksikliği olan sıçanlarda radyoaktif işaretli demirin eritrositlere katılması, kontrol hayvanlarına kıyasla %40 ila %50 oranında azalmıştır (26-28).

Daha sonraki çalışmalar AVE durumunda demir emiliminin arttığını bulmuştur (29, 30). A vitamini eksikliği yaşayan sıçanların A vitamini eksikliğinin giderilmesi, karaciğer ve dalaktaki demir depolarının kullanımını artırmıştır (31). Ancak daha sonraları Roodenburg ve arkadaşları tarafından yapılan bir çalışmada, A vitamininin eritropoezi etkilediğine dair herhangi bir kanıt saptanmamıştır (29). Ayrıca AVE'nin sıçanlarda demir durumunun herhangi bir indeksini şiddetlendirmediği de gösterilmiştir (32). Bununla birlikte demir eksikliği karaciğerde A vitamininin ayrılmasına neden olmuş ve artan retinol konsantrasyonları ile ilişkili bulunmuştur (32-34).

A Vitamini Besin Takviyesinin Anemi ve Demir Durumu Üzerine Etkisi

A vitamininin anemi üzerindeki etkisi ile ilgili literatürde çelişkiler mevcuttur. Çeşitli klinik deneylerde A vitamininin besin takviyesi olarak verilmesi çocuklarda ve hamile kadınlarda anemi ve demir durumu üzerinde olumlu bir etki göstermiştir (35-40). Ek olarak demir ve A vitamininin ikili takviyesinin, Hb konsantrasyonları ve demir durum indeksleri üzerinde, sadece demir veya sadece A vitamini takviyesinden daha büyük bir etkiye sahip olduğu gösterilmiştir. Bununla birlikte bazı çalışmalar A vitamininin tek başına veya demir ile kombinasyon halinde verildiğinde anemi üzerinde önemli bir etkisinin olmadığını rapor etmiştir (41-44).

Endonezyalı gebe kadınlar üzerinde yapılan bir çalışmada günlük 2,4 Retinol Eşdeğeri (RE) + 60 mg demir kombinasyonunun alımıyla Hb değerinde 1,5 g/dl'lik bir artış meydana geldiği; günlük 60 mg demir takviyesiyle Hb değerinde 1,0 g/dl'lik, günlük 2,4 RE takviyesiyle Hb değerinde 0,6 g/dl'lik ve plaseboyla ise Hb değerinde 0,2 g/dl'lik bir artış olduğu tespit edilmiştir (45). Takviyeden sonra artık anemik olmayan kadınların yüzdesinin 4 grupta

sırasıyla % 97, % 68, % 35 ve % 16 olduğu görülmüştür. Bu çalışma hamilelik sırasında tek başına A vitamini desteğinin Hb seviyelerini artırabildiğini ve anemi prevalansını azaltabildiğini, bunun yanında demir takviyesine ilaveten A vitamini verilmesinin ek bir koruyucu etki sağlayabildiğini öne sürmektedir (45). Benzer şekilde yapılan başka bir çalışmada, Batı Java'daki (Endonezya) hamile kadınlarda demir ve A vitamini düzeyini, demir ve A vitamini takviyesinin kombinasyon şeklinde verilmesinin demir ve A vitaminin tek başlarına takviye edilmesinden daha fazla geliştirdiği saptanmıştır (46).

Bunların yanı sıra başka bir araştırmada A vitamininin demir ve folik asitle kombinasyonunun Hb konsantrasyonları üzerinde etkileri araştırılmış ve Hb düzeylerinde düzelme olduğu gözlemlenmiştir (47). Yapılan bir başka çalışmada ise haftada bir A vitamini ve demir (ve folik asit) ile takviye edilen gebe kadınların Hb düzeylerinde, haftada bir demir veya günlük demir ile takviye edilen gebe kadınların Hb düzeylerine kıyasla daha büyük bir artış olduğu rapor edilmiştir. Demir ve A vitamini grubunda ferritinde bir azalma ve her 3 grupta sTfR'de bir artış gözlemlenmiştir. Bu veriler vücut depolarından ve artmış eritropoezden kaynaklanan artan muhtemel bir demir mobilizasyonu olduğunu öne sürmektedir (48). Muslimatun ve arkadaşları tarafından yapılan bir çalışmada, gebe kadınlarda A vitamini takviyesiyle gözlemlenen Hb konsantrasyonlarındaki düzelme lohusa dönemine kadar sürdürülememiştir (49). Zimbabve'de yapılan bir çalışmada ise emziren kadınlarda β-karotenden zengin besinlerin Hb üzerindeki etkisi araştırılmıştır. Kadınlar günlük olarak plasebo, 6 mg β-karoten kapsül, papaya püresi ve rendelenmiş havuç alanlar olarak 4 gruba ayrılmıştır. Karoten ve papaya gruplarında plasebo grubuna kıyasla Hb seviyeleri anlamlı olarak daha fazla artmıştır (50). Bu bulgular kadınların demir seviyelerini iyileştirmek için besine dayalı yaklaşımların önemini güçlendirmektedir.

A vitamininin tek başına hematolojik durumu iyileştirdiğinin rapor edildiği çalışmalardan biri olan Muhilal'in çalışmasında, 5 aydan fazla bir süre boyunca A vitamini ile monosodyum glutamatın (MSG) beraber verilmesi sonucunda Endonezya'daki okul öncesi çocuklar arasında Hb düzeyinin 1,0 g/dl arttığı saptanmıştır (51). Benzer şekilde yalnız A vitamini takviyesi Tanzanya'da ve Fas'ta Hb düzeyini iyileştirmiştir (23, 52).

Bunların dışında bazı başka çalışmalarda, A vitamininin Hb konsantrasyonları üzerinde ek bir anlamlı etkisi olmadığı gösterilmiştir. Semba ve arkadaşlarının yaptığı kontrollü bir klinik çalışmada, Malavi'de yüksek oranda anemi prevalansı olan gebeler arasında Hb veya EPO konsantrasyonlarında artış gözlemlenmemiştir (21). Benzer şekilde diğer bir çalışmada anemik olan gebe kadınlar günlük A vitamini takviyesi alan veya plasebo alan iki gruba randomize olarak dağıtılmıştır. Çalışma sonunda A vitamini takviyesinin anemi, ağır

anemi ve demir durumu üzerinde önemli bir etkiye sahip olmadığı tespit edilmiştir (53).

SONUÇ

Demir metabolizmasında A vitamininin rolüne ilişkin çalışmalar bu iki mikro besin arasındaki etkileşimin karmaşıklığını vurgulamaktadır. Bu tespite ek olarak tüm çalışmalar birlikte ele alındığında ise A vitamininin demir metabolizmasını dolayısıyla anemiyi olumlu yönde etkilediği söylenebilir. Bu nedenle, A vitamini besin takviyelerinin kandaki demir yetersizliği ve anemi gibi sorunların önlenmesi ve akut problemlerin giderilmesi adına potansiyel bir çözüm yöntemi olabileceği düşünülmektedir. Ancak sağlıklı ve kalıcı bir yol olarak bireylerin ve toplumların besin gereksinimleri A vitaminini de içerecek şekilde karşılamak adına kapsamlı ve dengeli bir beslenme yaklaşımı benimsenmelidir. Ayrıca A vitamini ve demir arasındaki karmaşık ilişkinin tam olarak anlaşılması için bu konuda daha fazla araştırma yapılması yararlı olacaktır.

