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Journal article on the Internet

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]; 102. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Website

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 Jul 2002]. Available from: www.cancer-pain.org

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The Intensive Care Society of Australia and New Zealand. Mechanical ventilation strategy in ARDS: Guidelines. Int Care J Aust 1996;164:282-4.

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Original Article / Orijinal Araştırma

Effect of Surfactant Protein B and D Genes Polymorphisms on Frequency and Severity of Acute Bronchiolitis

Surfaktan Protein B ve D Gen Polimorfizmlerinin Akut Bronşiolitin Sıklık ve Şiddeti Üzerine Etkileri

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Abstract

Aim: Acute bronchiolitis (AB) is the most common cause of hospitalization in infants. Varying bronchiolitis presentations in patients with similar demographic characteristics suggest genetic causes of individual differences.

Material and Method: The study included 106 infants diagnosed with AB and 107 healthy infants recruited from a pediatric outpatient clinic. Genotyping was conducted for intron 4 and C/A–18 in the SP-B gene, along with SP-D/160 (Ala160Thr) and SP-D/270 (Ser270Thr) polymorphisms in the SP-D gene.

Results: The SP-B intron 4 invariant polymorphisms of ins/ins and ins/del were 93.40% and 4.72% in the AB group and 84.11% and 15.89% in the control group, respectively (p=0.012). Frequency of polymorphism in the SP-D/270 (Ser270Thr) gene for Ser/Ser and Ser/Thr was 60% and 39.05% in the AB group and 79.44% and 18.69% in the control group, respectively (p=0.004). The frequencies of Ser and Thr alleles were 79.90% and 20.10% in the AB group and 88.79% and 11.21% in the control group, respectively (p=0.012). There was no observed correlation between the SP-B intron 4 and C/A-1, as well as the SP-D Ser270Thr and Ala160Thr polymorphisms, with the severity of AB (p>0.05).

Conclusion: SP-B gene polymorphisms were identified as risk factors for AB, while SP-D polymorphisms appeared to play a protective role. However, these polymorphisms were not linked to AB severity. Early identification of children at risk could enable close monitoring and preventive care.

Keywords: Acute bronchiolitis, surfactant protein, polymorphism, respiratory disease, infant

Öz

Amaç: Akut bronşiolit (AB), infantlarda en yaygın hastaneye yatış nedenidir. Benzer demografik özelliklere sahip hastalar arasında bronşiolitin farklı şekilde seyretmesi, bireysel farklılıklarda genetik faktörlerin rol oynayabileceğini düşündürmektedir.

Gereç ve Yöntem: Çalışmaya bir çocuk polikliniğinden alınan, AB tanısı almış 106 bebek ve sağlıklı 107 bebek dahil edilmiştir. SP-B genindeki intron 4 ve C/A–18, ayrıca SP-D genindeki SP-D/160 (Ala160Thr) ve SP-D/270 (Ser270Thr) polimorfizmleri için genotipleme yapılmıştır.

Bulgular: SP-B intron 4 sabit polimorfizmleri olan ins/ins ve ins/del oranları, AB grubunda sırasıyla %93,40 ve %4,72, kontrol grubunda ise %84,11 ve %15,89 olarak bulunmuştur (p=0,012). SP-D/270 (Ser270Thr) genindeki Ser/Ser ve Ser/Thr polimorfizmleri AB grubunda %60 ve %39,05, kontrol grubunda ise %79,44 ve %18,69 oranında tespit edilmiştir (p=0,004). Ser ve Thr allel frekansları AB grubunda sırasıyla %79,90 ve %20,10, kontrol grubunda ise %88,79 ve %11,21 olarak belirlenmiştir (p=0,012). SP-B intron 4, C/A–18 ile SP-D Ser270Thr ve Ala160Thr polimorfizmleri ile AB'nin şiddeti arasında herhangi bir ilişki bulunmamıştır

(p>0,05).

Sonuç: SP-B gen polimorfizmleri, AB için bir risk faktörü olarak belirlenirken, SP-D polimorfizmleri koruyucu bir rol oynamaktadır. Bununla birlikte, bu polimorfizmler AB'nin şiddeti ile ilişkili bulunmamıştır. Risk altındaki çocukların önceden tespit edilmesi ve yakından izlenmesi AB morbiditesi açısından önemli olabilir.

Anahtar Kelimeler: Akut bronşiolit, surfaktan protein, polimorfizm, solunum yolları

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INTRODUCTION

Acute bronchiolitis (AB) is characterized by bronchial obstruction with inflammation, edema, mucus, and cellular debris. AB is predominantly a viral disease. Respiratory syncytial virus (RSV) is responsible for >50% of cases.[1] The severity of AB is associated with the degree of immune response.[2] Research on genetic susceptibility in patients with lower respiratory tract (LRT) RSV infections has highlighted heterozygous surfactant protein (SP)-B-knockout mice exhibit decreased lung compliance and increased susceptibility to pulmonary infections and oxidative stress.[3-5]

Pulmonary surfactant is a mixture of phospholipids and proteins synthesized, packaged, and secreted by alveolar type II cells, which lower surface tension and prevent atelectasis at end-expiration.[6,7] Surfactants contain 80% lipids, 12% protein, and 8% neutral fats. They also contain serum proteins and SPs.[8] SP-B, located on human chromosome 2, is approximately a 9.5-kb gene that encodes a 2-kb mRNA transcript. This transcript is translated into a 381-amino-acid proprotein, which is glycosylated and undergoes a series of proteolytic cleavage to produce the 79-amino-acid hydrophobic mature SP-B protein.[9,10] SP-B enables the adsorption of phospholipids to the alveolar surface, provides surfactant stability, and is essential for tubular myelin formation.[11] SP-B enables the surfactant to spread on the alveolar surface.[6] Although not an acute respiratory distress syndrome (RDS), patients with AB have decreased amounts and functions of surfactant. Surfactants play a role in the opsonization of RSV.[12,13] Mutations and polymorphisms of exon 4 of SP-B are common and cause significant functional disorders.[6,14]

SP-D is a multimeric collectin that is a part of innate immunity and is expressed in pulmonary and extrapulmonary epithelia. SP-D exerts some antimicrobial effects and decreases inflammation through direct microbial interactions and modulation of inflammatory cell responses. SP-D increases phagocytosis of microbes and dying host cells.[15] Recent studies have shown that SP-D exerts antimicrobial and anti-inflammatory effects on various nonpulmonary organs. An important function of SP-D is binding to bacteria, viruses, fungi, and even helminthic parasites for their phagocytosis through opsonization.[16,17] SP-D/SP-A haplotypes, including the Met11 allelic SP-D variant, are protective against RDS development but detrimental to patients with bronchopulmonary dysplasia (BPD).[18] The surfactant protein-D (SFTPD) gene is located at the genomic position 10q22.2-23.1. Lower serum SP-D levels were observed in individuals homozygous for the RS721917 minor allele (threonine/Thr11), which affects the predominance of the trimeric structure of SP-D and its immunological ability to bind microbes.[19] The rs721917 major allele (methionine 11) has been associated with an increased risk of severe RSV bronchiolitis in infants.[20]

The individual differences in susceptibility to AB prompted the investigation in this study. We aimed to determine the association of SP B (SP-B) intron 4 and SP-D SP-D/270 (Ser270Thr) and SP-D/160 (Ala160Thr) polymorphisms with AB in infants.

MATERIAL AND METHOD

This study was conducted on infants diagnosed with AB and healthy infants recruited from pediatric outpatient and emergency clinics between January 1, 2015, and January 1, 2016. Data on subjects were derived from a prior thesis study conducted by our team.[21] Demographic, clinical, laboratory, and radiological data were collected. Infants in good health visiting the pediatric outpatient clinic for routine check-ups were enrolled in the study. A physician assessed patients for enrollment using a standardized questionnaire and clinical evaluation. In children aged <1 year, AB was diagnosed if at least one of the signs of increased respiratory effort such as wheezing, rhonchi, prolonged expiration, tachypnea, and intercostal or subcostal retractions and findings of upper respiratory tract infections such as fever, nasal discharge, and cough were present.[1,2,22] Exclusion criteria included existing cardiopulmonary diseases, immunodeficiency, congenital anomalies, prematurity, cystic fibrosis, and BPD. We excluded these diseases from the study as they could influence the diagnosis and severity of AB. Parental consent was obtained for participation in the study, which adhered to the Declaration of Helsinki and received approval from the Gaziosmanpasa University School of Medicine ethics committee (15-KAEK-040). The clinical severity score (**Table 1**), based on respiratory rate, wheezing, retraction, and general condition (irritability, poor feeding, and lethargy), was assessed upon admission, categorizing patients into mild, moderate, and severe groups.[2,23]

Table 1 Clinical severity scores(3)

Variables	Score			
	0	1	2	3
Respiratory rate (breaths/min)	<30	30–45	46–60	>60
Wheezing	None	Terminal respiratory or only with stethoscope	Entire expiration or audible on expiration without stethoscope	Inspiration and expiration without stethoscope
Retraction	None	Intercostal only	Tracheosternal	Severe with nasal flaring
General condition	Normal	Mild irritable	İrritable, poor feeding	Noon-feeding, alteration in consciousness

Genetic Analysis

Blood samples were collected, and DNA was extracted using a GeneAll® ExgeneTM Blood SV Genomic DNA Kit. SP-B intron 4, C/A-18, and SP-D/270 (Ser270Thr), and SP-D/160 (Ala160Thr) polymorphisms were analyzed through the polymerase chain reaction (PCR)-based restriction fragment length polymorphism method. The PCR reaction was conducted in a total volume of 25 µL, following specific guidelines and using designated primers (Fermentas, Shenzhen, China). The PCR primers and product sizes are shown in **Table 2**.

Table 2. PCR primers and product sizes for the SP-B intron4, SP-B C/A–18 and SP-D/270 (Ser270Thr), and SP-D/160 (Ala160Thr) polymorphisms.

Polymorphism	Primers	Product Size
SP-B intron4	F;5'TGTGTGTGAGAGTGAGGGTGTAAG3' R;5'CTGGTCATCGACTACTTCCA3'	604 bp (inv)
C/A–18	F;5' GTCCAGCTATAAGGGGCCGTG3' R;5' GTGAGTGGAGCTGCCTA3'	168 bp
SP- DAla160Thr	F;5'CTCGCAGGCCCTAAGGGAGAG3' R;5'CTGGACCCAGCCCAGCCCAG3'	107 bp
Ser270Thr	F;5'ACGGAGGCACAGCTGCTG3' R;5'GGAAAGCAGCCTCGTTCT3'	115 bp

Statistical Analysis

Statistical analyses were performed using Epi Info Software and Openepi for genetic data comparison, with the χ^2 test applied for genotype distribution and Fisher's exact tests for allele distribution. A p-value of <0.05 was deemed statistically significant. Analyses, except for genetic tests, were performed using IBM SPSS Statistics for Windows version 19 (IBM Corp, Armonk, NY, USA).

RESULTS

The study included 106 infants with AB admitted to Gaziosmanpasa University School of Medicine and 107 healthy controls from outpatient clinics. The gender distribution showed 42.5% female among the AB group. The mean ages for the patient and control groups were 7.66±2.80 months and 7.70±3.02 months, respectively (p=0.231).

The respective genotype frequencies of the inversion (inv)/inv, inv/(insertion [ins]/deletion [del]), ins/ins, and del/del genotypes of SP-B intron 4 were 93.40%, 4.72%, 0.94%, and 0.94% in the AB group and 84.11%, 15.89%, 0%, and 0% in the control group (p=0.012) (**Table 3**). The inv/inv polymorphism presented an odds ratio for AB 3.74 (CI: 95%; 1.33-10.55; p=0.029).

A significant difference in the genotype frequencies of intron 4 polymorphisms in SP-B was found between the AB and control groups (p=0.029) (**Table 3**). However, no significant difference in SP-B C/A-18 polymorphisms was observed between the control and AB groups (p=0.643) (**Table 3**).

Table 3. Frequency of Intron 4 Polymorphism in the SP-B Gene

Polymorphism INT4 Genotypes	Patients n=106(%)	Control n=107(%)	p
Inv/inv	99 (93,40)	90 (84,11)	
Inv/# (ins/del)	5 (4,72)	17 (15,89)	0.029
Ins/ins	1 (0,94)	0 (0)	
Del/del	1 (0,94)	0 (0)	
SP-B 18 (C/A) Genotypes	n=104 (%)	n=103 (%)	
CC	23 (22,12)	18 (17,48)	
CA	50 (48,08)	55 (53,40)	0.643
AA	31 (29,80)	30 (29,12)	
Alleles			
C	96 (46,15)	91 (44,17)	0.607
A	112 (53,85)	115 (55,83)	

χ^2 (Chi-Square) test applied for Two-Way Tables in genotype distribution, INT 4: Intron 4, inv: invariant, ins: insertion, del: deletion, SP: Surfactant protein, A: Adenine, C: Cytosine, T: Thymine.

SP-B C/A-18 polymorphisms did not influence the risk for AB (p=0.643). The genotype frequencies of the CC, CA, and AA genotypes of SP-B C/A-18 are summarized in **Table 3**. The frequencies of the C and A alleles were 46.3% in the AB group and 32.4% in the control group (p=0.607).

The SP-D/270 (Ser270Thr) polymorphism in SP-D showed a statistically significant difference (p<0.05) between the two groups (**Table 4**). The Ser genotype presented an odds ratio for AB 0,50 (CI: %95; 0.29-0.86; p =0.004). However, when examining the SP-D/160 (Ala160Thr) polymorphism in SP-D, no statistically significant difference was noted (p>0.05) (**Table 4**).

Table 4. SP-D/270 (Ser270Thr) polymorphism in the SP-D gene

Polymorphism SP-D/270 (Ser270Thr) Genotypes	Patients n=105 (%)	Control n=107 (%)	p
Ser/Ser	63 (60.00)	85 (79.44)	
Ser/Thr	41 (39.05)	20 (18.69)	0.004
Thr/Thr	1 (0.95)	2 (1.87)	
Alleles			
Ser	167 (79.90)	190 (88.79)	0.012
Thr	42 (20.10)	24 (11.21)	

χ^2 (Chi-Square) test applied for Two-Way Tables in genotype distribution, SP: Surfactant protein, Ser: Serine, Thr: Threonine.

No relationship was found between clinical severity and gene polymorphism. The χ^2 and p-value could not be calculated because of the insufficient number of patients included in the study (**Table 5**).

Table 5. SP-D/160 (Ala160Thr) polymorphism in the SP-D gene

Polymorphism SP-D/160 (Ala160Thr) Genotypes	Patients n=105 (%)	Control n=106 (%)	p
Ala/Ala	37 (35.24)	35 (33.02)	
Ala/Thr	50 (47.62)	53 (50.00)	0.933
Thr/Thr	18 (17.14)	18 (16.98)	
Alleles			
Ala	124 (59.05)	123 (58.02)	0.830
Thr	86 (40.95)	89 (41.98)	

χ^2 (Chi-Square) test applied for Two-Way Tables in genotype distribution, SP: Surfactant protein, Ala: Alanine, Thr: Threonine.

Table 6. Distribution of gene polymorphisms according to clinical severity

		Clinical severity			X2	p
		Mild N=58	Moderate N=32	Severe N=16		
	del/del	-	1 (100)	-		
	ins/ins	1 (100)	-	-		
Intron 4	inv/del	2 (66.67)	-	1 (33.33)	-	-
	inv/ins	2 (100)	-	-		
	inv/inv	53 (53.54)	31 (31.31)	15 (15.15)		
	AA	18 (58.06)	9 (29.03)	4 (12.91)		
C/A-18	CA	27 (54.00)	15 (30.00)	8 (16.00)	0.340	0.987
	CC	13 (56.52)	6 (26.09)	4 (17.39)		
	AA	8 (44.44)	7 (38.89)	3 (16.67)		
SP-D 160	TA	30 (60.00)	14 (28.00)	6 (12.00)	1.903	0.754
	TT	19 (51.35)	11 (29.73)	7 (18.92)		
	AA	37 (58.73)	20 (31.75)	6 (9.52)		
SP-D 270	AT	20 (48.78)	11 (26.83)	10 (24.39)	1.903	0.754
	TT	-	1 (100)	-		

χ^2 (Chi-Square) test applied for genotype distribution, SP: Surfactant protein, del: deletion, ins: insertion, inv: invariant, A: Adenine, C: Cytosine, T: Thymine.

DISCUSSION

AB is the most common LRT disease in infancy, and viral agents play a significant role in its etiology. Despite the known risk factors for AB and its inflammatory nature, the absence of disease in patients with similar demographics suggests that genetic factors may contribute to its etiology.

This study established a significant link between SP-B and SP-D polymorphisms and the frequency of AB. The inv/inv polymorphism in SP-B intron 4 was more prevalent in the AB group, while the Ser/Ser polymorphism in SP-D was less common. However, the study could not confirm any association between the severity of AB and these polymorphisms.

Previous studies have highlighted associations between certain alleles and increased risks of RDS and severe RSV bronchiolitis.[24] Moreover, the C allele of the SP-B 1580 site may act as a susceptibility factor for lung damage. Similarly, Cao et al.[25] identified an association between the C allele of the SP-B 1580 locus and early mortality in mice with viral pneumonia. Additionally, the C allele was associated with markedly elevated concentrations of inflammatory cytokines, such as tumor necrosis factor-α, interleukin (IL)-1β, IL-18, and IL-6, in the bronchoalveolar lavage fluid of mice affected by viral pneumonia. Another experimental study suggested that the A allele of C/A-18 is a risk factor for BPD.[26] But, the present study did not find similar associations between these alleles and AB and its severity. Moreover, some SFTPB variants may increase the incidence or severity of diseases (e.g., RDS) in genetically vulnerable individuals.[7] In combination with other variants and under appropriate conditions, individual variants in SFTPB may lead to sufficiently low SP-B expression and cause disease.

The C allele of rs1130866, located on chromosome 2 p11.2 in the exon region of the SP-B N region and associated with glycosylation at position 129 of the SP-B protein, is overrepresented in patients with severe influenza. Therefore, glycosylation may affect the function of this protein.[27] In Chinese Han infants, the homozygous del variant genotype for intron 4 was significantly higher in the BPD group than in the control group. Therefore, the homozygous del variant genotype of intron 4 might be associated with BPD.[28] The ins/del variants in intron 4 were more frequent in adult patients with RDS than in the control participants.[29] Another study reported a high frequency of CT and TT genotypes at the C/T locus in patients with COVID-19, suggesting increased susceptibility to COVID-19.[30] In this study, the ins/del polymorphism was more frequent in the control group than in the AB group. These results suggest that the ins/del polymorphism might offer protection against AB. However, the SP-B 18 (C/A) polymorphism did not influence the frequency of AB.

SP-D belongs to the C-type lectin superfamily and prevents lung collapse during expiration. SP-D plays a role in innate immunity and regulates inflammatory processes.[31] SP-D is thought to be associated with immunomodulatory functions. It binds to pathogens such as bacteria, fungi, viruses, and mycobacteria, facilitating their aggregation.[32] One main effect of SP-D is the aggregation and enhancement of the phagocytosis of microbes and dying host cells.[15]

According to the results of this study, the Thr polymorphism at SP-D/270 (Ser270Thr) can be considered a risk factor for bronchiolitis in the first year of life. Three SNPs have been identified in the coding region of SP-D, resulting in amino acid variations. The variation at codon 11 within the sequence encoding mature protein results in significantly different serum SP-D levels.[33] The SP-D allele coding for Thr has been suggested to increase the susceptibility to tuberculosis.[34,35] Most studies have suggested disease associations with the Thr11 allele.[15,32,36] Unlike these studies, no association was found between disease severity and the polymorphisms and alleles examined in this study. We think the small sample size of the present study significantly contributed to the absence of a meaningful relationship.

Conversely, the SP-D/160 (Ala160Thr) polymorphism is not associated with AB in infants. Consistent with our study, a study reported that the individual polymorphisms of amino acid residue 160 had no detectable influence on the oligomeric state of SP-D and no significant differences in serum SP-D levels were found in the population with variant genotypes of SP-D/160.[33]

Limitations and strengths of the study

Viral identification was not performed in this study. The immune responses and clinical courses of various viral infections differ significantly. So, it is difficult to suggest that the effects of these polymorphisms are valid in all AB patients. This is a limitation of this study. The roles of these polymorphisms in the pathogenesis of diseases caused by specific viruses remain unclear. Nevertheless, this prospective case–control study provides insights into whether these polymorphisms are risk factors for AB, regardless of the etiological agent.