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Kaynaklar

1. Biswas A, Tripathy I, Basu K. Effects on hematopoiesis in children suffering from iron deficiency anemia with vitamin A supplementation. Int J Med Res Prof. 2016;2(1):155-67.
2. Biswas A. Role of vitamin A supplementation in management of iron deficiency anemia in children. Int J Community Med Public Health. 2018;5(4):1477-80.
3. Villalpando S, Cruz Vde L, Shamah-Levy T, Rebollar R, Contreras-Manzano A. Nutritional status of iron, vitamin B12, folate, retinol and anemia in children 1 to 11 years old: results of the ensanut 2012. Salud Publica Mex. 2015;57(5):372-84.
4. Bondevik G, Eskeland B, Ulvik R, Ulstein M, Lie R, Schneede J, et al. Anaemia in pregnancy: possible causes and risk factors in Nepali women. Eur J Clin Nutr. 2000;54(1):3.
5. Dreyfuss ML, Stoltzfus RJ, Shrestha JB, Pradhan EK, LeClerq SC, Khatry SK, et al. Hookworms, malaria and vitamin A deficiency contribute to anemia and iron deficiency among pregnant women in the plains of Nepal. J Nutr. 2000;130(10):2527-36.
6. Semba RD, Kumwenda N, Hoover D, Taha T, Mtimavalye L, Broadhead R, et al. Assessment of iron status using plasma transferrin receptor in pregnant women with and without human immunodeficiency virus infection in Malawi. Eur J Clin Nutr. 2000;54(12):872.
7. Albalak R, Ramakrishnan U, Stein AD, Van der Haar F, Haber MJ, Schroeder D, et al. Co-occurrence of nutrition problems in Honduran children. J Nutr. 2000;130(9):2271-3.
8. Hodges RE, Sauberlich H, Canham J, Wallace D, Rucker R, Mejia L, et al. Hematopoietic studies in vitamin A deficiency. Am J Clin Nutr. 1978;31(5):876-85.
9. Wieringa FT, Dijkhuizen MA, West CE, Thurnham DI, Van der Meer JW. Redistribution of vitamin A after iron supplementation in Indonesian infants. Am J Clin Nutr. 2003;77(3):651-7.
10. Hinderaker S, Olsen B, Lie R, Bergsjø P, Gasheka P, Bondevik G, et al. Anemia in pregnancy in rural Tanzania: associations with micronutrients status and infections. Eur J Clin Nutr. 2002;56(3):192.
11. Cunha MS, Siqueira EM, Trindade LS, Arruda SF. Vitamin A deficiency modulates iron metabolism via ineffective erythropoiesis. J Nutr Biochem. 2014;25(10):1035-44.
12. Gutowska K, Formanowicz D, Formanowicz P. Interrelations between iron and vitamin A-studied using systems approach. Int J Mol Sci. 2022;23(3):223-31.
13. Pagani A, Nai A, Silvestri L, Camaschella C. Hepcidin and anemia: a tight relationship. Front Physiol. 2019;10(2):494-9.

14. Mendes J, Frossard R, Siqueira E, Machado A, Brito e Silva J, Gabriel M, et al. Vitamin A deficiency modulates iron metabolism independent of hemojuvelin (Hfe2) and bone morphogenetic protein 6 (Bmp6) transcript levels. Genes Nutr. 2016;11(3):1-7.
15. Gernand AD, Xu X, West Jr KP. Vitamin A in nutritional anemia. In: Karakochuk CD, Zimmermann MB, Moretti D, K. Nutritional anemia. 2nd ed. Switzerland: Springer; 2022. 153-71 p.
16. Josefsen D, Blomhoff HK, Lømo J, Blystad AK, Smeland EB. Retinoic acid induces apoptosis of human CD34+ hematopoietic progenitor cells: involvement of retinoic acid receptors and retinoid X receptors depends on lineage commitment of the hematopoietic progenitor cells. Exp Hematol. 1999;27(4):642-53.
17. Kambe T, Tada-Kambe J, Kuge Y, Yamaguchi-Iwai Y, Nagao M, Sasaki R. Retinoic acid stimulates erythropoietin gene transcription in embryonal carcinoma cells through the direct repeat of a steroid/thyroid hormone receptor response element half-site in the hypoxia-response enhancer. Blood. 2000;96(9):3265-71.
18. Okano M, Masuda S, Narita H, Masushige S, Kato S, Imagawa S, et al. Retinoic acid up-regulates erythropoietin production in hepatoma cells and in vitamin A-depleted rats. FEBS Lett. 1994;349(2):229-33.
19. Neumcke I, Schneider B, Fandrey J, Pagel H. Effects of pro-and antioxidative compounds on renal production of erythropoietin. Endocr. 1999;140(2):641-5.
20. Jelkmann W, Pagel H, Hellwig T, Fandrey J. Effects of antioxidant vitamins on renal and hepatic erythropoietin production. Kidney Int. 1997;51(2):497-501.
21. Semba RD, Muhilal M, West Jr KP, Winget M, Natadisastra G, Scott A, et al. Impact of vitamin A supplementation on hematological indicators of iron metabolism and protein status in children. Nutr Res. 1992;12(4):469-78.
22. Cusick SE, Tielsch JM, Ramsan M, Jape JK, Sazawal S, Black RE, et al. Short-term effects of vitamin A and antimalarial treatment on erythropoiesis in severely anemic Zanzibari preschool children. Am J Clin Nutr. 2005;82(2):406-12.
23. Zimmermann MB, Biebinger R, Rohner F, Dib A, Zeder C, Hurrell RF, et al. Vitamin A supplementation in children with poor vitamin A and iron status increases erythropoietin and hemoglobin concentrations without changing total body iron. Am J Clin Nutr. 2006;84(3):580-6.
24. Cañete A, Cano E, Muñoz-Chápuli R, Carmona R. Role of vitamin A/retinoic acid in regulation of embryonic and adult hematopoiesis. Nutrients. 2017;9(2):159.
25. Thurnham DI. Vitamin A, iron and haemopoiesis. Lancet. 1993;342(8883):1312-3.
26. Mejia LA, Hodges RE, Rucker RB. Role of vitamin A in the absorption, retention and distribution of iron in the rat. J Nutr. 1979;109(1):129-37.
27. Mejia LA, Hodges RE, Rucker RB. Clinical signs of anemia in vitamin A-deficient rats. Am J Clin Nutr. 1979;32(7):1439-44.
28. Gardner R, Hodges R, Rucker R. Fate of erythrocyte iron in vitamin A deficient rats. Fed Proc. 1979;38(3):762-.
29. Roodenburg A, West C, Beguin Y, Van Dijk J, Van Eijk H, Marx J, et al. Indicators of erythrocyte formation and degradation in rats with either vitamin A or iron deficiency. J Nutr Biochem. 2000;11(4):223-30.
30. Sijtsma K, Van den Berg G, Lemmens A, West C, Beynen A. Iron status in rats fed on diets containing marginal amounts of vitamin A. Br J Nutr. 1993;70(3):777-85.
31. Roodenburg AC, West CE, Hovenierl R, Beynen AC. Supplemental vitamin A enhances the recovery from iron deficiency in rats with chronic vitamin A deficiency. Br J Nutr. 1996;75(4):623-36.
32. Strube YNJ, Beard JL, Ross AC. Iron deficiency and marginal vitamin A deficiency affect growth, hematological indices and the regulation of iron metabolism genes in rats. J Nutr. 2002;132(12):3607-15.
33. Jang J-T, Green JB, Beard JL, Green MH. Kinetic analysis shows that iron deficiency decreases liver vitamin A mobilization in rats. J Nutr. 2000;130(5):1291-6.
34. Rosales FJ, Jang J-T, Piñero DJ, Erikson KM, Beard JL, Ross AC. Iron deficiency in young rats alters the distribution of vitamin A between plasma and liver and between hepatic retinol and retinyl esters. J Nutr. 1999;129(6):1223-8.
35. Ma G, Chen Y, Liu X, Gao Y, Deavila JM, Zhu M-J, et al. Vitamin a supplementation during pregnancy in shaping child growth outcomes: a meta-analysis. Crit Rev Food Sci Nutr. 2023;63(33):122-5.
36. Brownell JN, Schall JI, Mcanlis CR, Smith-Whitley K, Norris CF, Stallings VA. Effect of high-dose vitamin A supplementation in children with sickle cell disease: a randomized, double-blind, dose-finding pilot study. J Pediatr Hematol Oncol. 2020;42(2):83-91.
37. Silva AP, Pereira AdS, Simões BFT, Omena J, Cople-Rodrigues CdS, de Castro IRR, et al. Association of vitamin A with anemia and serum hepcidin levels in children aged 6 to 59 month. Nutr. 2021;91(2):111-4.
38. Tan PY, Loganathan R, Teng K-T, Mohd Johari SN, Lee SC, Selvaduray KR, et al. Supplementation of red palm olein-enriched biscuits improves levels of provitamin A carotenes, iron, and erythropoiesis in vitamin A-deficient primary schoolchildren: a double-blinded randomised controlled trial. Eur J Nutr. 2024;63(3):905-18.

39. Aggarwal S, Verma A, Tiwari S, Kaushik S, Garg S, Kumar S. Assessment of vitamin A status in patients with iron deficiency anemia. MAMC J Med Sci. 2023;9(1):50-6.
40. Kumar R, Oruna-Concha MJ, Niranjan K, Vimaleswaran KS. A review on vitamin A deficiency and depleted immunity in South Asia: from deficiency to resilience. Nutr. 2024;8(3):112-25.
41. Khan JR, Karim ME. A propensity score analysis of the effect of a single dose vitamin A supplementation on child hemoglobin status in Bangladesh. Child Care Pract. 2023;29(2):166-80.
42. McCauley ME, van den Broek N, Dou L, Othman M. Vitamin A supplementation during pregnancy for maternal and newborn outcomes. Cochrane Database Syst Rev. 2015;23(10):314-22.
43. Rai RK. Estimated effect of vitamin A supplementation on anaemia and anthropometric failure of Indian children. Pediatr Res. 2022;91(5):1263-71.
44. Ribaudo I, Aramburú-Duclos CB, Blitchtein D. Is vitamin A supplementation associated with anemia in children under 5 years of age in peru: secondary analysis of the "demographic health survey" 2015-2018? Glob Pediatr Health. 2021;8(1):233-7.
45. Suharno D, Karyadi D, West C, Hautvast JG. Supplementation with vitamin A and iron for nutritional anaemia in pregnant women in West Java, Indonesia. Lancet. 1993;34(8):132-8.
46. Tanumihardjo SA. Vitamin A and iron status are improved by vitamin A and iron supplementation in pregnant Indonesian women. J Nutr. 2002;132(7):1909-12.
47. Chawla P, Puri R. Impact of nutritional supplements on hematological profile of pregnant women. Indian Pediatr. 1995;32(7):876-80.
48. Muslimatun S, Schmidt MK, Schultink W, West CE, Hautvast JG, Gross R. Weekly supplementation with iron and vitamin A during pregnancy increases hemoglobin concentration but decreases serum ferritin concentration in Indonesian pregnant women. J Nutr. 2001;131(1):85-90.
49. Muslimatun S, Schmidt MK, West CE, Schultink W, Hautvast JG, Karyadi D. Weekly vitamin A and iron supplementation during pregnancy increases vitamin A concentration of breast milk but not iron status in Indonesian lactating women. J Nutr. 2001;131(10):2664-9.
50. Ncube T, Malaba L, Greiner T, Gebre-Medhin M. Evidence of grave vitamin A deficiency among lactating women in the semi-arid rural area of Makhaza in Zimbabwe. A population-based study. Eur J Clin Nutr. 2001;55(4):229.
51. Muhilal, Permeisih D, Idjradinata YR, Muherdiyantiningsih, Karyadi D. Vitamin A-fortified monosodium glutamate and health, growth, and survival of children: a controlled field trial. Am J Clin Nutr. 1988;48(5):1271-6.
52. Mwanri L, Worsley A, Ryan P, Masika J. Supplemental vitamin A improves anemia and growth in anemic school children in Tanzania. J Nutr. 2000;130(11):2691-6.
53. Van Den Broek N, White S, Flowers C, Cook J, Letsky E, Tanumihardjo S, et al. Maternal medicine: Randomised trial of vitamin A supplementation in pregnant women in rural Malawi found to be anaemic on screening by HemoCue. BJOG. 2006;113(5):569-76.

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REVIEW

Occupational Safety and Health Challenges Among Ageing Population in Asia

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ABSTRACT

The ageing workforce in Asia presents significant occupational safety and health (OSH) challenges, necessitating a comprehensive understanding of the risks, interventions, and policy responses. As demographic shifts lead to an increasing number of older workers remaining in employment, age-related physical, psychological, and social factors impact their workplace safety and well-being. This systematic review explores the primary OSH challenges faced by ageing workers across various industries in Asia, including physical vulnerabilities, cognitive decline, and socioeconomic constraints. Our systematic search of electronic databases yielded 19 relevant studies, which were analyzed to evaluate the extent of OSH risks and the effectiveness of workplace interventions. Findings indicate that musculoskeletal disorders, reduced adaptability to technological advancements, and social stigma related to ageing significantly affect older workers. The review highlights the need for age-sensitive workplace modifications, ergonomic interventions, mental health support, and inclusive OSH policies tailored to the needs of ageing workers. Successful initiatives in Japan and Singapore demonstrate the potential benefits of structured workplace adaptations and policy reforms. The study underscores the urgency of implementing targeted strategies to promote safer, healthier, and more productive work environments for older workers in Asia.