CONCLUSION

The inv/inv polymorphism in SP-B intron 4 may serve as a risk factor for AB, while the inv/del polymorphism could provide a protective effect against the condition in infants. Additionally, the Ser allele in SP-D appears less frequently in infants with AB, potentially indicating a lower risk. Continued monitoring and proactive measures may facilitate early detection of infants genetically predisposed to AB, although a definitive relationship between AB severity and these polymorphisms was not established.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval was received for this study from the Gaziosmanpasa University Faculty of Medicine Ethics Committee (Decision No: 15-KAEK-040).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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REFERENCES

1. Bria M, Coates LEC. Wheezing in Infants: Bronchiolitis, in Nelson Textbook of Pediatrics, Kliegman RM, Editor. Elsevier: Canada. 2016;2044-50.
2. Gul A, Takçı Ş, Altıntaş Seyyah B, Yılmaz R. Independent Predictors of Severity and Hospitalization in Acute Bronchiolitis: Neutrophil/Lymphocyte Ratio and Mean Platelet Volume. J Pediatr Infect Dis 2018;13(04):268-73.
3. Yusen RD, Cohen AH, Hamvas A. Normal lung function in subjects heterozygous for surfactant protein-B deficiency. Am J Respir Crit Care Med. 1999;159(2):411-4.
4. Tokieda K, Iwamoto HS, Bachurski C, et al. Surfactant protein-B-deficient mice are susceptible to hyperoxic lung injury. Am J Respir Cell Mol Biol. 1999;21(4):463-72.
5. Tokieda K, Whitsett JA, Clark JC, et al. Pulmonary dysfunction in neonatal SP-B-deficient mice. Am J Physiol. 1997;273(4):875-82.
6. Wright JR. Immunoregulatory functions of surfactant proteins. Nat Rev Immunol. 2005;5(1):58-68.
7. Hamvas A. Inherited surfactant protein-B deficiency and surfactant protein-C associated disease: clinical features and evaluation. Semin Perinatol. 2006;30(6):316-26.
8. Kültürsay N, Uygur Ö, Yalaz M. Yenidoğan döneminde sürfaktan kullanımı-bilinenler, halen araştırılanlar, araştırılması gerekenler. Türk Ped Arş 2014;49:1-12.
9. Weaver TE, Whitsett JA. Function and regulation of expression of pulmonary surfactant-associated proteins. Biochem J. 1991;273(Pt 2)(Pt 2):249-64.
10. Mallory GB Jr. Surfactant proteins: role in lung physiology and disease in early life. Paediatr Respir Rev. 2001;2(2):151-8.
11. Cole FS, Hamvas A, Nogee LM. Genetic disorders of neonatal respiratory function. Pediatr Res. 2001;50(2):157-62.
12. Ventre K, Haroon M, Davison C. Surfactant therapy for bronchiolitis in critically ill infants. Cochrane Database Syst Rev. 2006;(3):CD005150.
13. Davison C, Ventre KM, Luchetti M, Randolph AG. Efficacy of interventions for bronchiolitis in critically ill infants: a systematic review and meta-analysis. Pediatr Crit Care Med. 2004;5(5):482-9.
14. Hallman M, Haataja R. Surfactant protein polymorphisms and neonatal lung disease. Semin Perinatol. 2006;30(6):350-61.
15. Sorensen GL. Surfactant Protein D in Respiratory and Non-Respiratory Diseases. Front Med (Lausanne). 2018;5:18.
16. Hartshorn KL, Crouch E, White MR, et al. Pulmonary surfactant proteins A and D enhance neutrophil uptake of bacteria. Am J Physiol. 1998;274(6):958-69.
17. LeVine AM, Elliott J, Whitsett JA, et al. Surfactant protein-d enhances phagocytosis and pulmonary clearance of respiratory syncytial virus. Am J Respir Cell Mol Biol. 2004;31(2):193-9.
18. Pavlovic J, Papagaroufalis C, Xanthou M, et al. Genetic variants of surfactant proteins A, B, C, and D in bronchopulmonary dysplasia. Dis Markers. 2006;22(5-6):277-91.
19. Leth-Larsen R, Garred P, Jensenius H, et al. A common polymorphism in the SFTPD gene influences assembly, function, and concentration of surfactant protein D. J Immunol. 2005;174(3):1532-8.
20. Lahti M, Lofgren J, Marttila R, et al. Surfactant protein D gene polymorphism associated with severe respiratory syncytial virus infection. Pediatr Res. 2002;51(6):696-9.
21. Seyyah BA. The investigation of surfactant protein B and D gene polymorphism in infants with acute bronchiolitis, in Department of Pediatrics. Gaziosmanpasa University, Tokat Turkiye. 2016;72.
22. Okutan Ö, Çeltik C. Akut Bronşiolitlerde Güncel Bilgiler. STED 2005;14(1):5-7.
23. Wang EE, Law BJ, Boucher FD, et al. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) study of admission and management variation in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. J Pediatr. 1996;129(3):390-5.
24. Dahmer MK, O'cain P, Patwari PP, et al. The influence of genetic variation in surfactant protein B on severe lung injury in African American children. Crit Care Med. 2011;39(5):1138-44.
25. Cao B, Bao Y, Liu C, Qi Q, Zhao Y, Yang F. A gene polymorphism at SP-B 1580 site regulates the pulmonary surfactant tension of viral pneumonia through the cellular pyroptosis signaling pathway. Am J Transl Res. 2023;15(12):6949-58.
26. Steagall WK, Lin JP, Moss J. The C/A(-18) polymorphism in the surfactant protein B gene influences transcription and protein levels of surfactant protein B. Am J Physiol Lung Cell Mol Physiol. 2007;292(2):448-53.
27. To KKW, Zhou J, Song YQ, et al. Surfactant protein B gene polymorphism is associated with severe influenza. Chest. 2014;145(6):1237-43.
28. Cai BH, Chang LW, Li WB, et al. Association of surfactant protein B gene polymorphisms (C/A-18, C/T1580, intron 4 and A/G9306) and haplotypes with bronchopulmonary dysplasia in chinese han population. J Huazhong Univ Sci Technolog Med Sci. 2013;33(3):323-8.
29. Floros J, Veletza SV, Kotikalapudi P, et al. Dinucleotide repeats in the human surfactant protein-B gene and respiratory-distress syndrome. Biochem J. 1995;305 (Pt 2)(Pt 2):583-90.
30. Gerosa C, Fanni D, Cau F, et al. Immunohistochemical findings in the lungs of COVID-19 subjects: evidence of surfactant dysregulation. Eur Rev Med Pharmacol Sci. 2021;25(13):4639-43.
31. Takahashi H, Sano H, Chiba H, Kuroki Y. Pulmonary surfactant proteins A and D: innate immune functions and biomarkers for lung diseases. Curr Pharm Des. 2006;12(5):589-98.
32. McCormack FX, Whitsett JA. The pulmonary collectins, SP-A and SP-D, orchestrate innate immunity in the lung. J Clin Invest. 2002;109(6):707-12.
33. Leth-Larsen R, Garred P, Jensenius H, et al. A common polymorphism in the SFTPD gene influences assembly, function, and concentration of surfactant protein D. J Immunol. 2005;174(3):1532-8.
34. El Gayed E, Elhelbawy RH, Elhelbawy NG. Nicotinic acetylcholine receptors (rs1051730) gene polymorphism and surfactant protein D level in chronic obstructive pulmonary disease. Br J Biomed Sci. 2020;77(4):213-5.
35. Floros J, Lin HM, García A, et al. Surfactant protein genetic marker alleles identify a subgroup of tuberculosis in a Mexican population. J Infect Dis. 2000;182(5):1473-8.
36. El Saleeby CM, Li R, Somes GW, Dahmer MK, Quasney MW, DeVincenzo JP. Surfactant protein A2 polymorphisms and disease severity in a respiratory syncytial virus-infected population. J Pediatr. 2010;156(3):409-14.

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Original Article / Orijinal Araştırma

Evaluating Medical Faculty Students' Awareness and Professional Attitudes Towards Domestic Violence

Tıp Fakültesi Öğrencilerinin Aile İçi Şiddete İlişkin Farkındalıklarının ve Mesleki Tutumlarının Değerlendirilmesi

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Abstract

Aim: This study aimed to investigate the awareness, attitudes, and perceptions of medical students regarding domestic violence, with a focus on examining the associations between sociodemographic factors and attitudes towards domestic violence.

Material and Method: This descriptive study was conducted as an e-survey between 01 January 2023- 01 May 2023 on students' social media group. The population consists of 4th, 5th, and 6th-year medical students undergoing clinical practice education at a University Faculty of Medicine. Statistical analyses, including descriptive statistics and inferential tests, were conducted to explore the relationships between sociodemographic variables and domestic violence-related features with participants' scores on the The Domestic Violence Awareness Scale (DVAS) and The Attitude towards Domestic Violence Scale (DVAtS).

Results: A total of 225 medical students participated in the study, 54.7% of them female and the mean age was 23.04±1.54 (20;31). Of the students, 17.3% of them stated that they exposed, 34.7% of them witnessed to domestic violence. Total score of domestic violence awareness scale was 57.6±3.83 (25; 60). Women demonstrated higher awareness scores compared to men, and individuals not exposed to domestic violence exhibited lower tolerance for normalized forms of violence. Higher maternal education levels were associated with more favorable attitudes towards casualization of violence. Participants belonging to nuclear families showed higher awareness levels compared to non-nuclear family participants.

Conclusion: The study underscores the importance of addressing domestic violence awareness and education among medical students, particularly regarding the nuanced associations between sociodemographic factors and attitudes towards domestic violence. Targeted educational initiatives and intervention strategies are needed to enhance awareness, sensitivity, and professional attitudes towards addressing domestic violence in clinical practice, ultimately contributing to the promotion of health and well-being among affected individuals and communities.

Keywords: Medical faculty students, domestic violence, awareness, professional attitudes

Öz

Amaç: Bu çalışma, sosyodemografik faktörler ile aile içi şiddete yönelik tutumlar arasındaki ilişkilerin incelenmesine odaklanarak tıp öğrencilerinin aile içi şiddete ilişkin farkındalık, tutum ve algılarını araştırmayı amaçlamıştır.

Gereç ve Yöntem: Tanımlayıcı tipte olan bu çalışma, 01 Ocak 2023- 01 Mayıs 2023 tarihleri arasında öğrencilerin sosyal medya grubuna e-anket olarak uygulandı. Evreni bir Üniversite Tıp Fakültesi'nde klinik uygulama eğitimi alan 4., 5. ve 6. sınıf tıp öğrencilerinden oluşmaktadır. Sosyodemografik değişkenler ile aile içi şiddete ilişkin özellikler arasındaki ilişkileri, katılımcıların Aile İçi Şiddet Farkındalık Ölçeği (DVAS) ve Aile İçi Şiddete Yönelik Tutum Ölçeği (DVAtS) puanlarıyla araştırmak için tanımlayıcı istatistikler ve çıkarımsal testleri içeren istatistiksel analizler yapıldı.

Bulgular: Çalışmaya %54,7'si kadın olmak üzere toplam 225 tıp öğrencisi katıldı ve yaş ortalaması 23,04±1,54 (20;31) idi. Öğrencilerin %17,3'ü aile içi şiddete maruz kaldığını, %34,7'si ise aile içi şiddete tanık olduğunu belirtti. Aile içi şiddet farkındalık ölçeğinin toplam puanı 57,6±3,83 (25; 60) idi. Kadınlar erkeklere göre daha yüksek farkındalık puanlarına sahipken, aile içi şiddete maruz kalmayan bireylerin normalleştirilmiş şiddet biçimlerine karşı daha düşük tolerans sergiledikleri görüldü. Daha yüksek anne eğitim düzeyi, şiddetin gündelikleştirilmesine yönelik daha olumlu tutumlarla ilişkilendirildi. Çekirdek aileye mensup katılımcılar, çekirdek aileye sahip olmayan katılımcılara göre daha yüksek farkındalık düzeyi gösterdi.

Sonuç: Çalışma, özellikle sosyodemografik faktörler ile aile içi şiddete yönelik tutumlar arasındaki incelikli ilişkiler açısından, tıp öğrencileri arasında aile içi şiddet farkındalığı ve eğitiminin ele alınmasının önemini vurgulamaktadır. Klinik uygulamada aile içi şiddetin ele alınmasına yönelik farkındalığı, duyarlılığı ve profesyonel tutumları artırmak ve sonuçta etkilenen bireyler ve topluluklar arasında sağlık ve refahın geliştirilmesine katkıda bulunmak için hedefe yönelik eğitim girişimlerine ve müdahale stratejilerine ihtiyaç vardır.

Anahtar Kelimeler: Tıp fakültesi öğrencileri, aile içi şiddet, farkındalık, mesleki tutumlar

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INTRODUCTION

Domestic violence is defined by the Turkish Ministry of Family and Social Services as actions occurring between family members, including children, spouses, ex-spouses, and close relatives, resulting in physical, sexual, economic, or psychological harm or the likelihood of such harm. This definition encompasses threats, coercion, arbitrary deprivation of liberty, all forms of physical, sexual, psychological, verbal, or economic behaviors occurring in societal or private settings.[1] World Health Organization (WHO) defines violence as any behavior within an intimate relationship that causes physical, psychological, or sexual harm, including physical aggression, sexual coercion, psychological abuse, and controlling behaviors.[2,3]

Exposure to violence contributes to lifelong health problems and premature death, especially for women and children.[4] Leading causes of death such as heart disease, stroke, cancer, and HIV/AIDS often result from coping mechanisms like smoking, alcohol and drug use, and engaging in unsafe sexual practices due to the psychological impact of violence. Moreover, violence imposes a heavy burden on healthcare and criminal justice systems, social and welfare services, and the economic fabric of communities.[3]

Despite being a primary issue in Turkey, limited efforts have been made to address domestic violence, particularly violence against women.[5-8] The approach of healthcare professionals is crucial due to the prevalence of violence among a significant portion of the female population. This prevalence leads to serious health issues, impacting safe motherhood, family planning, HIV/AIDS prevention, and sexually transmitted infections.[5-11] Therefore, all healthcare providers, especially primary care physicians who often encounter patients across various stages of the family life cycle, play a key role in recognizing and addressing domestic violence.

Individuals experiencing domestic violence may seek help from healthcare facilities for various reasons but may refrain from disclosing their problems due to factors like embarrassment or fear of the perpetrator. Hence, it is essential for healthcare professionals to recognize and address domestic violence, providing support while ensuring the victim's privacy and safety.[7]

Healthcare professionals need to document domestic violence cases ethically and guide victims without inducing guilt, referring them to appropriate support systems when necessary. However, studies show that healthcare personnel often lack adequate training and knowledge in identifying and managing cases of abuse, neglect, and domestic violence.[5-11]

As future physicians, medical students should assess their awareness, perspectives, and attitudes towards victims of domestic violence, as they will inevitably encounter such cases in their careers. Although studies have explored awareness and attitudes towards domestic violence among students in various faculties like health sciences, law, engineering, and education in Turkey, no specific research has evaluated medical students' awareness and attitudes.[9-11]

This study aims to assess the awareness, perspectives, and attitudes of medical students undergoing clinical practice towards domestic violence and victims of violence.

MATERIAL AND METHOD

This descriptive study was conducted as an e-survey between 01 January 2023- 01 May 2023 on students' social media group. The population consists of 4th, 5th, and 6th-year medical students undergoing clinical practice education at Hacettepe University Faculty of Medicine. Each semester, there were approximately 480-490 students, totaling around 1440-1470 students in the target group. Sampling did not be performed, and students who voluntarily participate by filling out the form on designated dates in social media groups were included in the study. The research form was shared in student groups at 10-day intervals over a period of 2 months.

As data collection tools, student information form, The Domestic Violence Awareness Scale (DVAS) and The Attitude towards Domestic Violence Scale (DVAtS) and 6 questions about attitudes of students were used. Iınformation form was prepared by making use of the literature, including the socio-demographic information of the students and questions about the concept of domestic violence. Two scales were used:

The domestic violence awareness scale: Developed by Özyürek and Kurnaz (2019) to determine individuals' awareness of domestic violence among university students, this scale is a three-point Likert scale with responses categorized as Agree (1), Partially Agree (2), and Disagree (3).[12] The scale consists of 20 items grouped into 4 dimensions: Identification of Domestic Violence, Consequences of Domestic Violence, Acceptance of Domestic Violence, and Normalization of Domestic Violence. Scores from the scale can be totaled, and items 11 through 20 are reverse-scored. Higher scores indicate higher awareness of domestic violence. Confirmatory factor analysis was conducted to determine the validity of the scale, yielding the following goodness-of-fit indices: x^2=73.38 (sd=164, p<.001), (x^2 /sd)=0.44, RMSEA=0.00, RMR=0.20, SRMR=0.03, GFI=0.96, CFI=1.00, and AGFI=0.94. The reliability of the scale was assessed using Cronbach's alpha, which ranged between .71 and .92 for internal consistency. The overall reliability coefficient for the scale was calculated as .92, indicating that the scale provided valid and reliable results. For this study, the calculated Cronbach's alpha coefficient for the total scale was found to be 0.84.

The attitude towards domestic violence scale: Developed by Şahin and Dişsiz (2009) in a five-point Likert format to assess attitudes toward domestic violence.[13] Responses are categorized as "strongly agree" (1), "agree" (2), "undecided" (3), "disagree" (4), and "strongly disagree" (5). Scores are obtained by summing the items, with the highest possible score being 65 and the lowest 13. An increase in scores indicates a positive attitude toward domestic violence, while a decrease indicates a negative attitude. The Cronbach's alpha coefficient for reliability was found to be 0.72. The scale comprises 13 items grouped into 4 factors: Normalization of Violence (5 items - 1, 2, 3, 4, 5),

Generalization of Violence (3 items - 6, 7, 8), Rationalization of Violence (3 items - 9, 10, 11), and Concealment of Violence (2 items - 12, 13).

Data Analysis

The data obtained in the study were transferred to electronic media (data entry) and statistical analyses of the data were performed using the IBM SPSS Statistics Premium 23 V statistical computer package program licensed by Hacettepe University. In the analyses, descriptive statistics were expressed as distributions, percentage, mean, median, minimum-maximum values, and standard deviation. The compatibility of the variables with normal distribution was checked by Kolmogrow Smirnov and Shapiro Wilk tests. Independent groups t test was used to compare independent two-group continuous variables that conformed to normal distribution. ANOVA was used to compare the means of more than two independent groups. Alpha 0.05 was taken.

Ethics

This study protocol was examined by Hacettepe University Ethics Committee and was approved on July 05, 2022 with the report numbered GO22/73917.

RESULTS

Two hundred twenty five students were participated to study, 54.7% of them female; 83.1% of them had no chronical disease and the mean age was 23.04±1.54 (min=20; max=31). The sociodemographic characteristics of the students were presented at **Table 1**.

Of the students, 17.3% of them stated that they exposed, 34.7% of them witnessed to domestic violence. 32.9% of them stated that they took lesson on domestic violence during their medical school education. The features of students related with domestic violence were presented at **Table 2**.

Table 2. The features of students related with domestic violence (N=225)

	Number	Percent (%)
Have you ever been exposed to domestic violence (physical, sexual or psychological)?		
No	186	82.7
Yes	39	17.3
Have you ever witnessed domestic violence?		
No	147	65.3
Yes	78	34.7
Have you ever taken lesson on domestic violence during your medical school education?		
No	151	67.1
Yes	74	32.9
If you have taken lesson on domestic violence, do you consider this lesson sufficient?		
No	45	60.8
Yes	29	39.2
If you have not taken lesson on domestic violence, would you like to study?		
No	36	24.0
Yes	114	76.0

Table 1. Sociodemographic characteristics of the students (N=225)

	Number	Percent (%)
Gender		
Female	123	54.7
Male	102	45.3
Class		
Class 4	89	39.6
Class 5	65	28.9
Class 6	71	31.6
Marital Status		
Married	1	0.4
Single	224	99.6
Chronic Disease		
No	187	83.1
Yes	38	16.9
Maternal Education Status		
Primary School and Lower	32	14.2
Middle School and High School	52	23.1
University and Higher	141	62.7
Maternal Working Status		
Not Worker/ Housewife	81	36.0
Worker	99	44
Retired	43	19.1
Died	2	0.9
Paternal Education Status		
Primary School and Lower	14	6.2
Middle School and High School	39	17.3
University and Higher	172	76.4
Paternal Working Status		
Not Worker	7	3.1
Worker	154	68.4
Retired	54	24
Died	10	4.4
Parents Cohabitation Status		
Parents Living Together	197	87.6
Parents Living Apart	16	7.1
Mother Died	2	0.8
Father Died	10	4.4
Family Structure		
Nuclear Family	215	95.6
Extended Family	10	4.4

	Mean	SD	Min	Max
Age	23.04	1.54	20	31

SD: Standard Deviation; Min: minimum; Max: maximum

Total score of domestic violence awareness scale was 57.6±3.83 (min=25; max=60). The total score and subscale scores of domestic violence awareness scale and the subscale scores of domestic violence attitude scale were presented at **Table 3**.

Table 3. The total sore and subscale scores of domestic violence awareness scale and the subscale scores of domestic violence attitude scale

DVAS Subscales	Mean	SD	Min	Max
Definition of domestic violence	14.71	0.87	9.0	15.0
Results of domestic violence	14.72	0.96	5.0	15.0
Acceptance of domestic violence	13.92	1.71	5.0	15.0
Normalization of domestic violence	14.28	1.63	5.0	15.0
DVAS Total Score	57.6	3.83	25.0	60.0
DVAtS Subscales	**Mean**	**SD**	**Min**	**Max**
Normalization of the violence	23.20	2.89	5.0	25.0
Generalization of the violence	14.36	1.38	3.0	15.0
Casualization of the violence	12.50	1.61	5.0	15.0
Hiding violence	9.13	1.45	2.0	10.0

SD: standard deviation; Min: minimum; Max: maximum

The evaluation of the perception and professional attitude of the physician in the context of the domestic violence were presented at **Table 4**. 92.9% of them were stated that they consider that should the physician ask the presence of domestic violence in his/her patient whom he/she thinks has been exposed to violence.

Table 4. The evaluation of the perception and professional attitude of the physician in the context of the domestic violence

	Number	Percent (%)
Do you consider that should the physician ask the presence of domestic violence in his/her patient whom he/she thinks has been exposed to violence?		
No	2	0.9
Yes	209	92.9
Hesitant	14	6.2
If the physician thinks that the patient is a victim of domestic violence, what should he/she do next?		
He/she should inform the competent authorities (law enforcement etc.) without asking with the patient.	84	37.3
He/she should notify the competent authorities after obtaining the patient's consent.	141	62.7
Do you consider that low-income victims of domestic violence should benefit from free medical treatment?		
No	12	5.3
Yes	180	80
Hesitant	33	14.7
Do you consider that women who are victims of domestic violence are not given enough attention by the physician because they exaggerate their symptoms?		
No	96	42.7
Yes	34	15.1
Hesitant	95	42.2
Do you consider that victims of violence have difficulty in expressing themselves?		
No	1	0.4
Yes	212	94.2
Hesitant	12	5.3
In your opinion, how should the physician's approach be to patients who are victims of violence and have difficulty expressing themselves?		
Paternalistic Model	1	0.4
Deliberative Model	163	72.4
Hesitant	9	4.0
I don't know	44	19.6
Other	8	3.6

The relationship of sociodemographic variables and domestic violence related features of participants with DVAtS scores were presented at **Table 5**. Statistically significant higher scores of total and subgroup domestic violence attitude among women compared to men were found (respectively, p<0.001; p<0.001, p=0.098, p=0.089, p=<0.001). It was found that those not witnessing domestic violence had statistically significantly higher DVAtS attitude scores (p=0.020). Additionally, those not exposed to domestic violence had statistically significantly higher normalization of violence attitude scores (p=0.040). A higher education level (university and above) in mothers was found to be statistically significantly associated with higher scores for casual attitudes toward violence (p=0.008). Furthermore, those with chronic illnesses and those not witnessing domestic violence had statistically significantly higher hiding violence attitude scores (respectively; p=0.013, p=0.09).