Keywords: Ageing, Asian Elderly, Asian Population, Occupational Safety and Health in Asia, Wellbeing

ÖZET

Asya'da yaşlanan işgücü, risklerin, müdahalelerin ve politika yanıtlarının kapsamlı bir şekilde anlaşılmasını gerektiren önemli iş sağlığı ve güvenliği (İSG) zorlukları ortaya koymaktadır. Demografik değişimler, istihdamda kalan yaşlı işçi sayısının artmasına yol açarken, yaşa bağlı fiziksel, psikolojik ve sosyal faktörler işyeri güvenliğini ve refahını etkilemektedir. Bu sistematik inceleme, Asya'daki çeşitli sektörlerde yaşlanan işçilerin karşılaştığı fiziksel hassasiyetler, bilişsel gerileme ve sosyo-ekonomik kısıtlamalar da dahil olmak üzere başlıca İSG zorluklarını araştırmaktadır. Çalışmamızda elektronik veri tabanlarından İSG risklerinin kapsamını ve işyeri müdahalelerinin etkinliğini değerlendirmek üzere 19 ilgili çalışma tespit edilerek analiz edilmiştir. Bulgular, kas-iskelet sistemi rahatsızlıklarının, teknolojik gelişmelere uyum sağlama kabiliyetinin azalmasının ve yaşlanmaya bağlı sosyal damgalanmanın yaşlı çalışanları önemli ölçüde etkilediğini göstermektedir. İnceleme, yaşa duyarlı işyeri modifikasyonları, ergonomik müdahaleler, ruh sağlığı desteği ve yaşlanan çalışanların ihtiyaçlarına göre uyarlanmış kapsayıcı İSG politikalarına duyulan ihtiyacı vurgulamaktadır. Japonya ve Singapur'daki başarılı girişimler, yapılandırılmış işyeri uyarlamalarının ve politika reformlarının potansiyel faydalarını göstermektedir. Çalışma, Asya'daki yaşlı çalışanlar için daha güvenli, daha sağlıklı ve daha üretken çalışma ortamlarını teşvik etmek için hedeflenen stratejilerin uygulanmasının aciliyetinin altını çizmektedir.

Anahtar kelimeler: Yaşlanma, Asyalı Yaşlılar, Asyalı Nüfus, Asya'da İş Sağlığı ve Güvenliği, Refah

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INTRODUCTION

The ageing population represents one of the most significant demographic shifts globally, and it presents unique challenges for occupational safety and health (OSH). According to the World Health Organization (WHO), the proportion of people aged 60 and older will nearly double by 2050, reaching about 2.1 billion (1). This shift has a profound impact on the workforce, as older workers are staying employed for longer periods, either out of choice or necessity. Consequently, addressing occupational safety and health issues specific to this demographic has become an urgent priority (2). Elderly workers face higher risk of sustaining injuries at work compared to their younger counterparts (3). Moreover, fatal workplace accidents are more prevalent among older workers, with rates rising with age (4).

OSH is a critical concern globally, as it seeks to protect workers from hazards and risks associated with their jobs. As the global population ages, a growing segment of the workforce now comprises elderly individuals, the definition of "older adult" varies, depending on different perspectives and purposes, but generally includes individuals aged 60 and above, with subgroups such as "younger old" (ages 65-75), "older-old" (ages 75-85), and "oldest old" (ages 85+) (5).

As the world progresses towards more advanced industrial practices, the emerging challenges of Industry 4.0, characterized by increased automation and digitization, introduce new risks for older workers. Addressing these concerns requires the implementation of comprehensive and inclusive occupational safety policies, ergonomic workplace designs, and age-friendly interventions. By recognizing the occupational safety and health challenges facing the ageing population, organizations can foster a safer and healthier work environment that promotes active ageing, reduces injury rates, and maintains productivity among older workers (6).

In Asia, which has one of the most rapidly aging populations in the world, the issue is particularly pressing. It is reported that by 2030, the Asian continent would be the region with the largest elderly population in the world exceeding 4.9 billion, significantly impacting the workforce structure (7). Countries like Japan, South Korea, China, and Singapore are already experiencing the effects, as their older populations grow and the need for a sustainable workforce increases (8). Ensuring occupational safety and health for this age group is vital not only for their well-being but also for maintaining productivity and economic growth in the region (9).

Asia's demographic profile is diversifying as a result of the region's dual trends: while the number of elderly people is rising in several Asian nations, other Asian nations are seeing the opposite trend. This dynamic is pressing not just in the field of OSH, but also in the domain of health and safety at work, and it has a significant impact on the workforce (10).

People are more prone to have physical changes as they age, which makes it harder for them to complete tasks in a safe manner for the company. On the other hand, senior workers may have a larger probability of experiencing some health problems or injuries, which implies that it is also difficult to prevent their own OSH issues (11). As the number of older workers has increased and the need for age-friendly policies and environments has grown, the study of OSH issues among ageing workers is a recent field that has attracted a lot of attention (12). Although the field of OSH publishing is vibrant, the writers have not yet addressed any specific problems encountered by older Asian workers. The aim of this systematic review is to address the lack of research on relevant topics described above by examining the primary OSH challenges faced by older workers in various Asian sectors.

MATERIALS AND METHODS

To perform a robust systematic review, a well-planned search strategy is employed that will involve searching through various databases in order to pinpoint the vital literature. We use electronic databases like PubMed, Scopus, Science Direct, and Emerald to conduct a systemic search of the literature using a combination of keywords search as well as Medical Subject Headings (MeSH) terms related to occupational safety and health, an ageing workforce, and Asian countries. Apart from that, published articles relevant to the review are searched manually in association with reference lists of included studies so that potential studies that might have been missed in the electronic database search are not turned away.

Studies are included in the review if they meet the following criteria: 1) A thematic issue on occupational safety and health of the ageing workers in Asia is chosen for the project, 2) different quantitative, qualitative, or mixed-methods design are employed for the project, and 3) project material is provided in English. Studies which do not meet the above-mentioned criteria, such as those limiting themselves to non-Asian populations or particular topics are not considered. Moreover, there will be no limitation on the publication date as the aim is for an up-to-date summary of the existing issues.

The reviewer will conduct the data abstraction consisting of information retrieval from the included studies into a standardized form. Formed data will be study characteristics, sampling design specifications and research objectives including the methods used: author(s), publication year, study design (such as randomized controlled trial, quasi-experimental design, case studies), participant

characteristics, main barrier to OSH associated with occupation and norms, culture and socio-demographic determinants. If a disagreement arises in the data extraction process, the two reviewers will settle it by discussion and achieving agreement among them.

The quality of studies will be the methodologic one, particularly using the tools necessary for the type of study. In terms of the JBI critical appraisal tools that is used for the quantitative section, the JBI Critical Appraisal Checklist for Analytical Cross-Sectional Studies or any other applicable JBI appraisal checklist is employed. Qualitative studies shall be assessed by employing the JBI Critical Appraisal Checklist, which is designated for Qualitative Research. Mixed-methods studies will be evaluated by using the MMAT suggested by the Mixed Methods Appraisal Tool. Studies are grouped according to their methodological quality, and the findings of the lower-grade studies will be interpreted more cautiously while taking into account during the synthesis of results.

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines are applied as they are used to ensure that the systematic review and meta-analysis process is systematic and has high reporting quality. The PRISMA flow diagram will be utilized in visualizing the selection process and the PRISMA checklist will be used to the purpose of the application of reporting guidelines.

Research Questions

RQ1: What are the main occupational safety and health challenges experienced by ageing workers in various industries across Asia?

RQ2: How do cultural and socioeconomic factors influence the occupational safety and health experiences of ageing workers in Asian countries?

RQ3: What evidence exists regarding the effectiveness of interventions aimed at improving occupational safety and health outcomes for ageing workers in Asia?

Search Strategy

The search strategy is designed to encompass a wide range of databases and sources to ensure the inclusivity and comprehensiveness of the review. Electronic databases such as PubMed, Scopus, Science Direct and Emerald will be systematically searched using a combination of keywords and Medical Subject Headings (MeSH) terms related to occupational safety and health, ageing workers, and Asian countries. The search terms are tailored to the specific requirements and syntax of each database, and Boolean operators (AND, OR) will be used to combine search terms effectively. Additionally, the reference lists of included studies and relevant review articles are manually searched to identify any additional studies that may have been missed in the electronic database search.

Study Selection Criteria

Studies will be selected for inclusion in the review based on predefined criteria designed to ensure relevance and methodological rigor. The following inclusion criteria will be applied:

- Focus on occupational safety and health challenges among ageing workers in Asian countries.
- Employ quantitative, qualitative, or mixed-methods research designs.
- Written in English.

Studies that meet these criteria will be included in the review, while those that do not will be excluded. Exclusion criteria may include studies focusing solely on non-Asian populations, unrelated topics, or those with insufficient methodological rigor. This review included only peer-reviewed journal articles and conference proceedings. Grey literature, such as government reports, dissertations, and preprints, was excluded to ensure methodological rigor and consistency in the quality of the selected studies. No restrictions will be placed on publication date to ensure a comprehensive synthesis of the available evidence. Any discrepancies in study selection will be resolved through discussion and consensus between the reviewers.

RESULTS

The included studies varied in methodology, geographical coverage, and focus areas within OSH challenges among ageing workers in Asia. A summary of study characteristics is provided in Table 1. Study Designs: The review included meta-analyses (n=2), literature reviews (n=3), scoping reviews (n=2), case studies (n=3), cross-sectional studies (n=4), mixed-methods research (n=3), and intervention studies (n=2). Geographical Scope: The majority of studies focused on East Asia (e.g., Japan, China, South Korea), followed by Southeast Asia (e.g., Singapore, Thailand, Malaysia, Vietnam) and South Asia (e.g., India, Bangladesh). Occupational Sectors: Studies primarily examined OSH challenges in manufacturing, construction, healthcare, transportation, and service industries.