The relationship of sociodemographic variables and domestic violence related features of participants with DVAS scores were presented at **Table 6**. Statistically significant higher awareness scores of total and subgroup domestic violence among women compared to men were found (respectively, p<0.001; p=0.009, p=0.049, p=0.003, p=<0.001). Those belonging to nuclear families and those not exposed to domestic violence were found to have statistically significantly higher total DVAS awareness scores (respectively; p=0.030, p=0.038). It was found that those not exposed to and not witnessing domestic violence had statistically significantly higher Results of Domestic Violence awareness scores (p=0.018, p=0.041). Individuals who had lost their fathers were found to have statistically significantly higher Acceptance of Domestic Violence awareness scores (p=0.027). Additionally, those belonging to nuclear families were found to have statistically significantly higher Normalization of Domestic Violence awareness scores (p=0.003).

DISCUSSION

The present study aimed to investigate the awareness and attitudes of medical students towards domestic violence, as well as their perceptions and professional attitudes regarding physicians' roles in addressing domestic violence. The findings revealed several noteworthy observations regarding the participants' sociodemographic characteristics, exposure to domestic violence, educational background, and their scores on the Domestic Violence Awareness Scale (DVAS) and Domestic Violence Attitude Scale (DVAtS).

Regarding exposure to domestic violence, a notable proportion (52%) of students reported either being exposed to or witnessing domestic violence. This finding underscores the importance of addressing domestic violence awareness and education among medical students, as healthcare professionals play a crucial role in identifying and addressing such issues in clinical settings. In the literatüre, there are studies carried on nursing students[5,6,9,14-16] and medical students[17,18] the results were in accordance with our study. The study by Usta et al. (2014) conducted

among Lebanese medical students similarly highlights the significant exposure to domestic violence, although it does not specify a percentage. However, it provides crucial insights into the potential consequences of such exposure, particularly on students' ability to empathize with and assist survivors.[17] Similarly, Ambuel et al. (2003) explored the impact of exposure to violence on medical students' well-being and their perceived capacity to assist battered women. Their findings indicate that both female and male medical students who have been exposed to violence may experience diminished well-being, which in turn could affect their confidence and competence in helping survivors of domestic violence.[18]

The participants' educational level also revealed that a considerable percentage had received formal education on domestic violence during their medical school training.

In our study, total domestic violence awareness and domestic violence attitude scales and subscale scores were higher than literature.[19-21] For example, in Şahin and Dişsiz's (2009) [13] development study of the attitudes towards domestic violence scale among healthcare workers, and in Kay and Robin's (2000)[19] examination of attitudes towards domestic violence among Romanian and U.S. university students. Additionally, Gezgin Yazici, Batmaz, and Okten's (2022)[21] study on the awareness and attitudes towards domestic violence in Turkish society reported lower scores. One factor is that our study was conducted with clinical stage and final year (4th, 5th, 6th year) medical students, and it is a school preferred by successful students.

Table 5. The relationship of sociodemographic variables and domestic violence related features of participants and DVAtS

	DVAtS total		1.Normalization of the violence		2. Generalization of the violence		3. Causalization of the violence		4. Hiding violence	
	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P
Gender										
Female	60.86±3.31	<0.001	24.10±1.41	<0.001	14.57±0.78	0.098	12.69±1.37	0.089	9.48±1.01	<0.001
Male	57.20±7.74		22.11±3.74		14.09±1.93		12.27±1.84		8.71±1.77	
Chronic disease										
No	58.90±6.38	0.147	23.09±3.07	0.541	14.28±1.48	0.147	12.49±1.65	0.801	9.02±1.53	0.013
Yes	60.71±3.57		23.73±1.75		14.71±0.61		12.57±1.42		9.68±0.80	
Maternal education status										
Primary school and lower	57.37±9.17		22.46±4.08		14.00±1.93		12.06±2.09		8.84±2.18	
Middle school and high school	58.55±5.99	0.046	23.07±3.20	0.416	14.28±1.79	0.420	12.15±1.53	0.008	9.03±1.35	0.562
University and higher	59.86±5.01		23.41±2.41		14.46±1.00		12.73±1.48		9.24±1.28	
Paternal education status										
Primary school and lower	59.00±8.93		23.42±3.67		14.28±1.89		12.50±2.34		8.78±2.35	
Middle school and high school	57.12±9.04	0.241	22.33±4.45	0.228	13.87±2.35	0.254	12.15±1.82	0.368	8.76±1.88	0.534
University and higher	59.69±4.70		23.38±2.31		14.47±0.96		12.58±1.49		9.25±1.23	
Parents cohabitation status										
Parents living together	58.87±6.27		23.06±3.02		14.31±1.45		12.39±1.62		9.10±1.50	
Parents living apart	61.25±3.72	0.094	23.83±1.64	0.066	14.50±0.79	0.639	13.66±1.23	0.027	9.25±1.21	0.655
Mother died	60.75±4.19		23.50±2.38		14.50±1.00		13.50±1.29		9.25±0.95	
Father died	62.16±1.80		24.83±0.38		14.83±0.38		12.91±1.31		9.58±0.99	
Family structure										
Nuclear family	59.42±5.67	0.213	23.30±2.78	0.061	14.38±1.33	0.221	12.53±1.53	0.641	9.19±1.36	0.057
Extended family	54.60±10.77		21.00±4.37		13.80±2.14		11.80±2.93		8.00±2.62	
Q1.Have you ever been exposed to domestic violence (physical, sexual or psychological)?										
No	59.45±5.96	0.057	23.33±2.88	0.040	14.37±1.38	0.685	12.51±1.65	0.558	9.22±1.36	0.094
Yes	58.02±6.27		22.56±2.92		14.28±1.39		12.46±1.44		8.71±1.82	
Q2. Have you ever witnessed domestic violence?										
No	59.48±6.39	0.020	23.26±3.10	0.116	14.35±1.49	0.403	12.55±1.70	0.207	9.30±1.34	0.009
Yes	58.69±5.27		23.08±2.48		14.37±1.14		12.41±1.44		8.82±1.60	
Q3. Have you ever taken lesson on domestic violence during your medical school education?										
No	59.09±6.51	0.799	23.14±3.09	0.740	14.33±1.54	0.564	12.50±1.65	0.906	9.10±1.52	0.773
Yes	59.43±4.92		23.32±2.45		14.40±0.96		12.50±1.54		9.20±1.31	
Q4. If you have taken lesson on domestic violence, do you consider this lesson sufficient?										
No	59.22±4.66	0.390	23.31±2.45	0.824	14.33±1.04	0.566	12.44±1.34	0.326	9.13±1.23	0.205
Yes	59.75±5.37		23.34±2.48		14.51±0.82		12.58±1.84		9.31±1.44	
Q5. If you have not taken lesson on domestic violence, would you like to study?										
No	58.94±7.47	0.428	23.08±3.37	0.550	14.27±1.48	0.838	12.66±2.00	0.220	8.91±1.82	0.607
Yes	59.13±6.24		23.14±3.03		14.35±1.57		12.45±1.54		9.17±1.42	

Table 6. The relationship of sociodemographic variables and domestic violence related features of participants and DVAS

	DVAS total		1. Definition of domestic violence		2. Results of domestic violence		3. Acceptance of domestic violence		4. Normalization of domestic violence	
	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P	Mean (SD)	P
Gender										
Female	58.52±2.63	<0.001	14.85±0.58	0.009	14.84±0.54	0.049	14.23±1.37	0.003	14.59±1.37	<0.001
Male	56.57±4.71		14.53±1.10		14.57±1.28		13.53±1.99		13.92±1.83	
Chronic disease										
No	57.43±4.09	0.598	14.69±0.90	0.674	14.70±1.01	0.690	13.83±1.80	0.266	14.19±1.75	0.522
Yes	58.65±1.90		14.78±0.70		14.81±0.60		14.31±1.11		14.73±0.60	
Maternal education status										
Primary school and lower	57.28±6.11		14.59±1.18		14.62±1.77		13.65±2.00		14.40±1.68	
Middle school and high school	57.75±3.65	0.046	14.71±0.89	0.416	14.71±0.80	0.420	13.88±1.77	0.008	14.44±1.53	0.562
University and higher	57.68±3.22		14.73±0.78		14.75±0.73		13.99±1.62		14.20±1.66	
Paternal education status										
Primary school and lower	56.35±9.12		14.35±1.59		14.21±2.66		13.57±2.68		14.21±2.39	
Middle school and high school	58.17±2.28	0.241	14.76±0.66	0.228	14.84±0.48	0.254	13.94±1.33	0.368	14.61±0.74	0.534
University and higher	57.62±3.40		14.72±0.83		14.73±0.76		13.94±1.70		14.22±1.70	
Parents cohabitation status										
Parents living together	57.53±4.03		14.69±0.90		14.73±0.98		13.85±1.79		14.24±1.71	
Parents living apart	57.66±2.05	0.094	14.66±0.77	0.066	14.50±0.90	0.639	14.08±1.08	0.027	14.41±1.08	0.655
Mother died	59.00±1.54		15.00±0.00		15.00±0.00		14.50±1.00		14.50±1.00	
Father died	59.00±1.34		14.91±0.28		14.66±0.88		14.66±0.49		14.75±0.45	
Family structure										
Nuclear family	57.86±3.11	0.030	14.76±0.68	0.091	14.76±0.71	0.455	13.98±1.54	0.293	14.34±1.55	0.003
Extended family	52.80±10.44		13.50±2.46		13.80±3.15		12.50±3.80		13.00±2.70	
Q1.Have you ever been exposed to domestic violence (physical, sexual or psychological)?										
No	57.86±3.24	0.038	14.77±0.66	0.221	14.79±0.69	0.018	13.96±1.66	0.418	14.32±1.62	0.058
Yes	56.58±5.84		14.38±1.47		14.38±1.72		13.71±1.95		14.10±1.66	
Q2. Have you ever witnessed domestic violence?										
No	57.72±3.52	0.241	14.76±0.70	0.818	14.73±0.72	0.041	13.95±1.76	0.304	14.20±1.79	0.734
Yes	57.50±4.39		14.61±1.11		14.58±1.29		13.84±1.64		14.44±1.28	
Q3. Have you ever taken lesson on domestic violence during your medical school education?										
No	57.66±4.02	1.000	14.74±0.83	0.260	14.74±1.01	0.263	13.93±1.70	0.973	14.23±1.76	0.816
Yes	57.60±3.45		14.63±0.99		14.68±0.84		13.89±1.74		14.39±1i34	
Q4. If you have taken lesson on domestic violence, do you consider this lesson sufficient?										
No	87.75±3.01	0.561	14.66±0.92	0.727	14.62±0.96	0.467	13.95±1.44	0.676	14.51±1.01	0.772
Yes	57.37±4.40		14.58±0.98		14.79±0.61		13.79±2.16		14.20±1.73	
Q5. If you have not taken lesson on domestic violence, would you like to study?										
No	58.86±6.12	0.406	14.55±1.18	0.187	14.61±1.67	0.734	13.69±2.03	0.456	14.00±2.21	0.845
Yes	57.90±3.09		14.80±0.68		14.78±0.70		14.00±1.59		14.30±1.60	

Analysis of the participants' scores on the DVAS and DVAtS highlighted several significant findings. Firstly, women exhibited significantly higher scores on both total and subgroup domestic violence attitudes compared to men. This aligns with existing literature indicating that women tend to have greater awareness and sensitivity towards domestic violence issues, possibly due to their higher likelihood of experiencing or witnessing such incidents.[9,21]

Moreover, participants who reported not witnessing domestic violence had significantly higher DVAtS attitude scores, indicating a positive association between lack of exposure to domestic violence and more favorable attitudes towards addressing and combating it. Similarly, individuals not exposed to domestic violence exhibited higher scores on the normalization of violence attitude subscale, suggesting a lower tolerance for normalized forms of domestic violence among this subgroup.

Interestingly, higher maternal education levels (university and above) were associated with higher casualization of violence attitude scores among participants. This finding underscores the complex interplay between sociodemographic factors and attitudes towards domestic violence, highlighting the need for nuanced approaches in educational and intervention strategies. In the literature, no relationship has been found between family education level and domestic violence.[19-21]

Furthermore, participants with chronic illnesses and those not witnessing domestic violence had higher hiding violence attitude scores, indicating a potential reluctance or discomfort in acknowledging and addressing domestic violence issues among these subgroups.

Analysis of the participants' scores on the DVAS revealed significant gender differences, with women consistently exhibiting higher awareness scores across total and subgroup domestic violence categories compared to men. This gender disparity in awareness levels highlights the need for targeted educational initiatives and awareness campaigns to bridge this gap and enhance male participants' understanding and recognition of domestic violence issues.

Additionally, individuals not exposed to and not witnessing domestic violence exhibited higher scores on the Results of Domestic Violence awareness subscale, indicating a more comprehensive understanding of the consequences and impacts of domestic violence among this subgroup. This highlights the importance of fostering empathy and understanding among individuals with limited exposure to domestic violence to enhance their capacity to support and advocate for affected individuals.

Moreover, participants who had lost their fathers exhibited higher Acceptance of Domestic Violence awareness scores, suggesting a potential influence of familial experiences and dynamics on individuals' perceptions of domestic violence. This underscores the need for targeted interventions and support systems to address the unique needs and challenges faced by individuals who have experienced familial loss and trauma.

This study have some limitations. The study relied on voluntary participation via social media groups, potentially introducing sampling bias as individuals who actively engage in these platforms may not be representative of the entire student population and the findings are specific to medical students at Hacettepe University Faculty of Medicine, limiting the generalizability of the results to other student populations or institutions.

Overall, the findings of this study provide valuable insights into the awareness, attitudes, and perceptions of medical students regarding domestic violence, highlighting the need for comprehensive educational initiatives and intervention strategies to enhance awareness, sensitivity, and professional attitudes towards addressing domestic violence in clinical practice. Future research should continue to explore the multifaceted determinants and implications of domestic violence awareness and attitudes among healthcare professionals to inform targeted interventions and policy initiatives aimed at combating this pervasive societal issue.

CONCLUSION

This study sheds light on the awareness, attitudes, and perceptions of medical students regarding domestic violence, highlighting several key findings. These findings underscore the importance of targeted educational initiatives aimed at enhancing awareness, sensitivity, and professional attitudes towards addressing domestic violence in clinical practice. By equipping future healthcare professionals with the necessary knowledge and skills to identify, intervene, and support individuals affected by domestic violence, healthcare systems can play a vital role in addressing this pervasive societal issue.

Overall, this study contributes to the growing body of literature on domestic violence awareness and attitudes among medical students, providing valuable insights that can inform educational programs, policy initiatives, and clinical practice guidelines aimed at combating domestic violence and promoting the health and well-being of individuals and communities affected by this issue. Further research is warranted to explore the multifaceted determinants and implications of domestic violence awareness and attitudes among healthcare professionals, with a focus on developing targeted interventions and support systems to address this complex societal challenge.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study protocol was examined by Hacettepe University Ethics Committee and was approved on July 05, 2022 with the report numbered GO22/73917.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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REFERENCES

1. Ministry of Family and Social Services 2024 [cited 12 May 2024] Available from:https://www.aile.gov.tr/ksgm/siddete-maruz-kalindiginda/
2. Krug Etienne G, Dahlberg Linda L, Mercy James A, et al. World report on violence and health. 2002 [cited 12 May 2024]; World Health Organization. Available from:https://iris.who.int/handle/10665/42495
3. World Health Organization. Global status report on violence prevention 2014. 2014 [cited 12 May 2024]; World Health Organization. Available from:https://apps.who.int/iris/handle/10665/145086
4. Şahin N, Dişsiz M. Sağlık çalışanlarında aile içi şiddete yönelik tutum ölçeği geliştirme çalışması. Uluslararası İnsan Bilimleri Derg 2009;6(2):263-74.
5. Yaman EŞ. Acil servis hemşirelerinin kadına yönelik aile içi şiddete ilişkin rol ve sorumlulukları. FÜ Sağ Bil Tıp Derg 2012; 26(1):49-54.
6. Çatak A.T. Birinci basamakta çalışan hekim, ebe ve hemşirelerin kadına yönelik aile içi şiddeti tanıma ve bildirim konusundaki tutum ve davranışları. 2015. Pamukkkale Üniversitesi Yüksek Lisans Tezi. Denizli.
7. Kurt G, Gün İ. Sağlık personelinin istismar, ihmal ve aile içi şiddetle karşılaşma durum ve tutumları. J Forensic Med 2017;31:2.
8. Aşırdizer M. Acil servislere başvuran çocuk ve kadın istismarı olgularına hekimlerin yaklaşımı. Turkiye Klinikleri J Surg Med Sci 2006;2(50):39-48.
9. Tunçel Kaynar E, Dündar C, Peşken Y. Ebelik ve hemşirelik öğrencilerinin aile içi şiddet konusunda bilgi ve tutumlarının değerlendirilmesi. Genel Tıp Derg 2007;17(2):105-10.

10. Şahin Tezel F, Özyürek A. Üniversite öğrencilerinin aile içi şiddete yönelik görüşleri. Akademik Bakış Uluslararası Hakemli Sosyal Bilimler Derg 2014;40.
11. Toprak Ergönen A, Özdemir M, Sönmez E, Can İ, Köker M, Salaçin S. Dokuz Eylül Üniversitesi Hukuk Fakültesi Öğrencilerinin 'Aile İçi Şiddete' Yaklaşımları. Adli Bilimler Derg 2006;5(4):7-13.
12. Özyürek A, Kurnaz FB. Aile içi şiddet farkındalığı ölçeği: Güvenilirlik ve geçerlilik çalışması. Kalem Eğitim ve İnsan Bilimleri Derg 2019;9(1):227-50.
13. Şahin NH, Dişsiz M. Development study of attitudes towards domestic violence scale in healthcare workers. J Hum Sci 2009;6(2):263–74.
14. Ali P, McGarry J, Younas A, Inayat S, Watson R. Nurses', midwives' and students' knowledge, attitudes and practices related to domestic violence: A cross-sectional survey. J Nurs Manag 2022;30(6):1434-44.
15. Doran F, Hutchinson M. Student nurses' knowledge and attitudes towards domestic violence: results of survey highlight need for continued attention to undergraduate curriculum. J Clin Nurs 2017;26(15-16):2286-96.
16. Bahadır Yılmaz E, Öz F. Assessing the Relation Between Attitudes Towards Gender Roles and Domestic Violence of Nursing And Paramedic Students. Clin Exp Health Sci 2018;8(3):160-5.
17. Usta J, Hlais S, Farhat HA, Romani M, Bzeih H, Abdo L. Lebanese medical students' exposure to domestic violence: does it affect helping survivors? Fam Med 2014;46(2):112-9.
18. Ambuel B, Butler D, Hamberger LK, Lawrence S, Guse CE. Female and male medical students' exposure to violence: impact on well-being and perceived capacity to help battered women. J Comp Fam Stud 2003;34:113-41.
19. Kay MK, Robin LT. Attitudes toward domestic violence among romanian and U.S. university students. Women Politics 2000;21:3:27-52.
20. Lin K, Sun IY, Wu Y, Jianhong Liu. College students' attitudes toward ıntimate partner violence: a Comparative study of China and the U.S. J Fam Viol 2015;31:179-89.
21. Gezgin Yazici H, Batmaz M, Okten C. Awareness of and attitudes towards domestic violence in Turkish Society. Galician Med J 2022;29(3):E202234.

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Original Article / Orijinal Araştırma

Analytical Performance Evaluation of a Clinical Microbiology Laboratory Using Sigma Metrics

Sigma Metriklerini Kullanarak Bir Klinik Mikrobiyoloji Laboratuvarının Analitik Performansının Değerlendirilmesi

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Abstract

Aim: Six sigma is a quality metric for performance evaluation and comparison. It can be used as a guide in determining internal quality control (IQC) strategies and frequency. In our study, we aimed to perform analytical performance evaluation using six sigma method for frequently used test parameters in microbiology laboratory.

Material and Method: A six-month analysis was conducted on quality control data for HBsAg, Anti-HCV, and Anti-HIV tests. The Sigma metrics were calculated for the parameters tested on the Roche Cobas 601 autoanalyzer. The quality goal index (QGI) was calculated to identify the reason for analytes with low sigma values.

Results: The sigma metrics demonstrated varied performance across the tests. The HBsAg test sigma values ranged from 2.0 to 8.8, generally remaining within an acceptable range (≥3). The Anti-HIV test yielded mixed results, with some sigma values dropping below the acceptable threshold in certain months, indicating the necessity for periodic review and adjustment. In contrast, the Anti-HCV test demonstrated a consistently low sigma value (average 2.84). When the average sigma value was calculated over a six-month period, Anti-HCV was the only analyte with a sigma value less than 3 and considered unacceptable.

Conclusion: Our findings demonstrate the necessity of continuous monitoring, staff training, and rigorous quality control measures. By addressing the specific issues identified through Sigma metrics, we can achieve higher standards of accuracy and precision, which ultimately contributes to improved healthcare quality.

Keywords: Six sigma, sigma metrics, analytical performance, Quality control, quality goal index

Öz

Amaç: Altı sigma, performans değerlendirmesi ve karşılaştırması için bir kalite ölçütüdür. İç kalite kontrol (İKK) stratejilerinin ve sıklığının belirlenmesinde bir rehber olarak kullanılabilir. Çalışmamızda, mikrobiyoloji laboratuvarında sık kullanılan test parametreleri için altı sigma yöntemini kullanarak analitik performans değerlendirmesi yapmayı amaçladık.

Gereç ve Yöntem: HBsAg, Anti-HCV ve Anti-HIV testleri için kalite kontrol verileri üzerinden altı aylık bir analiz yapılmıştır. Roche Cobas 601 otoanalizöründe test edilen parametreler için Sigma metrikleri hesaplanmıştır. Düşük sigma değerlerine sahip analitlerin nedenini belirlemek için kalite hedef indeksi (QGI) hesaplanmıştır.

Bulgular: Sigma metrikleri testler arasında farklı performans göstermiştir. HBsAg testi sigma değerleri 2,0 ila 8,8 arasında değişmiş ve genellikle kabul edilebilir bir aralıkta (≥3) kalmıştır. Anti-HIV testi karışık sonuçlar vermiş, bazı sigma değerleri belirli aylarda kabul edilebilir eşiğin altına düşerek periyodik inceleme ve ayarlama gerekliliğine işaret etmiştir. Buna karşılık, Anti-HCV testi sürekli olarak düşük bir sigma değeri göstermiştir (ortalama 2,84). Altı aylık bir dönem boyunca ortalama sigma değeri hesaplandığında, Anti-HCV sigma değeri 3'ün altında olan ve kabul edilemez olarak değerlendirilen tek analit olmuştur.