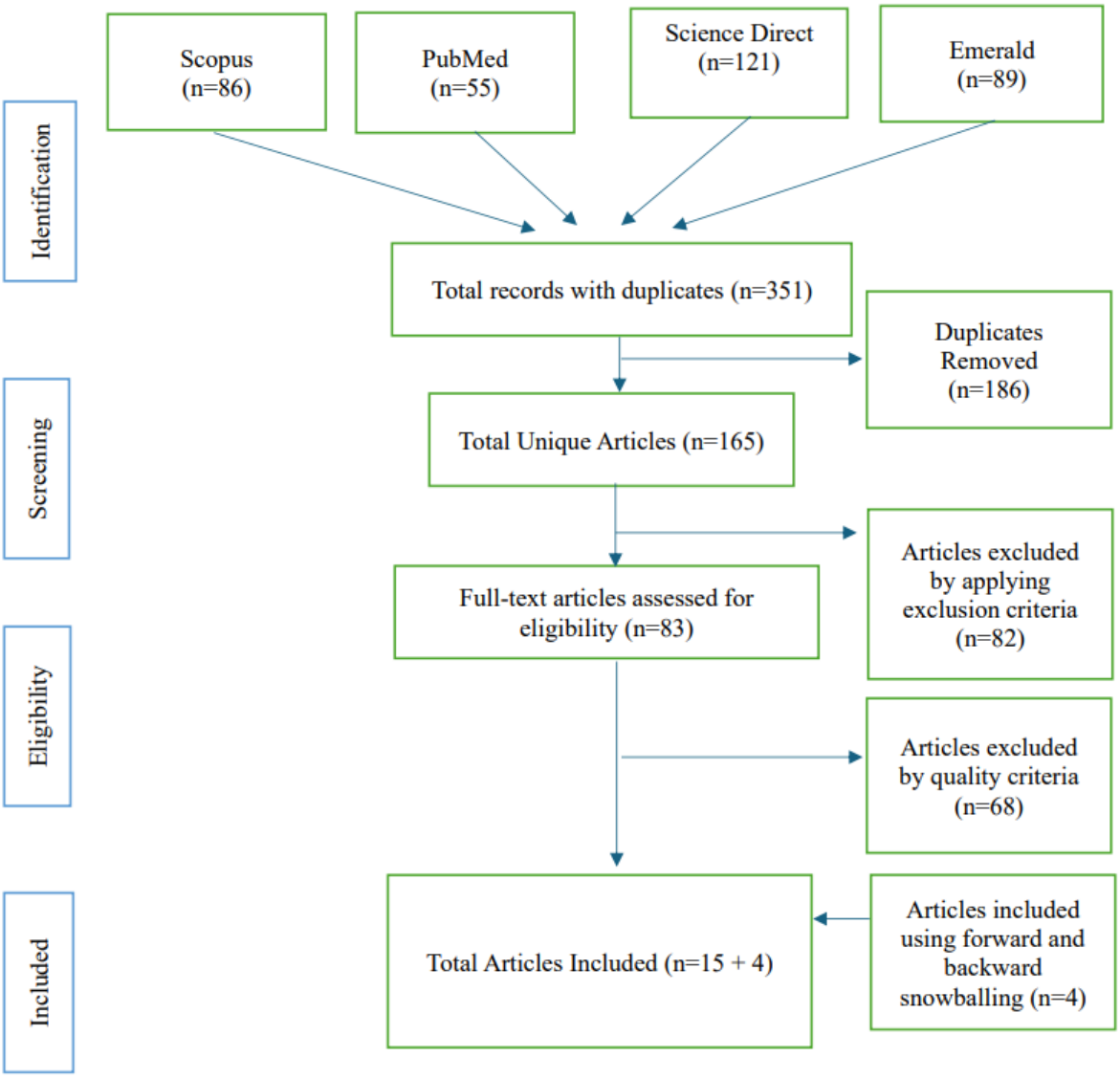

Figure 1. Article selection flowchart for the systematic literature review

Table 1. Review Article Summary

Author Name	Year	Title of Study	Study Design	Sample Size	Main Outcome
Peng L. & Chan A.H.	2019	A meta-analysis of the relationship between ageing and occupational safety and health	Meta-analysis	Multiple	Older workers face higher risks of injuries and health declines.
Chand M.	2018	Ageing in South Asia: challenges and opportunities	Literature review	Not specified	Identified socioeconomic and health challenges for aging workers in South Asia.
Romli M.H. et al.	2017	Falls amongst older people in Southeast Asia: a scoping review	Scoping review	Multiple	High prevalence of falls linked to physical decline in older workers.
Phillips D.R. et al.	2010	Ageing in a global context: The Asia-Pacific region	Comparative analysis	Not specified	Highlighted regional disparities in OSH policies for aging populations.
Anantanasuwong D.	2021	Population ageing in Thailand: critical issues in the twenty-first century	Case study	Not specified	Emphasized workplace adaptability gaps for older Thai workers.
Varianou-Mikellidou C.et al.	2019	Occupational health and safety management in the context of an ageing workforce	Mixed-methods	500+	Age-related vulnerabilities require tailored safety protocols.
Tiraphat S. et al.	2020	Age-friendly environments in ASEAN plus three: Case studies	Multi-country case study	5 countries	Cultural and environmental factors impact OSH outcomes.
Lim W.S. et al.	2020	COVID-19 and older people in Asia	Cross-sectional	1,200	Pandemic exacerbated mental and physical health risks for older workers.
Papadopoulou S.K.	2020	Sarcopenia: a contemporary health problem among older adult populations	Review	Not specified	Muscle loss increases injury risks in physically demanding jobs.
Cheng S.Y. et al.	2020	Advance care planning in Asian culture	Qualitative	150	Cultural norms influence retirement and healthcare decisions.

Seck P.A. et al.	2021	Gendered impacts of COVID-19 in Asia and the Pacific	Quantitative	2,000+	Highlighted gender disparities in work- related stress among older adults.
Rudnicka E. et al.	2020	The WHO approach to healthy ageing	Policy review	Not specified	Stressed holistic policies for aging workers' health.
Zhao D.	2021	Epidemiological features of cardiovascular disease in Asia	Epidemiolo-gical study	Not specified	Cardiovascular issues prevalent in aging workers with hazardous exposures.
Mao J.J. et al.	2022	Integrative oncology: Addressing global challenges of cancer prevention	Review	Not specified	Occupational carcinogen exposure risks for older workers.
Sepúlveda- Loyola W. et al.	2020	Impact of social isolation due to COVID-19 on health in older people	Mixed-methods	800	Social isolation worsened mental health outcomes.
Schwatka N.V. et al.	2012	An Aging Workforce and Injury in the Construction Industry	Longitudinal	5,000+	Older construction workers face higher injury rates.
Bravo G. et al.	2022	Do older workers suffer more workplace injuries?	Systematic review	Multiple	Confirmed higher injury rates and chronic conditions among older workers.
Kenji Kushida	2024	Japan's Aging Society as a Technological Opportunity	Literature Review & Case Study Analysis	Not specified	Japan's aging population presents challenges but also technological opportunities, particularly in automation and workforce augmentation.
Chng J & Sim BK	2018	Healthier Workers, Happier Workers' Programme: A Person-Centric Approach to Health & Safety at the Workplace for Bus-Drivers in Singapore	Intervention Study	2114	Improved chronic condition management and ergonomic training led to better health outcomes for bus drivers.

The results of the review were categorized into three main themes: physical, psychological, and social challenges. In terms of physical challenges, several studies indicated that ageing workers experience a decline in muscle strength, flexibility, and endurance, making them more vulnerable to workplace injuries. Musculoskeletal disorders such as osteoarthritis and osteoporosis were commonly reported, especially among those in physically demanding industries like construction and manufacturing. Studies also highlighted that falls, slips, and trips were more frequent among ageing workers due to reduced balance, coordination, and sensory acuity. Some interventions, such as ergonomic workplace adjustments, adjustable workstations, and exoskeletons, were found to effectively reduce strain and injury risks.

Psychological challenges were another significant concern. Cognitive decline, particularly in processing speed and memory, was reported as a barrier to adapting to new technologies and automated systems. Older workers also reported higher levels of job stress and anxiety, often stemming from job insecurity, rapidly changing work environments, and age discrimination. Some studies found that workplace training programs tailored to older workers improved their confidence and adaptability to new systems and processes, thus mitigating some of these psychological stressors.

Social challenges were also prominent, particularly in the context of cultural norms and family responsibilities, which significantly influenced work participation. In many Asian countries, traditional values such as filial piety and intergenerational support play a crucial role in older workers' decisions to remain employed. Many ageing workers in lower-income groups continued working out of financial necessity, increasing their exposure to workplace hazards. Age discrimination in the workplace was noted in several industries, negatively impacting job satisfaction and overall well-being. However, supportive work environments, including mentorship programs and intergenerational collaboration, were highlighted as effective strategies to promote inclusivity and ensure older workers feel valued.

The review highlights that ageing workers in Asia face complex OSH challenges that require targeted interventions, including ergonomic adjustments, mental health support, and age-friendly policies. Some countries, such as Japan and Singapore, have successfully implemented workplace interventions, policy reforms, and training programs to mitigate these risks. The findings emphasize the need for comprehensive workplace modifications, adaptive training, and stronger regulatory policies to enhance occupational safety and health outcomes for the ageing workforce in Asia. By adopting these strategies, organizations can create safer and more inclusive environments that support the continued participation of older workers in the labor force.

OCCUPATIONAL SAFETY AND HEALTH CHALLENGES OVERVIEW

The assessment of OSH problems in ageing workforce in Asia calls for a detailed consideration of factors related to the different aspects of this group which could be subdivided into physical, psychological, and social domains. Ageing workers merely encounter several challenges that can either be categorized under body changes, job stressors, or broad environmental factors that require an understanding of all these factors simultaneously to fully appreciate the elderlies at work.

Physical Challenges

Indication of an ageing process begins with a range of bodily fluctuations like reducing muscle strength, flexibility, sensory accurateness from which aged workers are prone to excessive injury risk and reduced functional capacities while on work. Musculoskeletal disorders of ageing workers with joint pain such as osteoarthritis and osteoporosis where ergonomic hazards are persistent and physically demanding job activities is an issue of concern. Also, the loss of balance and coordination is the thing that stands the way of the falling, slipping and tripping by the person and the control of their frequent falls. There ought to be target interventions of this kind.

Psychological Challenges

Older workers could face such a number of psychological pressure sources that might emerge from the inner complexities of the working environment, ambiguity about the job, and eventually the general public opinion towards ageing. Ageing adults themselves can become the target of age discrimination and stigma, and the by-product is their feelings of marginalization and decreased self-esteem, generating stress in the workplace and hamper its engagement. Nevertheless, the cognitive age-related changes, which are the declinations of the processing speed and memory, can create problems in the field of a rapidly growing work environment, so it is necessary to provide supportive measures to encourage cognitive health and the performers.

Social Challenges

The perception of occupational health and safety among ageing workers is significantly influenced by social demographic characteristics. Their views are impacted by societal norms, gender concerns, and family responsibilities, among other things. Filial piety and familial responsibilities are highly valued in many traditional Asian cultures, and these programs have a significant influence on work participation and retirement decisions, particularly when older workers may be compelled to continue working in order to support their families.

REVIEW REPORTS

Physical Health Challenges

Ageing workers in Asia face significant challenges related to physical health, which can impact their occupational

safety and well-being (13). Studies suggest that older workers experience a decline in physical abilities, including reduced strength, flexibility, and endurance (14). This decline makes them more susceptible to workplace injuries, particularly in physically demanding industries such as construction (15). Additionally, musculoskeletal disorders, hearing loss, and respiratory issues are prevalent among ageing workers, posing significant health concerns and affecting their ability to perform job tasks effectively (16).