Sonuç: Bulgularımız sürekli izleme, personel eğitimi ve titiz kalite kontrol önlemlerinin gerekliliğini ortaya koymaktadır. Sigma ölçümleri aracılığıyla belirlenen spesifik sorunları ele alarak, daha yüksek doğruluk ve kesinlik standartlarına ulaşabiliriz ve bu da sonuçta sağlık hizmetlerinin kalitesinin artmasına katkıda bulunur.

Anahtar Kelimeler: Altı sigma, sigma metrikleri, analitik performans, kalite kontrol, kalite hedef endeksi

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INTRODUCTION

The test results of clinical laboratories are indispensable for clinicians during screening, diagnosis and follow-up of patients.[1] The results obtained from clinical laboratories play a role in more than 70% of medical decisions, so the quality of laboratory services directly affects the quality of health care. Laboratory results that guide clinical decisions should be accurate, reliable and timely.[2]

The functioning in the medical laboratory is considered as preanalytical, analytical and post analytical processes and the approximate error rates in each of them are 62%, 23% and 15%, respectively.[3] In many laboratories, the follow-up of analytical quality-related processes is ignored unless there is no clinical feedback about the tests other than standard practices. It is assumed that automated systems used according to manufacturers' directives provide sufficiently high quality results, but it is the responsibility of the laboratory to ensure standards and implement quality procedures.

Defining quality specifications for a laboratory is a challenging process, and clinical laboratories routinely implement internal quality control (IQC) and external quality assessment (EQA), including proficiency testing programmes, to assess and improve analytical quality.[4] IQC is applied at least at two levels for all parameters. It helps to monitor test results immediately and to decide whether the results are reliable enough to be reported. On the other hand, EQA is performed by an independent organisation. Monthly or annually, a certain number of EQA provide information about the accuracy or bias in the laboratory's systems and methods, but do not give us a clear number of errors and biases in laboratory results.[5,6]

The 6 sigma methodology, which was first used in the evaluation of errors in the industrial field, has become a set of rules that have found widespread use in the classification of laboratory errors over time.[7] With sigma measurement, it is possible to objectively evaluate the performance of a method. This measure determines the process performance as the error rate per million opportunities.[8,9] The main analytical criteria in clinical laboratory test measurements are bias and repeatability (CV). The sigma value is calculated using the total permissible error (TEa), bias and CV.[3,10,11] The sigma value gives us an idea of the frequency of error occurrence; high sigma values mean low analytical error and acceptable test results, while low sigma values mean increased error and unacceptable results at the end of the process.[9]

6 sigma assessment can be used as an evaluation method to determine the frequency of IQC and to formulate quality control strategies. It is useful to apply these criteria in the daily analytical processes of clinical laboratories to obtain accurate and reliable measurement results.

In our study, we aimed to use this method, which is frequently used in analytical performance evaluation of parameters tested in clinical biochemistry laboratories, in analytical performance evaluation for certain test parameters in microbiology laboratories and to reveal quality control strategies to achieve desired/targeted quality test results according to Six sigma results.

MATERIAL AND METHOD

Internal and external quality control (IQC-EQA) data of HBsAg, Anti HCV and Anti HIV tests performed on Roche Cobas 601 (Roche Diagnostics, Tokyo, Japan) autoanalyzer in the Medical Microbiology Laboratory of Afyonkarahisar Health Sciences University Health Application and Research Centre (AFSU SUAM) for the period of 01 July - 31 December 2022 were retrospectively evaluated. The study was conducted with the approval of the Clinical Research Ethics Committee at Afyonkarahisar Health Sciences University (Decision: 2023/194).

CV (%) values were calculated using 2-level QC data for HBsAg and Anti HCV tests and 3-level QC data for Anti HIV tests analysed within 6 consecutive months, and Bias (%) values were calculated using the data in the EQA reports (RIQAS; Randox International Quality Assessment Scheme) for the same period.[12]

$$\text{CV\%} = \text{Standard Deviation/lab mean} \times 100$$

$$Bias = \left(\frac{\text{Lab EQAS Result} - \text{Peer group mean}}{\text{peer group mean}}\right) \times 100$$

The sigma value was calculated using the coefficient of variation (CV) obtained from the IQC data, the bias obtained from the target values of the EQA data and the total permissible error (TEa), as follows

$$\text{Sigma} = (\%TEa - \%Bias) \div \%CV$$

Sigma values ">5", "4-5", "3- 4" and "<3" shall be categorised as "very good", "good", "minimum" and "unacceptable" respectively. If a low sigma value is detected in the measurements, the reason for the low sigma value for the relevant test parameter will be determined by calculating the quality goal index (QGI). A QGI value <0.8 indicates that the problem is caused by imprecision, >1.2 by inaccuracy, and 0.8-1.2 by both.[4,13]

$$QGI = bias/1.5X\%CV$$

will be calculated with formula.

All calculations were performed using Microsoft Excel software programme.

Table 1. CV(%) values obtained from internal quality control studies in 6-month period

Parameters	July CV%		August CV%		September CV%		October CV%		November CV%		December CV%	
	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos
HBsAg	4.13	4.95	8.86	6.15	1.93	4.95	5.48	4.91	2.56	6.98	5.64	8.18
Anti-HCV	4.62	10.55	9.14	8.85	4.79	8.94	6.29	8.57	6.29	8.75	8.62	9.01
Anti-HIV	9.13	7.0	9.16	8.95	7.0	5.83	9.68	9.09	5.87	8.48	7.85	7.06

Table 2. 6-month average Bias (%) values obtained from external quality control studies

Parameters	July Bias%	August Bias%	September Bias%	October Bias%	November Bias%	December Bias%
HBsAg	1.41	2.44	5.15	3.63	3.7	6.6
Anti-HCV	-0.59	2.27	0	2.22	4.34	-2.08
Anti-HIV	2.02	2.79	3.62	5.55	0.23	2.56

Table 3. Sigma values obtained for each level of internal quality control in 6-month period

Parameters	July		August		September		October		November		December		Average	
	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos	Neg	Pos
HBsAg	6.0	6.0	2.88	3.83	20	5	4.4	5.5	11	3.67	3.8	2.38	8.0	4.4
Anti-HCV	6.25	2.5	2.56	2.88	6.25	3.13	3.83	2.88	3.5	2.63	3.38	3	4.3	2.84
Anti-HIV	2.56	3.29	2.56	2.88	3.14	4.4	2.22	2.22	5	3.13	3.29	3.29	3.13	3.20

RESULTS

For HBsAg, Anti HCV and Anti HIV parameters in 6 months period, %CV and %Bias values were calculated using both levels of IQC analysis data and %Bias values were calculated using EQA data and presented in **Tables 1** and **2**, respectively. TEa was taken as 25% according to ISO recommendations and sigma values were calculated (**Table 3**).

The sigma metrics derived from the internal quality control (IQC) and external quality assessment (EQA) data demonstrated varied performance across the tests. For instance, the HBsAg test showed sigma values ranging from 2.0 to 8.8, which fluctuated but were generally within an acceptable range (≥3) in most instances. In contrast, the Anti-HCV test showed consistently low sigma values (average 2.84), indicating persistent analytical issues. The Anti-HIV test had mixed results, with some sigma values dropping below the acceptable threshold in certain months, highlighting the need for periodic review and adjustment.

When the average sigma value was calculated over a six-month period, Anti-HCV was the only analyte with a sigma value less than 3 that was considered unacceptable and found to be problematic. The sigma values of the monthly two-level control samples for all three parameters were examined, and the results that were found to be less than 3 and considered unacceptable were presented in detail in **Table 4**. The QGI was calculated to pinpoint whether the low sigma values were due to imprecision or inaccuracy. For the Anti-HCV test, QGI values often indicated imprecision issues, as values were generally below 0.8.[4] This suggests that the variability within the test results (CV%) is a primary contributor to the low sigma performance rather than a consistent bias (error in accuracy). This distinction is crucial for developing corrective actions that are specific to the type of error encountered.[12]

Table 4: Parameters with low sigma values and its reason

Parameters / Time zone	QC level	CV%	Bias%	Sigma	QGI	Problem
HBsAg						
August	Neg	8.86	2.44	2.88	0.18	imprecision
December	Poz	8.18	6.6	2.38	0.53	imprecision
Anti-HCV						
July	Poz	10.55	-0.59	2.5	0.03	imprecision
August	Neg	9.14	2.27	2.56	0.20	imprecision
	Poz	8.85	2.27	2.88	0.17	imprecision
October	Poz	8.57	2.22	2.88	0.17	imprecision
November	Poz	8.75	4.34	2.63	0.33	imprecision
6-month average	Poz	9.11	1.02	2.84	0.07	imprecision
Anti-HIV						
July	Neg	9.13	2.02	2.56	0.14	imprecision
August	Neg	9.16	2.79	2.56	0.20	imprecision
	Poz	8.95	2.79	2.88	0.21	imprecision
October	Neg	9.68	5.55	2.22	0.38	imprecision
	Poz	9.09	5.55	2.22	0.40	imprecision

DISCUSSION

The application of sigma metrics in clinical laboratories has served as a pivotal tool in the reduction of errors, offering a multifaceted approach to quality assurance. They are utilized in the monitoring and auditing of test performance, the establishment of individual quality criteria, and the formulation of quality improvement plans.[14-16]

In the present study, the application of Sigma metrics to evaluate the analytical performance of clinical microbiology laboratories, specifically in the measurement of HBsAg, Anti-HCV, and Anti-HIV parameters, provides a quantitative framework for assessing and improving laboratory quality. This study conducted over six months highlights several critical findings and implications for laboratory practice.

The results indicate that most parameters achieved acceptable Sigma values, with the exception of Anti-HCV, which consistently showed a Sigma value of less than 3, categorizing it as unacceptable. The persistent low Sigma values for Anti-HCV suggest that this analyte is prone to higher analytical errors compared to HBsAg and Anti-HIV. The root cause analysis using the Quality Goal Index (QGI) identified imprecision as the primary issue, indicated by a QGI value significantly below 0.8 for multiple months. In accordance with the findings, the essential corrective and preventive measures were promptly implemented.

Imprecision in laboratory measurements can stem from various factors, including operator variability, instrument calibration, and reagent quality. The study's findings emphasize the need for targeted quality improvement initiatives for Anti-HCV testing. These could include more stringent internal quality control procedures, regular calibration and maintenance of analytical instruments, and enhanced training for laboratory personnel.

The evaluation also revealed that while HBsAg and Anti-HIV parameters generally met the acceptable Sigma criteria, occasional low Sigma values were still observed. For instance, HBsAg showed issues with imprecision in specific months, necessitating continuous monitoring and corrective actions to maintain high analytical performance consistently. This underscores the importance of regular performance evaluations and prompt responses to any identified issues to prevent them from affecting clinical decisions.

Furthermore, the use of Sigma metrics as a performance evaluation tool in clinical microbiology laboratories offers several advantages. It provides an objective measure of error rates, allowing for a clear identification of areas needing improvement. Implementing Six Sigma principles helps in systematically reducing errors, enhancing process efficiency, and ultimately leading to more reliable and accurate test results, which are crucial for patient care.

In the broader context of laboratory medicine, while the effectiveness of Six Sigma metrics in improving analytical performance in clinical biochemistry laboratories has been validated by numerous studies, no studies have yet addressed the potential of these metrics in microbiology laboratories.[12,15,17-19] Chauhan et al. highlighted the importance of Six Sigma in measuring and improving the quality of biochemistry assays, demonstrating significant error reduction and process improvement.[1] Similarly, Mao et al. evaluated the analytical quality in a clinical biochemistry laboratory using Six Sigma metrics, finding that the approach significantly enhanced the reliability of test results.[3] Moreover, Hens et al. underscored the critical role of Sigma metrics in assessing the analytical quality of clinical chemistry assays, emphasizing the importance of setting rigorous allowable total error (TEa) targets to achieve high standards of accuracy and precision.[10]

CONCLUSION

In conclusion, the study demonstrates that while Sigma metrics are a valuable tool for evaluating and improving laboratory performance, continuous efforts are necessary to address areas of imprecision and maintain high-quality standards. By focusing on the identified problematic areas and implementing targeted quality control strategies, clinical microbiology laboratories can enhance their analytical performance, ensuring accurate and reliable test results that are essential for effective patient management. This study's findings align with existing literature on Six Sigma's efficacy in biochemistry laboratories, reinforcing its applicability across various domains of clinical laboratory medicine.

The findings from our laboratory demonstrate the necessity of continuous monitoring, staff training, and rigorous quality control measures. By addressing the specific issues identified through Sigma metrics, laboratories can achieve higher standards of accuracy and precision, which ultimately contributes to improved healthcare quality.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was conducted with the approval of the Clinical Research Ethics Committee at Afyonkarahisar Health Sciences University (Date: 07.04.2024, Decision No: 2023/194).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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REFERENCES

1. Chauhan K P, Patel J D, Trivedi A, Six sigma in clinical biochemistry: It matters, measure it. Int J Clin Biochem Res 2017;4(3):270-4
2. International Organization for Standardization (ISO). ISO/IEC 17025. General requirements for the competence of testing and calibration of laboratories, 2005
3. Mao X, Shao J, Zhang B, Wang Y. Evaluating analytical quality in clinical biochemistry laboratory using Six Sigma. Biochem Med (Zagreb). 2018;28(2):020904.
4. Westgard S, Westgard QC. Six Sigma metric analysis for analytical testing processes. Abbott MS. 2009;9:04.
5. Yadav R, Bhartiya JP, Verma SK, Nandkeoliar MK. External quality assessment scheme (EQAS): Our experience as a participating laboratory. IJRRMS. 2013;3(4):1-4.

6. Wang RY, Strong DM. Beyond accuracy: what data quality means to data consumers. JMIS 1996:12(4):5–33.
7. Plebani M, Sciacovelli L, Aita A, Padoan A, Chiozza ML. Quality indicators to detect pre-analytical errors in laboratory testing. Clin Chim Acta. 2014;432:44-8.
8. Nar R, Emekli DI. The Evaluation of Analytical Performance of Immunoassay Tests by using Six-sigma Method. J Med Biochem. 2017;36(4):301-8.
9. Nevalainen D, Berte L, Kraft C, Leigh E, Picaso L, Morgan T. Evaluating laboratory performance on quality indicators with the six sigma scale. Arch Pathol Lab Med. 2000;124(4):516-9.
10. Hens K, Berth M, Armbruster D, Westgard S. Sigma metrics used to assess analytical quality of clinical chemistry assays: importance of the allowable total error (TEa) target. Clin Chem Lab Med. 2014;52(7):973-80.
11. Zhou B, Wu Y, He H, Li C, Tan L, Cao Y. Practical application of Six Sigma management in analytical biochemistry processes in clinical settings. J Clin Lab Anal. 2020;34(1):e23126.
12. Sharma LK, Datta RR, Sharma N. Evaluation of Sigma Metrics of Commonly Assayed Biochemical Parameters in a Clinical Laboratory. J Clin Chem Lab Med. 2020;3(1):42.
13. Aggarwal K, Patra S, Acharya V, Mahapatra SK. Application of Six sigma metrics and Method decision charts in improvising clinical Chemistry laboratory performance enhancement. Int J Adv Med 2019;6:1524-30.
14. Zhang C, Zhao H, Wang J, Zeng J, Wang Z. The Application of Six Sigma Techniques in the Evaluation of Enzyme Measurement Procedures in China. Clin Lab. 2015;61(5-6):461-5.
15. Tran MT, Hoang K, Greaves RF. Practical application of biological variation and Sigma metrics quality models to evaluate 20 chemistry analytes on the Beckman Coulter AU680. Clin Biochem. 2016;49(16-17):1259-66.
16. Korkmaz, S.2022. Sigma metric evaluation with different TEa targets in clinical biochemistry. Int J Med Biochem 2022;5(2):120-4.
17. Thomas V, Desai PB, Mithrason AT. Evaluation of clinical biochemistry laboratory performance using sigma metrics. Int J Clin Biochem Res. 2018;5(4):604-7.
18. Yücel Ç, Ercan M, Kızılgün M. The evaluation of analytical performance of Total PSA and Free PSA tests by using 6-sigma method Turk Hij Den Biyol Derg 2021;78(2):153-8.
19. Dundar B, Halipci Topsakal HN. Evaluation of analytical performance of tests worked on the same brand devices wıth six sigma metrics. Turk J Clin Lab 2023;2:321-9.

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Original Article / Orijinal Araştırma

Evaluation of Patients with Acute Rheumatic Fever: 13-Year Experience of a Single Center

Akut Romatizmal Ateş Tanılı Hastaların Değerlendirilmesi: 13 Yıllık Tek Merkez Deneyimi

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Abstract

Aims: This study aims to retrospectively evaluate acute rheumatic fever's epidemiological and clinical characteristics in the Eastern Black Sea Region.

Material and Method: Demographic, clinical and laboratory characteristics of patients diagnosed with acute rheumatic fever in our clinic between January 2005 and December 2017 were evaluated from archival records.

Results: Included in the study were 175 patients with a mean age of 11±3.52 years (26 months–17 years), with a female/male ratio of 1.38. Patients are most frequently presented in February, May and August. Carditis was the most common (80%) major finding, while arthritis was seen in 51.4% and chorea in 16%. Erythema marginatum was present in only one patient. While isolated mitral valve involvement (54.3%) was most common in the patients with carditis, simultaneous mitral and aortic valve involvement was found in 30.7% of the patients, and isolated aortic valve involvement in 10%. Tricuspid regurgitation was seen in three (2.1%) patients with mitral involvement. Recurrence was detected in four (57.1%) of the seven patients who were incompatible with secondary prophylaxis. During clinical follow-up, two patients underwent mitral and aortic valve replacement. No mortality was observed in the patients.

Conclusion: Despite improving socio-economic conditions in Turkiye in recent years, acute rheumatic fever remains a significant health problem for the Eastern Black Sea Region.

Keywords: Acute rheumatic fever, carditis, children, rheumatic heart disease

Öz

Amaç: Bu çalışmada, Doğu Karadeniz Bölgesi'nde akut romatizmal ateşin epidemiyolojik ve klinik özelliklerini retrospektif olarak değerlendirmeyi amaçlanmıştır.

Gereç ve Yöntem: Kliniğimizde Ocak 2005 ile Aralık 2017 tarihleri arasında akut romatizmal ateş tanısı alan hastaların demografik, klinik ve laboratuvar özellikleri arşiv kayıtlarından değerlendirildi.

Bulgular: Çalışmaya yaş ortalaması 11±3,52 yıl (26 ay-17 yıl), kadın/erkek oranı 1,38 olan 175 hasta dahil edildi. Hastalar en sık Şubat, Mayıs ve Ağustos aylarında başvurdu. En sık görülen majör bulgu kardit (%80) iken, artrit %51,4, kore ise %16 oranında görüldü. Sadece bir hastada eritema marjinatum mevcuttu. Kardit hastalarında en sık izole mitral kapak tutulumu (%54,3) görülürken, eş zamanlı mitral ve aort kapak tutulumu hastaların %30,7'sinde, izole aort kapak tutulumu ise %10 oranında saptandı. Mitral tutulumu olan üç (%2,1) hastada triküspit yetersizliği görüldü. Sekonder profilaksi ile uyumsuz olan yedi hastanın dördünde (%57,1) nüks tespit edildi. Klinik takip sırasında iki hastaya mitral ve aort kapak değişimi uygulandı. Hastalarda mortalite görülmedi.

Sonuç: Türkiye'de son yıllarda sosyo-ekonomik koşullardaki iyileşmeye rağmen akut romatizmal ateş, Doğu Karadeniz Bölgesi için önemli bir sağlık sorunu olmaya devam etmektedir.

Anahtar Kelimeler: Akut romatizmal ateş, kardit, çocuk, romatizmal kalp hastalığı

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INTRODUCTION

Acute rheumatic fever (ARF) is a late autoimmune response secondary to tonsillopharyngitis due to group A streptococci. The disease is characterized by such widespread systemic involvement as migratory joint involvement, carditis, chorea, erythema marginatum, subcutaneous nodules and fever.[1]

Although most of the clinical findings in the acute period improve with short-term medical treatments, cardiac valve damage can be permanent. Rheumatic heart disease is the main cause of ARF-related mortality and morbidity.[2] Deaths are most common in low- and middle-income countries.[3]

In developed countries, the frequency of ARF and the prevalence of rheumatic heart disease developing secondary to the disease have decreased significantly since the 20th century.[4] This decrease has been associated with improved medical care, the widespread use of benzathine penicillin in the treatment of streptococcal tonsillopharyngitis, a decrease in the number of households and other socioeconomic improvements.[5]

According to the latest Jones criteria, which were revised due to differences between countries, populations with ARF frequency ≤2/100,000 in school-age children, and rheumatic heart disease prevalence ≤1/1000 at all ages were low-risk; others were defined as moderate- to high-risk. In addition, it has been suggested that populations for which sufficient reliable epidemiological data are not available should be included in the moderate- to high-risk group.[6]

There is limited data on the incidence of ARF in Turkiye, and it is in the moderate-high risk group according to the 2015 Jones criteria.[7] We aimed to evaluate the clinical, laboratory results, demographic data and prognosis of the patients who were followed up with the diagnosis of ARF in our Pediatric Cardiology Clinic between 2005 and 2017.

MATERIAL AND METHOD

We present here a retrospective analysis of cases diagnosed with ARF in our Pediatric Cardiology Clinic between January 2005 and December 2017.

The cases included in the study were diagnosed according to the modified Jones criteria from 1992 until 2015, and according to the revised Jones criteria after 2015.

The patients' age at the time of hospital admission, gender, month of admission, socioeconomic status, complaint and history were ascertained from the records, along with (i) whether or not the patient had a history of tonsillopharyngitis, (ii) whether or not the patient consulted a doctor for tonsillopharyngitis (iii) whether or not antibiotics were recommended to the patient (iv) the duration/dose, if recommended; and (v) family history of acute rheumatic fever.

Since the start date of the study in January 2005, transthoracic echocardiography was performed by a pediatric cardiologist in our department on all patients with suspected ARF, as well as the presence or absence of a murmur. The criteria recommended by the World Heart Federation were used to define pathological valve regurgitation and to rate the severity of cardiac involvement.[8]

The hemogram, CRP, ESR, anti-streptolysin O titer and throat swab culture results of the patients were recorded. PR distance was evaluated from electrocardiogram recordings.

A single dose of benzathine penicillin was administered to all patients as primary prophylaxis, and salicylate was used for the treatment of arthritis. In the acute period, strict bed rest was applied to all patients. Although steroid treatment in mild carditis cases is controversial, our clinical observations are that mild carditis did not regress with salicylate, and all cases with carditis were treated with steroids. Haloperidol treatment was started in all cases diagnosed with chorea. In the follow-up, secondary prophylaxis was given to all cases.

Compliance used for patients receiving regular secondary prophylaxis. Recurrence defined as a new episode of ARF with group A streptococcal infection two months after the end of treatment.

Ethical approval was obtained from the local ethics committee of our hospital (Decision Number: 2017/99) and was conducted by the Declaration of Helsinki. Informed consent was obtained from the families of all children participating in the study.

IBM SPSS Statistics (Version 23.0. Armonk, NY: IBM Corp.) was used for the statistical analysis of the findings obtained in the study. While evaluating the data, in addition to complementary statistical approaches (mean, standard deviation, frequency), a Chi-Square test and Fisher's Exact Chi-Square test were used to compare qualitative data. In evaluating the results; p-values below 0.05 were considered to be statistically significant. Variables were presented as mean±standard deviation (SD), number (n), and percent (%).

RESULTS

Included in the study were 175 patients with a mean age of 11±3.52 years (2–17 years), of which 102 (58.2%) were female. When compared according to age groups, the largest group was between the ages of 10-14 with 82 (46.8%) patients (**Figure 1**).

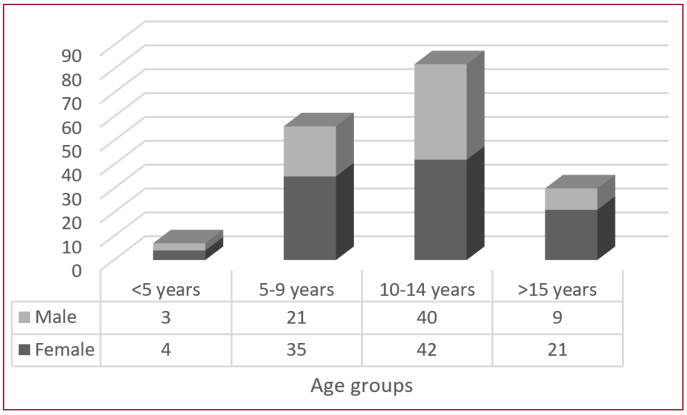

Figure 1. Distribution of ARF cases by age groups

The analysis of the distribution of cases by the years of diagnosis revealed the highest annual number of cases (n=28) was in 2017, while the lowest number of cases (n=7) was presented in 2005 (**Figure 2**). The disease was observed more often in spring (30%) and winter (29%), and mostly in February (13%), May (12%) and August (9%).

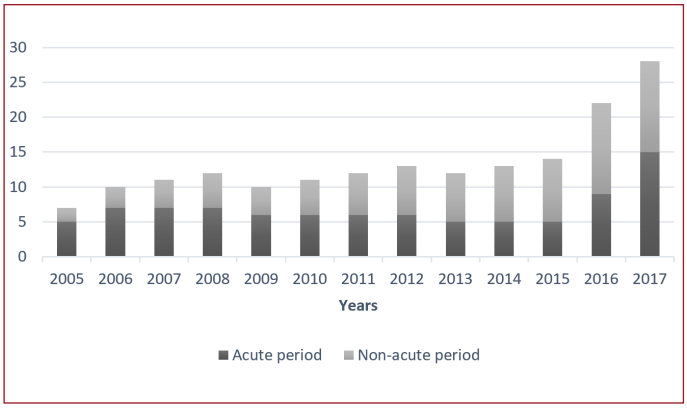

Figure 2. Distribution of ARF cases according to the years of diagnosis

Among the 47 (26.8%) patients with a history of tonsillopharyngitis before the diagnosis of acute rheumatic fever, 43 (24.6%) stated that they had consulted a doctor, and 28 (65.1%) of these were recommended antibiotics.

While 89 (51%) of the cases were in the acute period at the time of diagnosis, 86 (49%) cases were not in the acute period. Among the cases that were not in the acute period, 28 (16%) were referred to our department for chorea, and 18 (10.2%) incidentally detected murmur on physical examination. In these cases, valve involvement that could not be attributed to any other cause was diagnosed, and they were followed up with a diagnosis of acute rheumatic fever. Among the cases, 40 (22.8%) were diagnosed in another health center and administered to our hospital for follow-up. These cases were also included in the group not in the acute period. While the most common presenting complaint of cases diagnosed with acute rheumatic fever was joint pain/swelling (51%), other complaints were; involuntary movements (16%), palpitations/chest pain (12%), murmur (10%), fever (9%), fatigue (1.5%), rash (0.5%).

Carditis (n=140, 80%) was the most common major finding, followed by arthritis/polyarthralgia (n=90, 51.4%). Sydenham's chorea was observed in 28 (16%) cases, and erythema marginatum in one case, while no subcutaneous nodules were detected. When evaluated for the presence of more than one major criterion, carditis and arthritis were found to be coexistent in 65 (37.1%) cases, while chorea and valve involvement were coexistent in 18 (10.2%) cases (**Table 1**).

Table 1. Distribution of Major Manifestations in ARF Cases

Major manifestations	(n)	(%)
Carditis	140	80
Arthritis/Polyarthralgia	90	51.4
Chorea	28	16
Erythema marginatum	1	0.5
Subcutaneous nodules	-	-
Multiple major criteria		
Arthritis+Carditis	65	37.1
Chorea+Carditis	18	10.2

When the distribution of major findings by gender was examined, Sydenham's chorea was more common in females (F/M: 1.8/1), but the difference was not statistically significant ($p > 0.05$).

When the cases diagnosed with carditis were evaluated in terms of valve involvement; mitral regurgitation was present in 125 (89.3%), aortic regurgitation in 57 (40.7%), and tricuspid regurgitation in three (2.1%). The most common form of involvement was isolated mitral regurgitation (76 cases - 54.3%), while mitral and aortic regurgitation were observed concurrently in 43 (30.7%) cases, and isolated aortic regurgitation was observed in 14 (10%) cases. All three of the cases with tricuspid regurgitation had coexistent mitral regurgitation.

When the grade of valve involvement in echocardiography was evaluated; grade I mitral regurgitation was observed in 61 (43.6%) cases, grade II mitral regurgitation in 33 (23.6%) cases, grade III mitral regurgitation in 26 (18.6%) cases, and grade IV mitral regurgitation in five (3.6%) cases. In aortic valve involvements, grade I aortic regurgitation was detected in 48 (34.2%), grade II aortic regurgitation in seven (5%), and grade III aortic regurgitation in two (1.4%) cases (**Table 2**).

Table 2. Echocardiographic Evaluation of Valve Involvements

	Grade I- AR* n (%)	Grade II- AR n (%)	Grade III- AR n (%)	Isolated MR† n (%)
Grade I- MR	17 (12.1)	1 (0.7)	-	43 (30.7)
Grade II- MR	10 (7.1)	1 (0.7)	-	22 (15.7)
Grade III- MR	8 (5.7)	1 (0.7)	-	17 (12.1)
Grade IV- MR	1 (0.7)	2 (1.4)	2 (1.4)	-
Isolated AR	12 (8.6)	2 (1.4)	-	-

*AR: Aortic regurgitation, †MR: Mitral regurgitation

The severity of carditis was determined based on clinical and echocardiographic examinations. When carditis was classified according to clinical severity; mild carditis was observed in 94 (67%), moderate carditis in 31 (22%) and severe carditis in 15 (11%) cases.

When the 89 cases in the acute period were evaluated in terms of minor findings, monoarthralgia was observed in one (1.1%) case, while prolonged PR interval was found in four (9.5%) of 42 cases with accessible electrocardiogram recordings. While fever was detected in 17 (19%) cases, elevated CRP and/or ESR were present in all cases in the acute period.

Among the supporting findings, high anti-streptolysin O titer was detected in 100 (57.1%) cases. Group A streptococci was detected in six (9.2%) of the 65 patients from whom throat swab cultures were obtained.

All cases with cardiac involvement were treated with steroids. Supportive treatment was given to 15 (10.7%) cases with congestive heart failure. Mitral and aortic valve replacements were performed in two (1.7%) patients with grade IV mitral regurgitation and grade III aortic regurgitation that could not be controlled with medical treatment.

In terms of secondary prophylaxis, records of 112 cases were evaluated. While 115 (94.2%) of these cases had good treatment compliance, 7 (5.8%) cases had insufficient compliance. A single daily oral macrolide treatment was recommended for three of the cases due to penicillin allergies and for four cases who declined benzathine penicillin prophylaxis due to pain. Clarithromycin was used as macrolide therapy since erythromycin could not be supplied.

In the clinical follow-up, improvement in valve involvement was observed in 59 (48.3%) cases. In 45 (36.9%) of these cases, the grade of valve regurgitation regressed, while in 14 (11.4%) cases the valve involvement disappeared completely. The median time to the disappearance of valve regurgitation was 4 months (1–6 months). In the first month, improvement in valve regurgitation was detected in 37 (26.4%) cases. While no recurrence was observed in our patients with secondary prophylaxis compliance, it was detected in 4 (57.1%) of 7 non-compliant patients. While surgical intervention was required in two cases due to severe valve insufficiency and uncontrolled congestive heart failure, no mortality was observed in our cases.

DISCUSSION

Acute rheumatic fever and rheumatic heart disease are among the most common preventable reasons for cardiovascular mortality and morbidity, particularly in low- and middle-income countries.[9]

The incidence of ARF is estimated to be 8-51/100.000 worldwide.[10] The lowest incidence was reported as 0.5-3.1/100,000 in Western Europe and the United States.[11] Despite being developed countries, ARF is common among Aborigines in Australia, Maoris in New Zealand, and natives of the Pacific islands.[12] In a study in Australia between 1997 and 2010, the incidence of ARF was reported as 194/100,000 in Indigenous children aged 5-14 years.[13] However, it is not possible to state the true incidence worldwide, since sufficient data cannot be obtained from the African and Asian regions, where the disease is common.

Until 2015, mostly regional data was available on the incidence of ARF in Turkey. Saraçlar et al.[14] found the frequency of ARF to be 20/100.000 between 1972 and 1976. According to other studies, the incidence of the disease varies between 7.4/100.000 and 107.7/100.000.[15,16] The 2016 records of the Turkish National Statistics Institute were used to determine the incidence of ARF by various provinces and regions. The estimated incidence rate of ARF in Turkey is 8.84/100.000.[7]

We were unable to determine the incidence of the disease in our province and region for the years 2005–2017. During this period, the temporary presence of a second pediatric cardiologist in the region made our incidence assessment impossible. Again, since our center provides tertiary healthcare services, we observe that complicated carditis cases are often referred to our center.

Acute rheumatic fever is most commonly observed in the 5–15 years age group, being the period in which the risk of group A streptococci tonsillopharyngitis is highest. While the incidence of the disease before the age of 5 years is around 5%, cases under the age of 2 years are very rare.[17] In the study by Örün et al.[15] involving the highest number of cases in our country, 98.3% of cases were between the ages of 5 and 15 years, while 1.7% were under the age of 5 years. The youngest case in the literature is a nine-month-old female patient; she was diagnosed with fever, arthritis, and a 3/6 pansystolic murmur at the apex and mitral regurgitation.[18] Among the cases in the present study, 78.8% were in the 5–15 years age range. The youngest of the seven (4%) patients under the age of 5 years was 26 months old. She was admitted to the hospital with migratory arthralgia and fever. While acute phase reactants and anti-streptolysin O titers were high, the patient's echocardiography was normal. Although the diagnosis of ARF was considered in the patient, she was hospitalized and followed up, as migratory polyarthralgia was not among the major findings at the time of diagnosis. Due to the continued increase in anti-streptolysin O titers during follow-up and the progressive mitral regurgitation identified on repeated echocardiography, the patient was diagnosed with ARF and treatment was started.

In parallel with the fact that group A streptococci tonsillopharyngitis is observed mostly in the spring and winter, ARF is mostly observed in these seasons.[19] Concurring with the literature, the disease was observed mostly in spring (30%) and winter (29%) in our study. In the distribution according to months, the cases applied primarily in February (13%) and May (12%). In our study, it was seen that the cases were diagnosed during the summer season as well. These cases were not usually in acute period, and the majority of them were patients who were admitted with the diagnosis of Sydenham's chorea.

The history of tonsillopharyngitis undergone before ARF ranges from 24–81%.[20] In our study, a history of tonsillopharyngitis before ARF was noted in 26.8% of the cases, 24.6% of whom had consulted a doctor due to tonsillopharyngitis. The reasons why the rate of tonsillopharyngitis history is so low were; a significant portion of cases, tonsillitis resolves asymptomatically or were not admitted to hospital due to infection. Antibiotics

were recommended for 65.1% of the cases admitted to the health institution. According to the results of our study, the most important reasons for the high frequency of ARF in our region were: (i) asymptomatic group A streptococci tonsillopharyngitis or, (ii) antibiotic treatment was not recommended, or (iii) the treatment was not complied with in the appropriate dose and duration, although antibiotics were recommended. The preference of benzathine penicillin for primary prophylaxis in only four cases in the study group is quite low, and we believe that increasing the single dose of benzathine penicillin treatment will lead to significant improvements in the incidence of ARF.

Örün et al.[15] found the most common major finding to be carditis with a rate of 61.7%, followed by arthritis in 59.1%, chorea in 14.1%, erythema marginatum in 0.8%, and subcutaneous nodule in 0.6%, respectively. In our study, carditis was observed in 80%, arthritis in 51.4%, chorea in 16% and erythema marginatum in one case, while no subcutaneous nodule was detected.

The most common major coexisting findings were carditis and arthritis, while in a study conducted in Bursa between 1994 and 2000, coexisting arthritis and carditis was observed in 37% of 207 cases.[21] In the present study, the coexistence of carditis and arthritis was found at a rate of 37.1%. Carditis is reported in more than half of chorea patients in literature.[22] In a study by Caldas et al.[23] carditis was found in 64% of patients with chorea and the importance of performing echocardiography in patients with chorea was emphasized. Similarly in our study, carditis was detected in 64.2% of the patients with chorea.

Carditis is the most significant major finding of ARF due to its potential to cause sequelae.[24] In the study conducted by Erdem et al.[25] isolated mitral regurgitation was observed in 54.9% of cases, mitral and aortic regurgitation concurrently in 34% of cases and isolated aortic regurgitation in 5.7% of cases. In the same study, pericardial effusion with pancarditis was detected in 5.7% of cases, while tricuspid regurgitation was not observed. Similarly in our study, isolated mitral regurgitation was observed in 54.3% of cases with cardiac involvement, mitral and aortic regurgitation were observed concurrently in 30.7%, while isolated aortic regurgitation was detected in 10%. Furthermore, tricuspid regurgitation, among the rare involvements, was present in three (2.1%) cases with mitral regurgitation, while no pericardial effusion was observed.

Mild carditis is observed mostly in terms of clinical severity of carditis. In the study by Ekici et al.[26] between 2005 and 2008, 63% of 193 cases were evaluated as mild, 30.2% as moderate and 6.7% as severe carditis. When the 140 cases with carditis in the present study were classified according to clinical severity, the condition was evaluated as mild in 67%, moderate in 22% and severe in 11% of cases.

A review of literature assessing the frequency of minor findings, arthralgia was reported at rates in the range of 54.6–81.1%, fever in 40–62%, prolonged PR interval in 15.9–23%, ESR elevation in 81.8–95%, and CRP elevation in 72–81.8%.[27,28] These data, however, were reported according to the Jones criteria prior to the 2015 revision. In our study; monoarthralgia 1.1%, PR prolongation 9.5%, fever 19% and increased acute phase reactants were present in all cases. While acute phase reactants are the most common minor finding similar to the literature, monoarthralgia has been under-detected since it has been included in the diagnostic criteria since 2015.

As an indicator of previous group A streptococci infection, Güngör et al.[29] found elevated anti-streptolysin O titers in 92,2% of patients and group A streptococci in throat swab culture in 4.4%. In our study, while elevated anti-streptolysin O titers was observed in all of the cases in the acute period, group A streptococci was present in the throat culture of 9.2%.

One of the most important factors that cause mortality and morbidity in the follow-up of ARF is recurrences. Benzathine penicillin prophylaxis is the most effective prevention method to prevent recurrent attacks and severe consequences of the disease such as valve replacement.[30] In the study of Ekici et al.[26] compliance with secondary prophylaxis was 83.6%, and recurrence was observed in 16.7% of the cases. While the recurrence rate was 4.8% in cases that were compliant with prophylaxis, this rate was found to be 78% in non-compliant cases. In our study, compliance with secondary prophylaxis was 94.2%, recurrence as carditis was observed in 3.3% of our cases. Recurrence was not observed in our patients with secondary prophylaxis compliance, whereas recurrence was found in 57.1% of non-adherent patients.

Concerning the prognosis of ARF, among the 702 cases in Brazil that were followed for 1.3–16.9 years, the valve lesions resolved completely in 34.4% of the cases with mild carditis.[31] Bozabali et al.[32] reported that among 62 cases with mitral regurgitation who were followed up for an average of 3.4±2.7 years after treatment, 32.2% experienced a regression in the grade of valve involvement, while complete recovery was observed in 11.3%. In the present study, a regression in the grade of valve involvement was detected in 36.9% of cases, while complete improvement was observed in 11.4% of the cases. The median time to the disappearance of valve involvement was 4 months (1-6), while improvement in valve involvement in the first month occurred in 26.4% of the cases.

Although congestive heart failure is relatively rare (4.4–13.8%) in patients with ARF carditis, it can be observed.[33] Bostan et al.[21] reported that surgical intervention was performed in four (2%) patients whose levels of severe aortic insufficiency and progressive mitral stenosis. In our study, medical treatment was applied to 10.7% of the cases due to congestive heart failure, and mitral and aortic valve replacement was performed in two (1.7%) cases due to 4th degree mitral regurgitation and 3rd degree aort regurgitation that did not respond to treatment. No mortality was observed in our cases.

Subclinical carditis has gained importance after the revised Jones criteria. For this purpose, an echocardiographic screening study was conducted among Turkish school children, including 2550 students. The incidence of rheumatic heart disease is 15/1000, which is similar to studies in intermediate- and high-risk populations.[34] It has been emphasized that echocardiographic screening studies are necessary to reduce the burden of rheumatic heart disease and long-term follow-up of children diagnosed with subclinical rheumatic heart disease is necessary.

CONCLUSION

ARF remains a significant health concern in the Eastern Black Sea Region. The most important reasons for the high frequency of ARF are the fact that in most patients the group A streptococci tonsillopharyngitis is asymptomatic, that they do not admit to health institutions due to infection and do not use antibiotic therapy at the appropriate dose and time. We consider that increasing the single-dose benzathine penicillin treatment will lead to significant improvements in the incidence of ARF. In addition, increasing echocardiographic screening studies will contribute to reducing the burden of rheumatic heart disease.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of **XXXXXXXXXXXXXXX** Ethics Committee (Date: **XXXXXXXXXX**, Decision No: 2017/99).

Informed Consent: Informed consent was obtained from the families of all children participating in the study.

Referee Evaluation Process: Externally peer-reviewed.