Work Ability and Adaptability

Age-related changes can affect an individual's ability to adapt to new work environments or technologies, impacting their performance and safety on the job (17). Studies indicate that declining cognitive function and adaptability may hinder older workers' ability to cope with changing job demands and may lead to reduced productivity (18). As a result, interventions aimed at enhancing work ability and adaptability among ageing workers are crucial for maintaining their occupational health and well-being.

Increase Vulnerabality

Older workers in Asia are more vulnerable to chronic health conditions due to prolonged exposure to occupational hazards (2). Research suggests that in industries such as construction, where exposure to dust and harmful substances is common, older workers face a higher risk of developing conditions like chronic obstructive pulmonary disease (COPD) (19). This increased vulnerability underscores the importance of implementing targeted interventions and workplace accommodations to mitigate health risks and support the safety and well-being of ageing workers.

Mental Health Challenges

The mental well-being of ageing workers in Asia is a critical yet often overlooked aspect of occupational safety and health. Studies suggest that older workers may face unique mental health challenges related to job stress, insecurity, and work-related pressures (20). The transition to retirement may also evoke existential uncertainties and identity shifts, further impacting their psychological well-being (21). Implementing mental health intervention programs, such as individual support initiatives and health promotion activities, can play a pivotal role in addressing these challenges and fostering resilience among ageing workers (22).

Age Sensitive Work Environment

Creating age-sensitive work environments is paramount to ensuring the safety, health, and well-being of ageing workers in Asia (23). Studies indicate that adjusting work conditions, providing ergonomic support, and offering alternative work arrangements can help older workers maintain their productivity and work ability (24). Moreover, fostering a culture of inclusivity and respect in the workplace is essential for promoting age diversity and mitigating age-related stereotypes and discrimination (25). By prioritizing age-sensitive practices and accommodations,

organizations can create supportive environments that enable ageing workers to thrive and contribute effectively.

Policy And Program Development

Addressing occupational safety and health challenges among ageing workers in Asia necessitates concerted efforts in policy development and program implementation (26). Studies suggest that age-friendly policies, training programs, and collaborative initiatives are essential for promoting a culture of safety and well-being in the workplace (27). Policy interventions may include measures to enhance ergonomic standards, provide training on age-related health and safety issues, and establish support networks for ageing workers (28). Additionally, fostering partnerships between employers, policymakers, and healthcare providers is crucial for creating a supportive ecosystem that prioritizes the needs of ageing workers and ensures their continued engagement and contribution to the workforce (29). By embracing proactive policy and programmatic approaches, stakeholders can address the evolving needs of ageing workers and foster sustainable, age-inclusive workplaces across Asia.

Japan has proactively addressed the challenges of its rapidly ageing workforce through amendments to the Industrial Safety and Health Act, mandating employers to implement ergonomic adjustments and health monitoring for older employees. For instance, Toyota introduced exoskeletons to reduce physical strain during assembly tasks, adjustable workstations to accommodate mobility limitations, and flexible shift schedules to align with older workers' energy levels. The company also launched annual health check-ups focused on chronic conditions like hypertension and arthritis, coupled with tailored exercise programs. These measures contributed to a 30% reduction in musculoskeletal injuries among workers aged 50+ between 2018 and 2022. Nationally, Japan's occupational injury rate for workers over 60 fell by 15% from 2015 to 2020, reflecting systemic efforts to adapt workplaces to demographic shifts (30).

In Singapore, successful occupational health and safety (OHS) policies for older workers have been exemplified through a comprehensive health intervention program targeting bus drivers, a significant demographic of the aging workforce. The policy focused on a person-centric approach, understanding and addressing the unique needs of older drivers by implementing a nine-month onsite Health Intervention Programme, which included chronic disease health screenings and monthly group health coaching. Following this initiative, results indicated that approximately 50% of participants with abnormal screening outcomes showed improvement in at least one chronic condition after the program, with 25% improving from abnormal to normal health status within nine months. Additionally, workplace risk assessments conducted during the program led to the implementation of short-term interventions, such as driving ergonomics training and feedback protocols on

health and safety issues, ultimately fostering a safer and healthier work environment for older bus drivers in Singapore (31).

DISCUSSION

Challenges and Future Research Direction

The thorough analysis has uncovered the exceedingly intricate issue of aging workers in Asia, characterized by numerous challenges related to physical health, mental health, adaptability, and environmental elements. We must persist in enhancing our progress, which requires concerted efforts from several domains. Subsequent research initiatives ought to concentrate on numerous crucial domains. Initially, it is essential to conduct longitudinal studies that will significantly elucidate the sequential problems of occupational safety and health among aging workers, while simultaneously identifying critical junctures where treatments can be most effectively implemented. Long-term monitoring of OSH results may facilitate the early detection of signals to anticipate hazard preventive efforts aimed at mitigation.

A comprehensive study should examine the interconnections among aging, gender, and class to ascertain how various identities, considered over the lifespan, influence the distinct occupational safety and health experiences of workers nearing retirement age. Interventions that specifically address the circumstances of disadvantaged segments of the aging labor force can be identified through an intersectional approach. Furthermore, conclusive research on the effects of age-friendly policies, workplace adjustments, and psychological intervention programs addressing the rising occupational safety and health issues among aging workers is a paramount concern. The combination of findings and resilience will provide proof of a desirable trait for the mainstream. Conversely, the research should vary the emphasis on technological methods in occupational safety and health for the aging workforce, encompassing assistive technology, wearable devices, and computer displays tailored to older individuals, with the objective of enhancing workplace safety.

Limitation of Study

This study, while yielding positive results, possesses significant limitations that elucidate the accuracy of the findings. One key limitation is the exclusion of non-English literature, which may have introduced publication bias. The reliance solely on English-language sources could have resulted in the omission of relevant studies published in other languages, potentially leading to an incomplete representation of existing research. Additionally, papers may have been eliminated without clear justification solely due to the foreign language of publication, further restricting the comprehensiveness of the review. The other aspect of the issue is that the quality of research study methodologies varied, with many exhibiting methodological flaws or biases that predisposed them to distorted outcomes.

CONCLUSION

In conclusion, this comprehensive analysis provides an integrated overview of the most significant digital OSH concerns that are currently being faced by workers in Asia who are getting older. By incorporating a wide range of case studies, theoretical models, and policies, the review has been able to shed light on the heterogeneity of occupational safety and health challenges that are encountered by an ageing labor force. These issues include issues pertaining to physical and mental health, adaptability, and diversity among workers and the working environment. For the purpose of explicitly tailoring interventions and initiatives to the specific demands and issues of the ageing workforce in Asian countries, the results highlight the need of bringing pressed activities and policies in the area of productivity to the forefront. A considerable number of age-sensitive procedures, work settings that are accommodating to people from various walks of life, and the implementation of treatments that are supported by evidence are all ways in which the stakeholders may contribute to the development of surroundings that are conducive to the safety and health of this particular group.