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

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Webb RH, Grant C, Harnden A. Acute rheumatic fever. BMJ 2015;351:h3443.
2. Arvind B, Ramakrishnan S. Rheumatic fever and rheumatic heart disease in children. Indian J Pediatr 2020;87:305-11.
3. Zühlke LJ, Beaton A, Engel ME, et al. Group A Streptococcus, acute rheumatic fever and rheumatic heart disease: epidemiology and clinical considerations. Curr Treat Options Cardiovasc Med 2017;19:15.
4. Woldu B, Bloomfield GS. Rheumatic Heart Disease in the Twenty-First Century. Curr Cardiol Rep 2016;18:96.
5. Lahiri S, Sanyahumbi A. Acute Rheumatic Fever. Pediatr Rev 2021;42:221-32.
6. Gewitz MH, Baltimore RS, Tani LY, et al. Revision of the Jones Criteria for the diagnosis of acute rheumatic fever in the era of Doppler echocardiography: a scientific statement from the American Heart Association. Circulation 2015;131:1806-18.
7. Gürses D, Koçak G, Tutar E, Özbarlas N. Turkish ARF study group. Incidence and clinical characteristics of acute rheumatic fever in Turkey: Results of a nationwide multicentre study. J Paediatr Child Health 2021;57:1949-54.
8. Reményi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease--an evidence-based guideline. Nat Rev Cardiol 2012;9:297-309.
9. Karthikeyan G, Guilherme L. Acute rheumatic fever. Lancet 2018;392:161-74.
10. Kumar RK, Tandon R. Rheumatic fever & rheumatic heart disease: the last 50 years. Indian J Med Res 2013;137:643-58.
11. de Loizaga SR, Beaton AZ. Rheumatic Fever and Rheumatic Heart Disease in the United States. Pediatr Ann 2021;50:98-104.
12. Rising Ethnic Inequalities in Acute Rheumatic Fever and Rheumatic Heart Disease, New Zealand, 2000-2018. Emerg Infect Dis 2021;27:36-46.
13. Oliver J, Osowicki J, Cordell B, Hardy M, Engelman D, Steer AC. Incidence of acute rheumatic fever and rheumatic heart disease in Melbourne, Australia from 1937 to 2013. J Paediatr Child Health 2020;56:1408-13.
14. Saraçlar M, Ertuğrul A, Özme ve Ajun A. Akut romatizmal ateş insidansı ve romatizmal kalp hastalıklarının prevalansı. Türk Kardiyoloji Dern Arş 1978;7:50-5.
15. Orün UA, Ceylan O, Bilici M, et al. Acute rheumatic fever in the Central Anatolia Region of Turkey: a 30-year experience in a single center. Eur J Pediatr 2012;171:361-8.
16. Narin N, Mutlu F, Argun M, et al. Incidence and clinical features of acute rheumatic fever in Kayseri, Central Anatolia, 1998-2011. Cardiol Young 2015;25:745-51.
17. Tani LY, Veasy LG, Minich LL, Shaddy RE. Rheumatic fever in children younger than 5 years: is the presentation different? Pediatrics 2003;112:1065-8.
18. Abdin ZH, Eissa A. Rheumatic fever and rheumatic heart disease in children below the age of 5 years in the tropics. Ann Rheum Dis 1965;24:389-91.
19. Bono-Neri F. Acute Rheumatic Fever: Global Persistence of a Preventable Disease. J Pediatr Health Care 2017;31:275-84.
20. Bennett J, Rentta N, Leung W, et al. Structured review of primary interventions to reduce group A streptococcal infections, acute rheumatic fever and rheumatic heart disease. J Paediatr Child Health 2021;57:797-802.
21. Bostan MÖ, Çil E. Bursa ilindeki çocuklarda akut romatizmal ateşin değerlendirilmesi. T Klin Kardiyoloji 2001;14:276-81.
22. Teixeira AL, Vasconcelos LP, Nunes MDCP, Singer H. Sydenham's chorea: from pathophysiology to therapeutics. Expert Rev Neurother 2021;21:913-22.
23. Caldas AM, Terreri MT, Moises VA, et al. What is the true frequency of carditis in acute rheumatic fever? A prospective clinical and Doppler blind study of 56 children with up to 60 months of follow-up evaluation. Pediatr Cardiol 2008;29:1048-53.
24. Hung LC, Nadia R. A Review of Acute Rheumatic Fever and Rheumatic Heart Disease Research in Malaysia. Med J Malaysia 2016;71:79-86.
25. Erdem S, Demir F, Ayana M, et al. Acute rheumatic fever in south-east of Turkey: clinical features and epidemiological evaluation of the patients over the last 25 years. Cardiol Young 2020;30:1086-94.
26. Ekici F, Kale Y, Kocabaş A. Changing face of acute rheumatic fever: our clinical observations. Anadolu Kardiyol Derg 2013;13:506-7.
27. Grassi A, Fesslovà V, Carnelli V, et al. Clinical characteristics and cardiac outcome of acute rheumatic fever in Italy in the last 15 years. Clin Exp Rheumatol 2009;27:366-72.
28. Yildirim A, Aydin A, Demir T, et al. Acute rheumatic fever: a single center experience with 193 clinical cases. Minerva Pediatr 2016;68:134-42.
29. Güngör Ş, Doksöz O, Fettah A, Nacaroğlu HN, Örün UA, Karademir S. Akut romatizmal ateş tanısı ile izlenen hastaların geriye dönük olarak değerlendirilmesi: Beş yıllık tek merkez deneyimi. İzmir Dr. Behçet Uz Çocuk Hast. Dergisi 2014; 4:87-96.
30. Bennett J, Rentta NN, Leung W, et al. Early diagnosis of acute rheumatic fever and rheumatic heart disease as part of a secondary prevention strategy: Narrative review. J Paediatr Child Health 2021;57:1385-90.

31. Mota CC, Meira ZM, Graciano RN, Graciano FF, Araújo FD. Rheumatic Fever prevention program: long-term evolution and outcomes. Front Pediatr 2015;2:1-5.
32. Bozabalı S, Mammadova A, Turan C, Sahan YO, Levent E. Akut Romatizmal Ateşe Bağlı Kardit Gelişen Hastalarda Penisilin Profilaksisinin Etkinliğinin Değerlendirilmesi. Türkiye Çocuk Hast Derg 2016;1:7-12.
33. Leal MTBC, Passos LSA, Guarçoni FV, et al. Rheumatic heart disease in the modern era: recent developments and current challenges. Rev Soc Bras Med Trop 2019;52:e20180041.
34. Atalay S, Tutar E, Uçar T, Topçu S, Köse SK, Doğan MT. Echocardiographic screening for rheumatic heart disease in Turkish schoolchildren. Cardiol Young. 2019;29(10):1272-7.

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Original Article / Orijinal Araştırma

Do Accompanying Traumas Affect Mortality in cases of Blast-Induced Head Trauma?

Blast Etkiyle Oluşan Kafa Travmalarında Eşlik Eden Travmalar Mortaliteyi Etkiler Mi?

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Abstract

Aim: In today's wars, there are more civilian victims of war than soldiers. Most war-related deaths occur in civilians and children are the most affected. Although military injuries in the battlefield are usually penetrating, blast-induced blunt trauma is common in civilian injuries. In this study, the frequency of thoracic and abdominal trauma in children with blast-induced head trauma was analysed.

Material and Method: Twenty-five paediatric patients with blast head trauma in war were retrospectively reviewed.

Results: Sixteen of the patients were male and 9 were female. The mean age was 9.4±5 years. All patients had head trauma. In terms of type of trauma, 84% had multiple trauma (head, chest, abdomen) and 16% had only head trauma. Head trauma was accompanied by lung contusion in 60% and free abdominal fluid in 32%. Eleven patients (44%) died

Conclusion: Bomb blast injuries affect the whole body and have a high mortality rate. Developing children are the focus of war and terrorism, which increases mortality rates. In such injuries, the whole body should be carefully examined for damage, not only the parts with external cuts.

Keywords: Blast trauma, head trauma, gunshot wounds

Öz

Amaç: Günümüz savaşlarında askerlerden çok sivil savaş mağdurları görülmektedir. Savaşla ilgili ölümlerin çoğu sivillerde meydana gelir ve en çok etkilenenler çocuklardır. Savaş alanındaki askeri yaralanmalar genellikle delici olsa da, patlama etkisi olan künt travmalar sivil yaralanmalarda yaygındır. Bu çalışmada, savaşta blast etkisiyle kafa travması geçiren çocuklarda torasik ve abdominal travma sıklığı incelenmiştir

Gereç ve Yöntem: Savaşta patlama kafa travması geçiren 25 pediatrik hasta retrospektif olarak incelenmiştir.

Bulgular: Hastaların 16'sı erkek , 9'u kadındır. Ortalama yaş 9,4±5 idi. Tüm hastalarda kafa travması vardı. Travma türü açısından, %84'ünde çoklu travma (kafa, göğüs, karın) ve %16'sında sadece kafa travması vardı. Kafa travmasına %60 ile akciğer kontüzyonu ardından %32 ile serbest abdominal sıvı eşlik etmekteydi. On bir hasta (%44) kaybedildi

Sonuç: Bomba etkisine bağlı patlama yaralanmaları, tüm vücudu etkiler ve yüksek ölüm oranına sahiptir. Gelişme çağında çocuklar, savaş ve terörizmin odak noktasıdır ve bu da ölüm oranlarını artırır. Bu tür yaralanmalarda, yalnızca dış kesiklerin olduğu kısımlar değil tüm vücut hasar açısından dikkatlice incelenmelidir..

Anahtar Kelimeler: Blast travma, kafa travması, ateşli silah yaralanmaları

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INTRODUCTION

The vast majority of modern wars now take place in areas close to civilian settlements.[1] In these wars, blast injuries, particularly among civilians, as well as penetrating and burn injuries, are common.[2] In today's wars, more civilians than soldiers are killed. Most war-related deaths occur among civilians, and children are the most affected.[3]

The explosion of high-energy explosives creates a shock wave in the air or water. The blast propagates at a speed greater than the speed of sound and has three components. The first stage is the overpressure stage of the blast wave. The pressure can be hundreds of bar per square centimetre and decreases as the blast moves away from the source. The second stage is the negative pressure stage with a relative vacuum effect that sucks in air after the positive component. The third stage is the blast flow stage. The rapidly expanding gases caused by the explosion displace an equal volume of air. It has a lower pressure than a positive pressure blast wave but can travel further.[4,5]

Blast injuries cause trauma by 4 different mechanisms. Primary blast injuries are injuries caused by excessive blast waves, secondary blast injuries are injuries caused by flying particles as a result of the explosion, and tertiary blast injuries occur as a result of the displacement of the victim's body by the blast wave. These are quaternary injuries resulting from burns, toxic inhalation and radiation exposure.[10]

Blast induced traumatic brain injury has been a common form of injury in many wars.[11] However, all parts of the body are affected when the blast wave passes over people. A victim exposed to the blast effect may not have any external injuries. However, fatal injuries may occur.

This study investigated the incidence of head trauma associated with blast injury to the thorax and abdominal organs in children who sustained blast head trauma during the Syrian civil war and were followed up at the neurosurgery clinic.

MATERIAL AND METHOD

The study was carried out with the permission of Hatay Mustafa Kemal University Ethics Committee (Date: 25.12.2023, Decision No: 09). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Our study retrospectively analysed patients aged 1-17 years who were brought to the Faculty of Medicine Hospital by 112 emergency services between 2010 and 2021 with injuries related to the Syrian civil war. Among the available patients, 25 patients with blast injuries were included in our study and their computed tomography, magnetic resonance, radiographs and biochemical values in the hospital database were analysed. The treatments given to our patients in our hospital were evaluated with epicrisis notes.

In the statistical analyses, numbers and percentages were used to show frequency distributions among the descriptive statistics, and mean and standard deviation among the distribution criteria. The Fisher exact test was used to compare percentages of two discontinuous variables, and the Mann-Whitney U test was used to compare two independent continuous variables, since the number of samples was less than 30, the data were considered incompatible with normal distribution, and $p>0.05$ was considered significant.

RESULTS

16 patients were male and 9 were female. The mean age of the 25 patients included in the study was 9.4±5.0 years (min:1, max:16). All patients suffered from head trauma. Regarding the type of trauma, 84.0% had mixed trauma (head, thorax, abdomen) and 16.0% had only head trauma. When we analysed the trauma conditions other than head trauma, pulmonary contusion was the most common trauma with 60.0%, followed by free abdominal fluid with 32.0% (**Table 1**). When we analysed the head trauma of the patients, we found fractures of various types and locations in 80.0%, subarachnoid haemorrhage (SAH) in 36.0%, haematoma of various levels in 24.0% and cerebral contusion in 24.0% (**Figure 1**, **2**).

Table 1. Other trauma conditions of the patients accompanying head trauma

Trauma Type	Number	Percent
Lung contusion	15	60.0
İntra abdominal free fluid	8	32.0
Pneumothorax	6	24.0
Retroperitonel haematoma	3	12.0
Pericardial effusion	2	8.0
Liver laceration	2	8.0
Spleen laceration	1	4.0

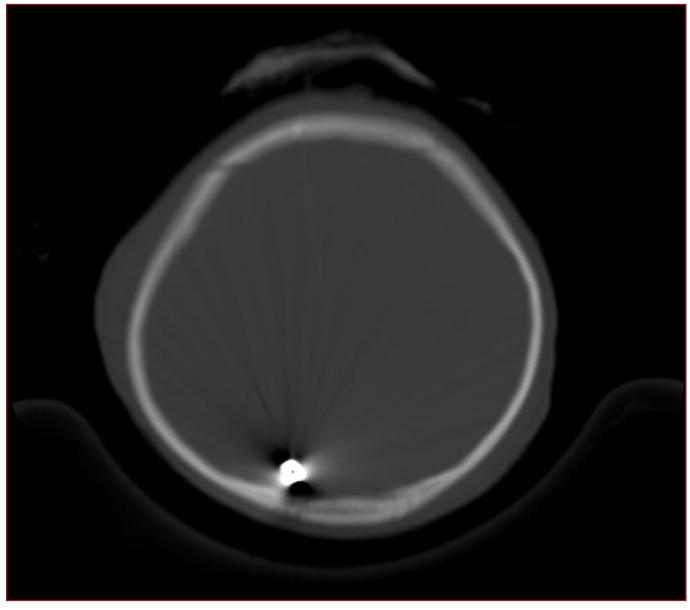

Figure 1: Presence of a foreign body approximately 7.5 mm in diameter in the left posterior parietal region with dense metallic artefacts

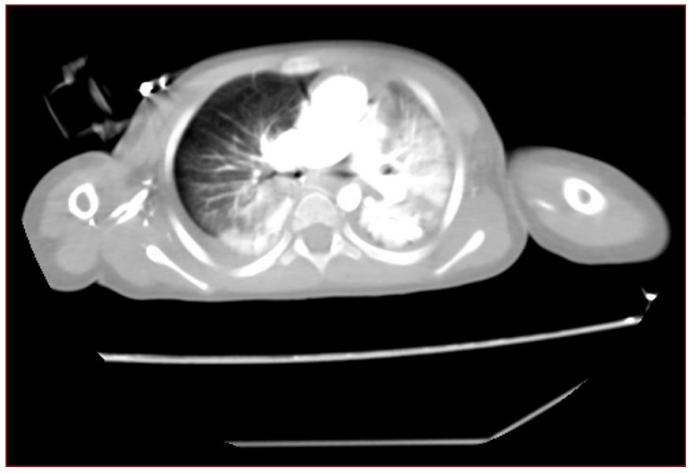

Figure 2: Lung tissue in the lower lobe of the right lung and in all lobes of the left lung has an atelectatic appearance.

11 patients (44.0%) died. The mean duration of ex was 7.9±7.1 days. When comparing the relationship between type of trauma and ex status, no statistical relationship was found between any type of trauma and the presence of ex (p>0.05) (**Table 2**). The mean Glasgow Coma Scale (GCS) score of the patients was 7.9±3.7. When the relationship between the types of trauma and GCS was compared between the mean GCS of the patients with and without each type of trauma, no statistical relationship was found for any type (p>0.05).

Table 2. The relationship between the type of trauma and exitus status

		Death				P**
		+		-		
		N*	%	N*	%	
Mixed Trauma	+	8	38.1	13	61.9	0.288
	Isolyted Head	3	75.0	1	25.0	
Lung Contusion	+	7	46.7	8	53.3	1.000
	-	4	40.0	6	60.0	
Liver Laceration	+	1	50.0	1	50.0	1.000
	-	10	43.5	13	56.5	
İntra Abdominal Free Fluid	+	3	37.5	5	62.5	1.000
	-	8	47.1	9	52.9	
Pneumothorax	+	1	16.7	5	83.3	0,180
	-	10	52.6	9	47.4	
Retroperitoneal Haematoma	+	1	33.3	2	66.7	1.000
	-	10	45.5	12	54.5	
Pericardial Effusion	+	1	50.0	1	50.0	1.000
	-	10	43.5	13	56.5	

* Line Percentage, **Fisher Exact Test

DISCUSSION

Explosions create a shock wave due to the compression of the air, which travels outwards from the explosion site at the speed of sound, hitting any object in front of it. The force of this shock wave is directly proportional to the amount of explosive and inversely proportional to the distance. In the second stage, which begins after the first stage has ended, the vacuum effect created in the blast zone hits everything in front of it again, creating an inward pressure wave that causes forced displacement. The destructive effect of these pressure storms forms the basis of blunt and penetrating injuries, which constitute secondary and tertiary injuries.[8]

In blast injuries, head/neck and extremity injuries and burns are common in children under 16 years of age, in contrast to extremity injuries, which are more common in adults.[9-11] The mortality rate in our study was very high at 44%, which is very close to the range of 0.6%-40% in the.[12-14] The main reason for the high mortality rate is secondary and tertiary injuries unrelated to the primary blast injury.[12-14] The cause of mortality in primary blast injury is severe head and brain trauma.[15] In our study, 84% of patients had mixed trauma and 16% had isolated head trauma. The mortality rate of patients with only head and brain injury was 75%, and the Glasgow coma score of these patients in the emergency department was 3. In addition, the mortality rate increased from 38.1% to 46.7% in patients with head and brain injury with the addition of pulmonary contusion, which correlates with information in the literature.[16]

In a study conducted in Israel, it was reported that 33% of the people affected after the explosion had serious injuries and could be transported to the hospital alive, 26% of those who reached the hospital required intensive care, 55% had open wounds, 31% had internal injuries and 50% underwent surgery.[17] In our study, 84% of the patients admitted to our hospital had mixed injuries. 16% of the patients had isolated head trauma. In mixed type trauma, all patients had head and brain injury and the most common associated pathology was pulmonary contusion (60%), followed by intra-abdominal free fluid (32%) and pneumothorax (24%).

On the other hand, while intra-abdominal organ injury in bomb victims is reported in the literature to be between 5% and 12%, mostly in the liver and small intestine, in our study intra-abdominal free fluid was found in 32%, liver laceration in 8% and splenic laceration in 4%10.[18]

When we analysed the head trauma, we found that 80% of the patients with head trauma had fractures of various types and locations, 36% had subarachnoid haemorrhage, 24% had intracerebral, subdural and/or epidural haemorrhage and 24% had cerebral contusion. These rates are higher than in adults, probably because children are more vulnerable and can be more easily and violently thrown by the blast effect due to their lighter weight.[19] Mortality from primary blast injury is therefore higher in children than in adults.

The data we have on primary blast injury are from patients who could be admitted to hospital. However, the mortality rate of primary blast injury is even higher than we have determined. This is because if we add to the mortality rate children who died at the scene, those who died before reaching medical assistance or during transport, the rate is even higher.

If we think about the reasons for such a wide range of values in the literature and the different results in our study, we can consider the severity of the blast as the most important one. In fact, as the intensity increases, the primary blast intensity increases and the mortality at the scene is higher. On arrival at the hospital, victims of a higher intensity blast may suffer more damage and mortality may increase. The second reason is the lack of protective instinct in the paediatric age group. In recent terrorist attacks and war bombings, children have been targeted. Children are more affected by primary blast injuries because they are lighter and more vulnerable.

CONCLUSION

While primary blast injuries in the adult population are mainly extremity and external injuries, in the paediatric age group they can cause mixed trauma and significantly increase mortality rates. In the developing world, children are at the centre of war and terrorism, increasing mortality rates.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Hatay Mustafa Kemal University Ethics Committee (Date: 25.12.2023, Decision No: 09).
Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.
Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: The authors have no conflicts of interest to declare.
Financial Disclosure: The authors declared that this study has received no financial support.
Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Hinsley DE, Rosell PA, Rowlands TK, Clasper JC. Penetrating missile injuries during asymmetric warfare in the 2003 Gulf conflict. Br J Surg. 2005;92(5):637-42.
2. Scope A, Farkash U, Lynn M, Abargel A, Eldad A. Mortality epidemiology in low-intensity warfare: Israel Defense Forces' experience. Injury. 2001;32(1):1-3.
3. Santa Barbara J. Impact of war on children and imperative to end war. Croat Med J. 2006;47(6):891-4.
4. Volgas DA, Stannard JP, Alonso JE. Ballistics: a primer for the surgeon. Injury. 2005;36(3):373-9.
5. Santucci RA, Chang YJ. Ballistics for physicians: myths about wound ballistics and gunshot injuries. J Urol. 2004;171(4):1408-14.
6. Milwood Hargrave J, Pearce P, Mayhew ER, Bull A, Taylor S. Blast injuries in children: a mixed-methods narrative review. BMJ Paediatr Open. 2019;3(1):e000452.
7. Arriola VD, Rozelle JW. Traumatic Brain Injury in United States Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Hispanic Veterans-A Review Using the PRISMA Method. Behav Sci (Basel). 2016;6(1):3.
8. Phillips YY. Primary blast injuries. Ann Emerg Med. 1986;15(12):1446-50.
9. Owens BD, Kragh JF Jr, Wenke JC, Macaitis J, Wade CE, Holcomb JB. Combat wounds in operation Iraqi Freedom and operation Enduring Freedom. J Trauma. 2008;64(2):295-9.
10. Bilukha OO, Brennan M, Anderson M, Tsitsaev Z, Murtazaeva E, Ibragimov R. Seen but not heard: injuries and deaths from landmines and unexploded ordnance in Chechnya, 1994-2005. Prehosp Disaster Med. 2007;22(6):507-12.
11. Stansbury LG, Lalliss SJ, Branstetter JG, Bagg MR, Holcomb JB. Amputations in U.S. military personnel in the current conflicts in Afghanistan and Iraq. J Orthop Trauma. 2008;22(1):43-6.
12. Stapczynski JS. Blast injuries. Ann Emerg Med. 1982;11(12):687-94.
13. Hadden WA, Rutherford WH, Merrett JD. The injuries of terrorist bombing: a study of 1532 consecutive patients. Br J Surg. 1978;65(8):525-31.
14. Cooper GJ, Maynard RL, Cross NL, Hill JF. Casualties from terrorist bombings. J Trauma. 1983;23(11):955-67.
15. Hill JF. Blast injury with particular reference to recent terrorist bombing incidents. Ann R Coll Surg Engl. 1979;61(1):4-11.
16. Peleg K, Aharonson-Daniel L, Michael M, Shapira SC; Israel Trauma Group. Patterns of injury in hospitalized terrorist victims. Am J Emerg Med. 2003;21(4):258-62.
17. de Ceballos JP, Turégano-Fuentes F, Perez-Diaz D, Sanz-Sanchez M, Martin-Llorente C, Guerrero-Sanz JE. 11 March 2004: The terrorist bomb explosions in Madrid, Spain--an analysis of the logistics, injuries sustained and clinical management of casualties treated at the closest hospital. Crit Care. 2005;9(1):104-11.
18. Turégano-Fuentes F, Pérez-Diaz D, Sanz-Sánchez M, Alfici R, Ashkenazi I. Abdominal blast injuries: different patterns, severity, management, and prognosis according to the main mechanism of injury. Eur J Trauma Emerg Surg. 2014;40(4):451-60.
19. Eastridge BJ, Salinas J, Wade CE, Blackbourne LH. Hypotension is 100 mm Hg on the battlefield. Am J Surg. 2011;202(4):404-8.

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Original Article / Orijinal Araştırma

Comparing the Effectiveness of Two Culture Media Techniques in the Diagnosis of Prosthetic Joint Infection

Protez Eklem Enfeksiyonunun Tanısında İki Kültür Ortamı Tekniğinin Etkinliğinin Karşılaştırılması

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Abstract

Aim: When infectious diseases are suspected, culture studies ensure the selection of the appropriate antimicrobial treatment and confirm the diagnosis. There are various differences in medium, sample collection technique, enrichment, and evaluation techniques. Culture sampling makes important contributions to the diagnosis and treatment of prosthetic joint infections, the frequency of which has increased in recent years as a result of the increased rate of arthroplasty. After evaluating the preoperative and intraoperative criteria together, prosthetic joint infections can be diagnosed in suspected cases without culture positivity. This study aims to evaluate different culture samplings efficiency for the diagnosis of prosthetic joint infection.

Material and Method: This study retrospectively evaluated 946 patients who had been sampled in our department between January 2005 and May 2015. These patients were divided into two groups according to their final diagnoses: group one (prosthetic joint infection) and group two (suspected but non-infected prosthetic joint replacement). Considering patients' final diagnoses, this study aimed to compare the results of the blood culture bottle (BCB) method and the standard sterile fluid culture method.

Results: When cultivated in a blood culture flask, the sensitivity of the culture test was 28.09%, specificity was 95.77%, and accuracy was 58.13%. When cultivated in a solid medium, sensitivity was 10.11%, specificity was 100%, and accuracy was 50%.

Conclusions: When prosthetic joint infection is suspected, BCB usage is a preferable, safer method compared to the standard sterile fluid culture method because it has the power to isolate more bacteria with a higher diagnostic value.

Keywords: Bacterial identification, blood culture bottles, culture assay, diagnostic accuracy, prosthetic joint infection

Öz

Amaç: Bulaşıcı hastalıklardan şüphelenildiğinde, kültür çalışmaları uygun antimikrobiyal tedavinin seçilmesini sağlar ve tanıyı doğrular. Ortam, örnek toplama tekniği, zenginleştirme ve değerlendirme tekniklerinde çeşitli farklılıklar vardır. Kültür örneklemesi, son yıllarda artroplasti oranının artmasıyla sıklığı artan protez eklem enfeksiyonlarının tanı ve tedavisine önemli katkılar sağlar. Ameliyat öncesi ve sırasındaki kriterlerin birlikte değerlendirilmesiyle, şüpheli vakalarda kültür pozitifliği olmadan protez eklem enfeksiyonları teşhis edilebilir. Bu çalışma, protez eklem enfeksiyonunun tanısı için farklı kültür örneklemelerinin etkinliğini değerlendirmeyi amaçlamaktadır.

Gereç ve Yöntem: Bu çalışmada, Ocak 2005 ile Mayıs 2015 arasında bölümümüzde örneklenen 946 hasta retrospektif olarak değerlendirildi. Bu hastalar nihai tanılarına göre iki gruba ayrıldı: birinci grup (protez eklem enfeksiyonu) ve ikinci grup (şüpheli ancak enfekte olmayan protez eklem replasmanı). Hastaların son tanıları göz önünde bulundurularak, bu çalışmada kan kültürü şişesi (BCB) yöntemi ile standart steril sıvı kültür yönteminin sonuçları karşılaştırılmıştır.

Bulgular: Kan kültürü şişesinde kültür yapıldığında, kültür testinin duyarlılığı %28,09, özgüllüğü %95,77 ve doğruluğu %58,13 olarak bulunmuştur. Katı bir ortamda kültür yapıldığında, duyarlılığı %10,11, özgüllüğü %100 ve doğruluğu %50 olarak bulunmuştur.

Sonuç: Protez eklem enfeksiyonundan şüphelenildiğinde, BCB kullanımı daha yüksek tanı değerine sahip daha fazla bakteri izole etme gücüne sahip olduğundan standart steril sıvı kültür yöntemine kıyasla tercih edilen, daha güvenli bir yöntemdir.

Anahtar Kelimeler: Bakteriyel tanımlama, kan kültürü şişeleri, kültür testi, protez eklem enfeksiyonu, tanısal doğruluk

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INTRODUCTION

Bacterial isolation in musculoskeletal system infections positively contributes to diagnosis and treatment direction. The increase in the prevalence of prosthetic joint infection (PJI), secondary to the increase in arthroplasty rates in recent years, suggests that this issue will remain relevant.[1]

PJI after primary arthroplasty has been reported at a rate of 1.5-2.5%. It is the most common cause of implant failure within the first five years after knee arthroplasty.[2] In cases of suspected PJI, a culture examination of synovial fluid is a routinely performed standard practice. Flora contamination, low-virulence bacteria, and uninterrupted antibiotherapy before joint aspiration can lead to uncertainty in culture sampling results.[3,4]

For PJI, the time of diagnosis affects the choice of treatment. It is generally accepted that infections observed within the first four weeks are called "early PJIs," while infections observed after the fourth week are called "late PJIs".[5,6] Apart from acute cases, PJIs are usually treated with staged surgeries that require implant removal. For this reason, it is important to reach a rapid diagnosis in cases that are suspected during the early period of infection.

Culture negativities are more common, especially in late-stage and delayed PJIs, due to the presence of a biofilm layer.[1] These negativities are usually caused by low-virulence bacteria.[2] Late PJI may be caused by low-virulent skin flora (coagulase-negative staphylococci, *Propionibacterium* species, and coryneform bacteria).[2–4] The long incubation time requirements of bacteries in late-stage prosthetic infections may lead to culture negativities and their presence in the normal skin flora may lead to a misdiagnosis as contamination.[5]

The importance of the culture is not limited to diagnosis; the culture and antibiogram are also important for guiding antibiotic therapy after implant removal and for determining the antibiotics in the spacer that will be applied into the joint during debridement-implant removal surgery.

Sampling type (tissue sampling, tissue swab samples, synovial fluid aspirate, implant sonication), incubation time, and medium type (solid, semi-solid, liquid, blood culture bottle) may affect the results of culture sampling.[7-12]

In the selection of media, the blood culture bottle (BCB) has the advantages of being easily obtained in many centers and of being able to offer a more objective evaluation of the automated system. It has been established that cultivation in a BCB contributes positively to non-blood sterile body fluid sampling.[13,14]

Despite all technical innovations, different types of specimens, long incubation periods, and enrichment methods, there are still patients who are diagnosed with prosthetic infections without reproduction in culture. This condition is defined as culture-negative PJI.

Culture-negative PJIs have been reported at relatively high rates, especially in late-stage PJIs. For this reason, the need to set out various criteria has emerged to define this group of patients. The most well-known of these criteria was defined by the Musculoskeletal Infection Society (MSIS) working group in 2011 and subsequently included in clinical practice.[15] These criteria were redefined in 2018.[16]

According to the 2011 MSIS criteria, the diagnosis of PJI can be performed under three main titles (**Table 1**).

Table 1. 2011 Musculoskeletal Infection Society (MSIS) criteria[15]

Main Criteria Group	Criteria	Status of meeting criteria	Final diagnosis
1.	The presence of sinus tract infections associated with the prosthesis	Positive	PJI
2.	The same pathogen is detected in two different samples	Positive	PJI
3.	**a)** Increased erythrocyte sedimentation rate (ESR) or C-Reactive Protein (CRP) in serum; **b)** Increased leukocyte count in synovial fluid; **c)** Increased neutrophil percentage in synovial fluid (PMN%); **d)** Presence of purulence in the affected joint; **e)** Reproduction in a single culture; **f)** More than five neutrophils appear per area at 400 x magnification	Presence of 4 or more	PJI

When these criteria are evaluated, the diagnosis of PJI can be made without culture positivity. Judging from the modifications to the criteria in 2018, it can be observed that the effectiveness of intraoperative findings increased and that the diagnosis of PJI can still be made without culture positivity.[16]

This group of patients, who have to be diagnosed without culture positivity, may benefit from different practices that will contribute to pathogen isolation. Choosing culture methods with higher sensitivity, specificity, and accuracy may positively contribute to PJI diagnosis.

This study compares the results of standard sterile body fluid culture and transplantation to a BCB by sampling synovial fluid of patients suspected of having a PJI. Furthermore, this study aimed to consider whether the patients' final diagnoses were PJI while comparing the diagnostic efficiency of their examinations.

The hypothesis of this study was the following: In the preliminary diagnosis of PJI, sowing into a blood culture bottle in synovial fluid sampling provides a greater number and variety of bacterial isolation.

MATERIAL AND METHOD

Before to the start of the study, approval was obtained from the institutional ethics committee with decision number 20-KAEK-092. This retrospective study examined patients' blood culture samplings between January 2005 and May 2015.

Patients with suspicious findings for PJI (joint pain, warmth, erythema, induration, oedema at the incision site, persistent wound drainage, wound dehiscence, joint effusion and/or fever) who had a sterile joint fluid culture performed from their synovial fluid samples and who agreed to participate in the study were

included in the study. Patients with oncological bone diseases who had undergone a tumour resection prosthesis, patients with a follow-up period of less than 2 years and those who had lost follow-up, patients who were taking immunomodulating drugs and patients who had taken antibiotics within the last seven days were not included in the study.

The following data were evaluated: the presence of sinus tracts, culture results, serum CRP and ESR values, synovial leukocyte count, synovial leukocyte ratio, the presence of purulence during surgery, and the neutrophil count per area at 400 times magnification.

When we started our study, it was found that 946 blood culture tests were performed at the Orthopaedics and Traumatology Clinic. 728 samples that were performed for reasons other than suspected PJI and did not contain synovial fluid samples were excluded from the study in the first phase. 218 samples collected with suspected PJI were analysed according to the MSIS criteria described in 2011. 160 patients with sufficient data in the hospital records who met the criteria were included in the study.

All samples included in the study were taken under fluoroscopy control in the operating room after appropriate sterilization and draping.

The patients included in the study were divided into two groups according to their MSIS criteria. Group I comprised patients diagnosed with PJI, while Group II comprised patients suspected of having PJI but not infected. Group I patients underwent two-stage revision arthroplasty, while Group II patients were treated conservatively and patients whose symptoms did not improve underwent one-stage revision arthroplasty.

A second study was performed based on the results of bacteriological examinations of synovial fluid samples collected with BCB and standard medium. Accordingly, the sowing with BCB was analysed in two groups as group B and the sowing with conventional medium in group C and the growth results were recorded.

In Group B, samples were inoculated and incubated in Bactec 9240 (Becton Dickinson, USA) automated blood culture system at 35°C for 7 days. Bottles that showed a positive signal were subjected to Gram staining and subcultured on Blood agar (Himedia, India) and Eosin Methylene-blue Lactose Sucrose (EMB) agar (Himedia, India) plates and incubated in 35°C for 24 hours. Identificatian of isolates were performed by conventional methods and the automated VITEK2® system (bioMerieux, France).

In Group C sample was subjected to Blood agar and EMB agar plates and incubated in 35°C for 24 hours. Identificatian of isolates were performed by conventional methods and the automated VITEK2® system (bioMerieux, France).

The results of culture sampling were tested with diagnostic parameters (sensitivity, specificity, positive predictive value and negative predictive value, diagnostic accuracy). The day bacteria isolation in positive cultures was also recorded.

Statistical Analysis

Each descriptor for the two groups of anchors is represented as average±standard deviation. Averages were compared using the independent sample t-test. The significance test of the difference between the two means or one-way analysis of variance (ANOVA) was used. P values less than 0.05 were accepted as statistically significant. The diagnostic test evaluation calculator was used to evaluate diagnostic tests. All statistical analyses were performed using the software package IBM SPSS Statistics 19 (SPSS Inc., an IBM Co., Somers, NY).

RESULTS

The analysis of the results of the culture samples taken from the patients, the characteristics of the wound site and the laboratory results from the hospital database showed that 89 (55.6%) patients were diagnosed with PJI and belonged to group I, while 71 (44.4%) patients belonged to group II.

Group I included 60 knee arthroplasty cases and 29 hip arthroplasty cases, while Group II included 52 cases of knee arthroplasty and 19 cases of hip arthroplasty. (p>0.05)

The average age of the patients in Group I was 67.58 (± 7.16) years and 64.91 (± 9.74) years in Group II. (p >0.05)

Four-eyed tables were prepared to examine whether patients were diagnosed with PJI and to determine the culture results (**Table 2**).

Table 2. Distribution of examination results according to final diagnosis

	Positive	Negative	Total
Technique 1			
Positive	25	3	28
Negative	64	68	132
Total	89	71	160
Technique 2			
Positive	9	0	9
Negative	80	71	151
Total	89	71	160
Evaluation together			
Positive	25	3	28
Negative	64	68	132
Total	89	71	160

Diagnostic test evaluation was performed according to technique one, technique two, and the evaluation of both techniques together. The sensitivity of technique B was 28.09%, with a specificity of 95.77%, a positive likelihood ratio of 6.65, a negative likelihood ratio of 0.75, a prevalence of 55.63, a positive predictive value of 89.29%, and an accuracy of 58.13%. The sensitivity of technique C was 10,11%, with a specificity of 100%, a positive likelihood ratio of 0, a negative likelihood ratio of 0.9, a prevalence of 55.63%, a positive predictive value of 100%, and an accuracy of 50%. When evaluated together, the diagnostic results of both tests were the same as when sowed only in a blood culture bottle (**Table 3**).

Table 3. Diagnostic test results according to culture techniques

Statistics	Result	95% Trust Interval
Technique 1		
Sensitivity	28.09%	19.07% - 38.62%
Specificity	95.77%	88.14% - 99.12%
Positive Likelihood Rate	6.65	2.09 - 21.13
Negative Likelihood Rate	0.75	0.65 - 0.86
Prevalence	55.63%	47.57% - 63.47%
Positive Predictive Value	89.29%	72.39% - 96.36%
Negative Predictive Value	51.52%	48.05% - 54.97%
Accuracy	58.13%	50.08% - 65.87%
Technique 2		
Sensitivity	10.11%	4.73% - 18.33%
Specificity	100%	94.94% - 100%
Positive Likelihood Rate		
Negative Likelihood Rate	0.9	0.84% - 0.96%
Prevalence	55.63%	47.57% - 63.47%
Positive Predictive Value	100%	
Negative Predictive Value	47.02%	45.29% - 48.76%
Accuracy	50%	42% - 58%
Evaluation together		
Sensitivity	28.09%	19.07% - 38.62%
Specificity	95.77%	88.14% - 99.12%
Positive Likelihood Rate	6.65	2.09 - 21.13
Negative Likelihood Rate	0.75	0.65 - 0.86
Prevalence	55.63%	47.57% - 63.47%
Positive Predictive Value	89.29%	72.39% - 96.36%
Negative Predictive Value	51.52%	48.05% - 54.97%
Accuracy	58.13%	50.08% - 65.87%

While the mean bacterial isolation day with technique B was 3.72±1.59, it was calculated as 2.2±0.45 for technique C (**Table 4**).

Table 4. Reproduction days with different techniques by species

Pathogen	Reproduction Day	
	n	Avg.±SD
Technique 1		
Acinetobacter baumanni	1	5±.
Brucella spp.	3	6±0
E. coli	1	3±.
Enterococcus faecium	2	4.5±0.71
Salmonella species	1	5±.
Staphylococcus aureus	7	2.86±0.69
Staphylococcus capitis ssp urealyticus	1	4±.
Staphylococcus chromogenes	2	2.5±0.71
Staphylococcus epidermidis	5	2.6±0.89
Staphylococcus hominis	1	3±.
Staphylococcus warneri	1	8±.
Total	25	3.72±1.59
Technique 2		
Acinetobacter baumanni	0	.±.
Brucella spp.	0	.±.
E. coli	1	2.±.0
Enterococcus faecium	2	3.±.0
Salmonella species	0	.±.
Staphylococcus aureus	4	2.25±0.5
Staphylococcus capitis ssp urealyticus	0	.±.
Staphylococcus chromogenes	1	2±.0
Staphylococcus epidermidis	0	.±.
Staphylococcus hominis	0	.±.
Staphylococcus warneri	0	.±.
Total	8	2.2±0.45

In 13 different patients, seven different bacteria were produced only in technique B, namely *Acinetobacter baumanni*i, *Brucella* ssp., *Salmonella* ssp., *Staphylococcus capitis Ureolyticus* ssp., *Staphylococcus epidermidis*, *Staphylococcus hominis*, and *Staphylococcus warneri* (**Table 5**).

Table 5. Results of samples with reproduction only in the blood culture bottle technique

Pathogen	Reproductive positivity
Acinetobacter baumanni	1
Brucella spp	3
Salmonella species	1
Staphylococcus capitis ssp urealyticus	1
Staphylococcus epidermidis	5
Staphylococcus hominis	1
Staphylococcus warneri	1
Total	13

DISCUSSION

Looking at our results, we found that we diagnosed PJI in 89 patients as a result of cultures from aspiration of synovial fluid performed when PJI was suspected. In the tests performed with BCB, it was found that 13 patients grew bacteria that could not be obtained in the cultures performed with conventional media. Nowadays, the problem can be solved with less morbidity by diagnosing joint surgery and prosthesis infections, which increase in parallel, at an early stage and performing interventions before a biofilm layer forms.

The classical method used for culture evaluation in sterile body fluids other than blood is to sow different solid mediums without enrichment. Concentration-enhancing methods such as filtration or centrifugation can be used before planting.[11] If necessary, the need to check reproduction daily after planting on standard media and to conduct a subculture study represent additional burdens on the laboratory. For this reason, systems that will reduce laboratory workload and contribute to international standardization are frequently needed.

A study by Von Essen has revealed that patients who presented to the rheumatology clinic due to the synovial effusion retrospectively analyzed the culture results and that the cultivation made in the blood culture bottle yielded a greater variety of culture positivity compared to the solid medium and swab cultures.[17] Although this patient population, which was referred to the rheumatology clinic without PJI, is different from that evaluated in our study, sensitivity of cultivation to the BCB medium was also higher.

Çetin et al. have compared the evaluation of sterile body fluids with conventional culture cultivation and blood culture bottle systems and pointed out that blood culture bottle systems are faster and more diverse, emphasizing that bacteria such as *Brucella* and *Streptococcus pneumoniae* only grow in BCB systems.[18] Similarly, in this study, *Staphylococcus warneri*, *Staphylococcus capitis*, *Ureolyticus* ssp., *Staphylococcus*

epidermidis, *Staphylococcus hominis*, *Brucella* ssp., and *Salmonella* ssp. were only produced in the blood culture bottle, suggesting that this technique has higher pathogen sensitivity when comparing sterile fluid culture technique.

Birgisson et al. have reported that in case series consisting of five pediatric patients with septic arthritis, osteomyelitis and sepsis, Kingella kingea isolation was only successful via cultivation in the blood culture bottle.[19] Similarly, Yagupsky et al. have reported a high frequency of Kingella kingea infection obtained only by the blood culture system in the synovial fluid analysis.[20] Many bacteria did not reproduce in standard sterile body fluid culture procedure but concominant blood culture bottle procedure results were positive. The fact that *Staphylococcus epidermidis*, which is frequently isolated in PJI, was detected only in the cultivation of the BCB in five different patients suggests that direct cultivation alone can be misleading.[21,22]

In this study, the presence of *Brucella* spp. and *Staphilococcus epidermidis* were only detected using the BCB technique which suggests that this technique is more preferable for PJI diagnosis. In 13 different patients, seven different bacteria were produced only in the BCB technique suggesting that the contribution of the standard sterile fluid culture assessment technique is limited in the diagnosis of PJI.

Therefore, the results of this study suggest that BCB usage is beneficial in diagnosing PJI. Similar to this finding, BCB usage was found to be favorable in the sampling of pleural fluid[23] and synovial fluid.[24,25]

With the exceptions of the positive predictive value and the negative likelihood values, all diagnostic tests of standard sterile fluid culture assessment have found lower than the BCB technique. The low pathogen diversity of standard sterile fluid method suggests that this technique's contribution to diagnosing PJI is limited.

The main limitation of this study was the retrospective design of the criteria assessment for patients suspected of having PJI. Considering that the patients with synovial sampling were clinically observed for at least two years, the authors of this study concluded that this limitation did not adversely affect the study's results.

CONCLUSION

In the case of suspected PJI, BCB usage is a preferable and safe method that has the power to isolate more bacteria with higher diagnostic value and a greater variety of microorganisms.

Increasing rates of PJI suggest that diagnostic accuracy will become more important issue. Improvement of microbiological identification contributes both diagnosis and treatment of PJI.

Microbiological identification studies performed using only sterile fluid technique may lead to limitations in the diagnosis of PJI.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Gaziosmanpaşa University Clinical Research Ethics Committee (Date: 30.04.2020, Decision No: 20-KAEK-092).
Informed Consent: Informed consent for this study was obtained from all subjects for this study.
Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: The authors have no conflicts of interest to declare.
Financial Disclosure: The authors declared that this study has received no financial support.
Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Hanssen A. Evaluation and treatment of infection at the site of a total hip or knee arthroplasty. Instr Course Lect. 1999 48:111-22
2. Saleh KJ, Rand JA, McQueen DA. Current status of revision total knee arthroplasty: how do we assess results? J Bone Joint Surg Am. 2003;85 (suppl_1):S18-S20.
3. Barrack RL. The value of preoperative knee aspiration: don't ask, don't tell. Orthopedics. 1997;20 (9):862-4
4. Duff GP, Lachiewicz PF, Kelley SS. Aspiration of the knee joint before revision arthroplasty. Clin Orthop Relat Res. 1996;331:132-9.
5. Cui Q, Mihalko WM, Shields JS, Ries M, Saleh KJ. Antibiotic-impregnated cement spacers for the treatment of infection associated with total hip or knee arthroplasty. J Bone Joint Surg Am. 2007;89 (4):871-82.
6. Hanssen AD, Osmon DR. Evaluation of a staging system for infected hip arthroplasty. Clin Orthop Relat Res. 2002;403:16-22.
7. Peel TN, Dylla BL, Hughes JG, et al. Improved diagnosis of prosthetic joint infection by culturing periprosthetic tissue specimens in blood culture bottles. Am Soc Microbiol. 2016;1:e01776-01715.
8. Fuerst M, Fink B, Rüther W. The value of preoperative knee aspiration and arthroscopic biopsy in revision total knee arthroplasty. Z Orthop Ihre Grenzgeb. 2005;143(1):36-41
9. Williams JL, Norman P, Stockley I. The value of hip aspiration versus tissue biopsy in diagnosing infection before exchange hip arthroplasty surgery. J Arthroplasty. 2004;19 (5):582-6.
10. Gollwitzer H, Diehl P, Gerdesmeyer L, Mittelmeier W. Diagnostic strategies in cases of suspected periprosthetic infection of the knee. A review of the literature and current recommendations. Der Orthopade. 2006;35(9):904, 906-8, 910-6.
11. Forbes B. Processing specimens for bacteria. Manual of Clinical Microbiology. 1995;6th ed:265-81
12. Isenberg, Henry D. Clinical microbiology procedures handbook. American Society of Microbiology, 1992.
13. Bourbeau P, Riley J, Heiter BJ, Master R, Young C, Pierson C. Use of the BacT/Alert blood culture system for culture of sterile body fluids other than blood. J Clin Microbiol. 1998;36 (11):3273-7.
14. Simor AE, Scythes K, Meaney H, Louie M. Evaluation of the BacT/Alert® microbial detection system with FAN aerobic and FAN anaerobic bottles for culturing normally sterile body fluids other than blood. Diagn Microbiol Infect Dis. 2000;37(1):5-9.
15. Parvizi J, Zmistowski B, Berbari EF, et al. New definition for periprosthetic joint infection: from the Workgroup of the Musculoskeletal Infection Society. Clin Orthop Relat Res. 2011;469(11):2992.
16. Parvizi J, Tan TL, Goswami K, et al. The 2018 definition of periprosthetic hip and knee infection: an evidence-based and validated criteria. J Arthroplasty. 2018;33(5):1309-14. e1302.
17. von Essen R, Hölttä. Improved method of isolating bacteria from joint fluids by the use of blood culture bottles. Ann Rheum Dis. 1986;45(6):454-

7.