It is necessary to conduct a number of studies in the future in order to investigate whether the occupational safety and health issues are becoming more severe or, on the other hand, whether the number of cases of occupational diseases is decreasing. Additionally, it is necessary to clarify the possible interaction of age with gender or socioeconomic status, as well as to establish some of the contemporary practices that are based on evidence or to create some of the new ones using modern technologies. In spite of the fact that language restrictions and bias in the publication of literature may have the effect of limiting the implications of this review, the consolidated knowledge that was gathered can still be a valuable resource for policymakers, practitioners, and researchers who are contemplating new strategies to deal with an ageing workforce in Asia. By adhering to proactive and joined-up tactics, stakeholders might develop a working environment that would be sustainable and inclusive regardless of age as well. Additionally, workers who are getting older would be able to participate in the workforce and community, sharing their experiences with others. To effectively address the challenges faced by an ageing workforce, policymakers should consider implementing specific strategies, including ergonomic adjustments to workstations, flexible work arrangements such as remote work or reduced hours, and mental health support programs tailored to older employees. Additionally, targeted training programs can help older workers adapt to new digital technologies, while age-friendly workplace policies can promote intergenerational collaboration and knowledge transfer. By integrating these measures, organizations can create a safer, healthier, and more productive work

environment for ageing workers while ensuring long-term sustainability and workforce participation.

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References

1. Noto S. Perspectives on Aging and Quality of Life. Healthcare. 2023;26;11(15):2131.
2. Varianou-Mikellidou, C, Boustras G, Dimopoulos C, Wybo JL, Guldenmund FW, Nicolaidou O, et al. Occupational health and safety management in the context of an ageing workforce. Safety science. 2019;116, 231-244.
3. Schwatka NV, Butler LM, Rosecrance JR. An Aging Workforce and Injury in the Construction Industry. Epidemiologic Reviews. 2012;1;34(1):156–67.
4. Bravo G, Viviani C, Lavallière M, Arezes P, Martínez M, Dianat I, et al. Do older workers suffer more workplace injuries? A systematic review. International Journal of Occupational Safety and Ergonomics. 2022;28(1):398–427.
5. Anurag Upadhyay RS. Mental Health of Elderly People. Journal of Psychosocial Research. 2024;19(1):61– 70.
6. Adem A, Çakit E, Dağdeviren M. Occupational health and safety risk assessment in the domain of Industry 4.0. Springer Nature Applied Sciences. 2020;1;2(5).
7. Jayawardhana T, Anuththara S, Nimnadi T, Karadanaarachchi R, Jayathilaka R, Galappaththi K. Asian ageing: The relationship between the elderly population and economic growth in the Asian context. PLoS One Journal. 2023;24;18(4):e0284895.
8. Chand M, Tung RL. The Aging of the World's Population and Its Effects on Global Business. Academy of Management Perspectives. 2014;28(4):409–29.
9. Rogers B, Marshall J, Garth K, Mopkins D, Remington J, Siemering K, et al. Focus on the Aging Worker. Official Journal of the American Association of Occupational Health Nurses. 2011;59(10):447–57.
10. Wei Y, Wang Z, Wang H, Li Y, Jiang Z. Predicting population age structures of China, India, and Vietnam by 2030 based on compositional data. PLoS One Journal. 2019;14(4).
11. Peng L, Chan AHS. A meta-analysis of the relationship between ageing and occupational safety and health. Safety Science. 2019;112:162–72.
12. G JW. Advancing safe and healthy work for all ages. Industrial Health. 2020;58(2):89–90.
13. Peng L, & Chan AH. A meta-analysis of the relationship between ageing and occupational safety and health. Safety Science. 2019;112, 162-172.
14. Chand M. Ageing in South Asia: challenges and opportunities. South Asian Journal of Business Studies. 2018;7(2), 189-206.
15. Romli MH, Tan MP, Mackenzie L, Lovarini M, Suttanon P, Clemson L. Falls amongst older people in Southeast Asia: a scoping review. Royal Society for Public health. 2017;145, 96-112.
16. Phillips DR, Chan AC, Cheng ST. Ageing in a global context: The Asia-Pacific region. The handbook of gerontology. 2010;430-446.
17. Anantanasuwong D. Population ageing in Thailand: critical issues in the twenty-first century. Education for the Elderly in the Asia Pacific. 2021;31-56.
18. Phillips DR. Overview of health and ageing issues in the Asia-Pacific region. In Singapore's Ageing Population. Routledge, CRC Press. 2011;7-30
19. Tiraphat, S, Buntup D, Munisamy M, Nguyen TH, Yuasa M, Nyein Aung M, et al. Age-friendly environments in ASEAN plus three: Case studies from Japan, Malaysia, Myanmar, Vietnam, and Thailand. International journal of environmental research and public health. 2020;17(12), 4523.

20. Lim WS, Liang CK, Assantachai P, Auyeung TW, Kang L, Lee WJ, et al. COVID-19 and older people in Asia: Asian Working Group for Sarcopenia calls to action. Geriatrics & gerontology international. 2020; 20(6), 547-558.
21. Papadopoulou SK. Sarcopenia: a contemporary health problem among older adult populations. Nutrients. 2020;12(5), 1293.
22. Cheng SY, Lin CP, Chan HYL, Martina D, Mori M, Kim SH, et al. Advance care planning in Asian culture. Japanese Journal of Clinical Oncology. 2020;50(9), 976-989.
23. McCallum J. Australia's new aged: issues for young and old. Routledge. 2023; 55-59
24. Seck PA, Encarnacion JO, Tinonin C, Duerto-Valero S. Gendered impacts of COVID-19 in Asia and the Pacific: Early evidence on deepening socioeconomic inequalities in paid and unpaid work. Feminist Economics. 2021;27(1-2), 117-132.
25. Findling MG, Blendon RJ, Benson J, Koh HK. COVID-19 has driven racism and violence against Asian Americans: perspectives from 12 national polls. Health Affairs Forefront. 2023;13(1):3–8
26. Rudnicka E, Napierała, P, Podfigurna A, Męczekalski B, Smolarczyk R, Grymowicz M. The World Health Organization (WHO) approach to healthy ageing. An International Journal of Midlife Health and Beyond. 2020;139, 6-11.
27. Zhao D. Epidemiological features of cardiovascular disease in Asia. Journal of the American College of Cardiology. 2021; Asia, 1(1), 1-13.
28. Mao JJ, Pillai GG, Andrade CJ, Ligibel JA, Basu P, Cohen L, et al. Integrative oncology: Addressing the global challenges of cancer prevention and treatment. CA: A Cancer Journal for Clinicians. 2022;72(2), 144-164.
29. Sepúlveda-Loyola W, Rodríguez-Sánchez I, Pérez-Rodríguez P, Ganz F, Torralba R, Oliveira DV, et al. Impact of social isolation due to COVID-19 on health in older people: mental and physical effects and recommendations. The journal of nutrition, health and ageing. 2020; 24(9), 938-947.
30. Kushida, Kenji. 2024. Japan's Aging Society as a Technological Opportunity. Carnegie Endowment for International Peace. 2024; 20-26
31. Chng J, Sim BK. Healthier workers, happier workers' programme: A person-centric approach to approaching health & safety at the workplace for bus drivers in Singapore. Occupational and Environmental Medicine 2018;75(2):A516