18. Çetin ES, Kaya S, Demirci M, Aridogan BC. Comparison of the BACTEC blood culture system versus conventional methods for culture of normally sterile body fluids. Adv Ther. 2007;24 (6):1271-7.
19. Birgisson H, Steingrimsson O, Gudnason T. Kingella kingae infections in paediatric patients: 5 cases of septic arthritis, osteomyelitis and bacteraemia. Scand J Infect Dis. 1997;29 (5):495-8.
20. Yagupsky P, Dagan R, Howard CW, Einhorn M, Kassis I, Simu A. High prevalence of Kingella kingae in joint fluid from children with septic arthritis revealed by the BACTEC blood culture system. J Clin Microbiol. 1992;30(5):1278-81.
21. Harris LG, El-Bouri K, Johnston S, et al. Rapid identification of staphylococci from prosthetic joint infections using MALDI-TOF mass-spectrometry. Int J Artif Organs. 2010;33(9):568-74.
22. Tande AJ, Patel R. Prosthetic joint infection. Clinical microbiology reviews. 2014;27 (2):302-45
23. Menzies SM, Rahman NM, Wrightson JM, et al. Blood culture bottle culture of pleural fluid in pleural infection. Thorax. 2011;66 (8):658-62.
24. Hughes JG, Vetter EA, Patel R, et al. Culture with BACTEC Peds Plus/F bottle compared with conventional methods for detection of bacteria in synovial fluid. J Clin Microbiol. 2001;39 (12):4468-71.
25. Portillo ME, Salvadó M, Trampuz A, et al. Improved diagnosis of orthopedic implant-associated infection by inoculation of sonication fluid into blood culture bottles. J Clin Microbiol. 2015;53 (5):1622-7.

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Original Article / Orijinal Araştırma

Ultrasonography in Anesthesiology: A Bibliometric Analysis of the Most Cited Articles

Anesteziyolojide Ultrasonografi: En Çok Atıf Alan Makalelerin Bibliyometrik Analizi

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Abstract

Aim: Ultrasonography (USG) has become a critical tool in anesthesiology, enhancing the safety and efficacy of nerve blocks, vascular interventions, and perioperative procedures. This study aims to perform a bibliometric analysis of the most cited articles on USG use in anesthesiology to identify trends and impactful research.

Material and Method: A bibliometric, descriptive, and analytical study was conducted using the Scopus database. The search terms "ultrasonography and anesthesiology" yielded 704 articles. After excluding reviews, letters, editorials, notes, conference papers, book chapters, and retracted papers, 337 original research articles remained. These were ranked by citation count and analyzed. Data collected included the first author, publication year, article title, journal title, main subject, academic specialization of the first author, institution, country of origin, and citation information. The median number of citations per year and journal impact factors were calculated.

Results: The median number of citations for the 100 most cited articles was 18. The most cited article, authored by Ramsing D., received 91 citations. Anesthesiologists authored 78% of these top-cited articles. The primary focus areas included peripheral nerve blocks, central nerve blocks, and catheterization. The median number of citations per year was 2.85.

Conclusion: The increasing use of USG in anesthesiology is reflected in the high citation rates of related studies, most of which were published in reputable journals. This trend underscores the importance of USG in enhancing clinical practice and the influence of robust financial and technical support on research impact.

Keywords: Anesthesiology, ultrasonography, nerve blocks, bibliometric analysis, citation analysis

Öz

Amaç: Ultrasonografi (USG); anesteziyolojide sinir blokları, vasküler girişimler ve perioperatif işlemlerin güvenliği ve etkinliğini arttıran önemli bir araç halini almıştır. Bu çalışma, anesteziyolojide USG kullanımına ilişkin en çok alıntı yapılan makalelerin bibliyometrik analizinin yapılması amaçlanmıştır.

Gereç ve Yöntem: Scopus veri tabanı kullanılarak bibliyometrik, tanımlayıcı ve analitik bir çalışma yapıldı. "Ultrasonografi ve anesteziyoloji" arama terimleri için, 704 makale listelendi. İncelemeler, mektuplar, başyazılar, notlar, konferans makaleleri, kitap bölümleri ve geri çekilmiş makaleler dışlandığında geriye 337 orijinal araştırma makalesi kaldı. Bunlar alıntı sayısına göre sıralanarak, analiz edildi. Toplanan veriler arasında ilk yazar, yayın yılı, makale başlığı, dergi başlığı, ana konu, ilk yazarın akademik uzmanlığı, kurumu, menşe ülkesi ve atıf bilgileri yer almaktadır. Ayrıca, yıllık ortalama atıf sayısı ve dergi etki faktörleri de hesaplandı.

Bulgular: En çok atıf alan 100 makalenin ortanca atıf sayısı 18 oldu. En çok atıf alan Ramsing D.'nin makalesi ise 91 atıf almıştı. En çok alıntı yapılan makalelerin %78'inin, anestezistler tarafından yazıldığı saptandı. Bu makalelerin primer olarak periferik sinir blokları, merkezi sinir blokları ve kateterizasyon konularına odaklandığı saptandı. Ayrıca, yıllık ortalama atıf sayısının da 2,85 olduğu görüldü.

Sonuç: Anesteziyolojide USG kullanımdaki artış, saygın dergilerde yayınlanmış olan ilgili çalışmaların yüksek atıf oranlarına da yansımaktadır. Bu trend, USG'nin klinik uygulamaları geliştirmedeki önemini vurgulamaktadır. Ve ayrıca, güçlü mali ve teknik desteğin araştırmalarını üzerindeki etkisini de göstermektedir.

Anahtar Kelimeler: Anesteziyoloji, ultrasonografi, sinir blokları, bibliometrik analiz, atıf analizi

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INTRODUCTION

Innovative technologies in recent years have caused significant advances in the field of health care, as in many other fields. Especially, imaging methods have enabled interventional procedures to be performed more safely and effectively with lesser complications.[1] Ultrasonographic imaging methods are used in many areas of medicine. The use of ultrasonography (USG) in anesthesiology and reanimation has also increased in recent years. High-resolution real-time imaging of anatomical structures with USG, especially before interventional invasive procedures, ensures successful and rapid completion of nerve blocks, vascular interventions, and perioperative procedures performed in anesthesiology.[2,3] In parallel with the widespread use of USG in anesthesiology, the number of publications in this field has also increased. Bibliometric analyses provide guidance to academicians about the content and quality of publications on a particular subject.[4] In this context, this bibliometric analysis was conducted to identify the top 100 articles with the highest number of citations on the use of USG in anesthesiology and describe the characteristics of these articles.

MATERIAL AND METHOD

This study was designed as a bibliometric, descriptive, and analytical analysis. The study material consisted of 704 articles obtained as a result of the search conducted in the Scopus citation database using the keywords "ultrasonography and anesthesiology" on January 1st, 2023.

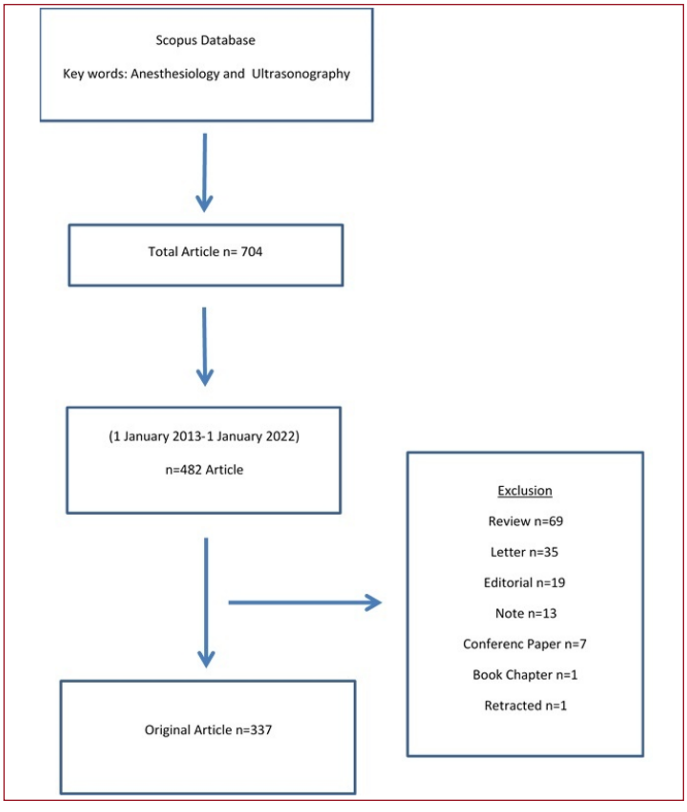

Figure 1. Flow Chart

482 articles were published between 2013 and 2022.[5] While articles focusing on the use of USG in anesthesiology were included in the study, publications such as reviews, letters, editorials, notes, conference papers, book chapters, and retracted papers were excluded from the study (**Figure 1**). The remaining 337 original research articles were listed in **Table 1**. And, all articles were reviewed in detail by an anesthesiologist. For each article, descriptive data such as the first author, publication year and title of the article, the title, main subject, genre and publication language of the journal in which the article was published, the academic specialization of the first author of the article and the institution where he/she was working at the time of submission of the article, country of origin of the article and citation information were obtained from the Scopus database and recorded. The median number of citations received by the article per year was calculated with using the formula below:

Median number of citations per year=total number of citations/[2023-year of publication])

The impact factors (IF) of the journals where the articles were published were viewed on the official websites of the journals. The articles were classified according to the academic specializations of their first authors, i.e., [1] Anesthesiology and Reanimation, [2] Biomedical Engineering, [3] Electrical and Computer Engineering, [4] Emergency Medicine, [5] Surgery and [6] Others, as well as their country of origin.

The research data evaluated online and collected on data forms were expressed using descriptive statistics such as median [interquartile range (IQR), 25th-75th percentile] and frequency (n) and percentage (%) values. Bar and pie charts were used to represent the data graphically.

RESULTS

Of the 337 original research articles on the use of USG in anesthesiology reviewed within the scope of the research, top 100 articles with the highest number of citations were listed in descending order for citations (**Table 1**). The median number of citations per year of the all articles was 18 (14-27.75). While the article by Ramsing D.[6] was the most cited article with 91 citations in the list, the article by Woodland DC.[7] was the least cited (**Table 1**). Among the all study articles, Frykholm P.'s article,[8] the most recently published article, which was published in 2022, received 17 citations. The number of first authors with two articles on the list was 7. These authors are Batker M, Lufting J, Mariano E, Ramsing D, Tran D, Woodworth G.E, and Yu S.[6,9,10-14] Thus, the 100 most cited articles were authored by 93 first authors. Ramsing D. stood out in that two articles, of which he was the first author, were included in the 100 most cited articles, and one of these articles was the most cited article in the list. Two of the 100 most cited articles were published in French, one in German, and the others in English.

Table 1.The most-cited 100 manuscript on ultrasound in anesthesiology between 2012 and 2023 years

Rank	First Author	Total Citations	Title	Journal	Year
1	Ramsingh D	91	Impact assessment of perioperative point-of-care ultrasound training on anesthesiology residents	Anesthesiology	2015
2	Marhofer D	83	Magnetic resonance imaging analysis of the spread of local anesthetic solution after ultrasound-guided lateral thoracic paravertebral blockade: A volunteer study	Anesthesiology	2013
3	Mahmood F	77	Perioperative ultrasound training in anesthesiology: A call to action	Anesth Analg	2016
4	Bouvet L	71	Real-time detection of gastric insufflation related to facemask pressure-controlled ventilation using ultrasonography of the antrum and epigastric auscultation in nonparalyzed patients	Anesthesiology	2014
5	Luftig J	68	Successful emergency pain control for posterior rib fractures with ultrasound-guided erector spinae plane block	Am J Emerg Med	2018
6	Berk D	65	Ultrasound-guided radial arterial cannulation: Long axis/in-plane versus short axis/ out-of-plane approaches?	J Clin Monit Comput	2013
7	Sahin L	54	Ultrasound-guided transversus abdominis plane block in children: A randomised comparison with wound infiltration	Eur J Anaesthesiol	2013
8	Tiran E	51	Transcranial Functional Ultrasound Imaging in Freely Moving Awake Mice and Anesthetized Young Rats without Contrast Agent	Ultrasound Med Biol	2017
9	Lamb A	51	Accuracy of identifying the cricothyroid membrane by anesthesia trainees and staff in a Canadian institution	Can J Anesth	2015
10	Yu S	45	Lumbar Ultrasound Image Feature Extraction and Classification with Support Vector Machine	Ultrasound Med Biol	2015
11	Andruszkiewicz P	41	Effectiveness and validity of sonographic upper airway evaluation to predict difficult laryngoscopy	J Ultrasound Med	2016
12	Sultan S	41	Simulators for training in ultrasound guided procedures	Med Ultrasonography	2013
13	Mariano E	38	A randomized comparison of proximal and distal ultrasound-guided adductor canal catheter insertion sites for knee arthroplasty	J Ultrasound Med	2014
14	Wong S	34	Real-time ultrasound-guided spinal anesthesia using the SonixGPS needle tracking system: A case report	Can J Anesth	2013
15	Dres M	34	Usefulness of Parasternal Intercostal Muscle Ultrasound during Weaning from Mechanical Ventilation	Anesthesiology	2020
16	Ramsingh D	34	Comparison of the didactic lecture with the simulation/model approach for the teaching of a novel perioperative ultrasound curriculum to anesthesiology residents	J Clin Anesth	2014
17	Smistad E	32	Real-Time Automatic Artery Segmentation, Reconstruction and Registration for Ultrasound-Guided Regional Anaesthesia of the Femoral Nerve	IEEE Trans Med Imaging	2016
18	Batker M	32	Routine pre-operative focused ultrasonography by anesthesiologists in patients undergoing urgent surgical procedures	Acta Anaesthesiol Scand	2014
19	Zimmerman J	31	The Nuts and Bolts of Performing Focused Cardiovascular Ultrasound (FoCUS)	Anesth Analg	2017
20	Tran D	31	Primary failure of thoracic epidural analgesia in training centers: The invisible elephant?	Reg Anesth Pain Med	2016
21	Peters C	31	Ultrasound guidance versus direct palpation for radial artery catheterization by expert operators: a randomized trial among Canadian cardiac anesthesiologists	Can J Anesth.	2015
22	Sviggum H	31	Needle echogenicity in sonographically guided regional anesthesia blinded comparison of 4 enhanced needles and validation of visual criteria for evaluation	J Ultrasound Med	2013
23	Yu X	30	Performance of Lung Ultrasound in Detecting Peri-Operative Atelectasis after General Anesthesia	Ultrasound Med Biol	2016
24	Aksu C	29	Analgesic effect of the bi-level injection erector spinae plane block after breast surgery: A randomized controlled trial	Agri	2019
25	Goettel N	28	Monitoring of cerebral blood flow autoregulation in adults undergoing sevoflurane anesthesia: a prospective cohort study of two age groups	J Clin Monit Comput	2016
26	Pesteie M	27	Automatic Localization of the Needle Target for Ultrasound-Guided Epidural Injections	IEEE Trans Med Imaging	2018
27	Diaz gomez J	27	Impact of a focused transthoracic echocardiography training course for rescue applications among anesthesiology and critical care medicine practitioners: A prospective study	J Cardiothorac Vasc Anesth	2015
28	Kessler J	27	Ultrasound-guided regional anesthesia: Learning with an optimized cadaver model	Surg Radiol Anat	2014
29	Woodworth G	26	Efficacy of computer-based video and simulation in ultrasound-guided regional anesthesia training	J Clin Anesth	2014
30	Conway D	26	A comparison of noninvasive bioreactance with oesophageal Doppler estimation of stroke volume during open abdominal surgery: An observational study	Eur J Anaesthesiol	2013
31	Mariano E	26	A randomized comparison of longand short-axis imaging for in-plane ultrasound-guided femoral perineural catheter insertion	J Ultrasound Med	2013
32	Dobson G	25	Guidelines to the Practice of Anesthesia - Revised Edition 2017	Can J Anaesth	2017
33	Munirama S	25	Physical properties and functional alignment of soft-embalmed Thiel human cadaver when used as a simulator for ultrasound-guided regional anaesthesia	Br J Anaesth	2016
34	Dal Moro F	24	Ultrasound-guided transversus abdominis plane block (US-TAPb) for robot-assisted radical prostatectomy: a novel four-point technique results of a prospective, randomized study	J Rob Surg	2019

Table 1.The most-cited 100 manuscript on ultrasound in anesthesiology between 2012 and 2023 years (Cont...)

Rank	First Author	Total Citations	Title	Journal	Year
35	Borg LK	24	Preliminary Experience Using Eye-Tracking Technology to Differentiate Novice and Expert Image Interpretation for Ultrasound-Guided Regional Anesthesia	J Ultrasound Med	2018
36	Corvetto M	24	Simulation-based training program with deliberate practice for ultrasound-guided jugular central venous catheter placement	Acta Anaesthesiol Scand	2017
37	Lee D	24	Ultrasound evaluation of the radial artery for arterial catheterization in healthy anesthetized patients	J Clin Monit Comput	2016
38	McGraw R	23	Development and evaluation of a simulation-based curriculum for ultrasound-guided central venous catheterization	Can J Emerg Med	2016
39	McVicar J	22	Novice performance of ultrasound-guided needling skills: Effect of a needle guidance system	Reg Anesth Pain Med	2015
40	Edrich T	22	A Comparison of Web-Based with Traditional Classroom-Based Training of Lung Ultrasound for the Exclusion of Pneumothorax	Anesth Analg	2016
41	Harrison T	22	Feasibility of eye-tracking technology to quantify expertise in ultrasound-guided regional anesthesia	J Anesth	2016
42	Kan J	22	An in vitro study to evaluate the utility of the "air test" to infer perineural catheter tip location	J Ultrasound Med	2013
43	Batker M	21	Implementing point-of-care ultrasonography of the heart and lungs in an anesthesia department	Acta Anaesthesiol Scand	2017
44	Ramlogan R	20	A virtual reality simulation model of spinal ultrasound: Role in teaching spinal sonoanatomy	Reg Anesth Pain Med	2017
45	Wang Q	19	Comparison of the effects of ultrasound-guided erector spinae plane block and wound infiltration on perioperative opioid consumption and postoperative pain in thoracotomy,	J Coll Phys Surg Pak	2019
46	Tran D	19	Beyond Ultrasound Guidance for Regional Anesthesiology	Reg Anesth Pain Med	2017
47	Defosse J	19	A Germany-wide survey on anaesthesia in thoracic surgery	Anaesthesist	2014
48	Laurent DA	19	A valid and reliable assessment tool for remote simulation-based ultrasound-guided regional anesthesia	Reg Anesth Pain Med	2014
49	Uppal V	18	Effect of beam steering on the visibility of echogenic and non-echogenic needles: a laboratory study	Can J Anesth	2017
50	Gopalasingam N	18	Ultrasound-guided radial artery catheterisation increases the success rate among anaesthesiology residents: A randomised study	J Vasc Access	2017
51	Kant A	18	Application of the continual reassessment method to dose-finding studies in regional anesthesia: An estimate of the ED95 dose for 0.5% bupivacaine for ultrasound-guided supraclavicular block,2013,	Anesthesiology	2013
52	Ashab H	18	An augmented reality system for epidural anesthesia (AREA): Prepuncture identification of vertebrae	Anesthesiology	2013
53	Frykholm P	17	Pre-operative fasting in children: A guideline from the European Society of Anaesthesiology and Intensive Care	IEEE Trans Biomed Eng	2022
54	Mok D	17	Point-of-care ultrasonography in Canadian anesthesiology residency programs: a national survey of program directors	Eur J Anaesthesiol	2017
55	Gurkan Y	17	One operators experience of ultrasound guided lumbar plexus block for paediatric hip surgery	J Clin Monit Comput	2017
56	Barrington M	17	Determining the Learning Curve for Acquiring Core Sonographic Skills for Ultrasound-Guided Axillary Brachial Plexus Block	Reg Anesth Pain Med	2016
57	Udani AD	17	Comparative-effectiveness of simulation-based deliberate practice versus self-guided practice on resident anesthesiologists' acquisition of ultrasound-guided regional anesthesia skills	Reg Anesth Pain Med	2016
58	Kokofer A	17	Ropivacaine 0.375% vs. 0.75% with prilocaine for intermediate cervical plexus block for carotid endarterectomy: A randomised trial	Eur J Anaesthesiol	2015
59	Alvarez-Diaz N	17	Comparison between transthoracic lung ultrasound and a clinical method in confirming the position of double-lumen tube in thoracic anaesthesia. A pilot study	Rev Esp Anestesiol Reanim	2015
60	Dolu H	17	Comparison of an ultrasound-guided technique versus a landmark-guided technique for internal jugular vein cannulation	J Clin Monit Comput	2015
61	Yu S	17	Automatic Identification of Needle Insertion Site in Epidural Anesthesia with a Cascading Classifier	Ultrasound Med Biol	2014
62	Steinfelt T	17	Nerve localization for peripheral regional anesthesia. Recommendations of the German Society of Anaesthesiology and Intensive Care Medicine	Anaesthesist	2014
63	Barbe N	17	Locating the cricothyroid membrane in learning phase: Value of ultrasonography?	Ann Fr Anesth Reanim	2014
64	Liu Y	17	Comparison of the development of performance skills in ultrasound-guided regional anesthesia simulations with different phantom models	Simul Healthc	2013
65	Whittaker S	17	An ultrasound needle insertion guide in a porcine phantom model	Anaesthesia	2013
66	Adler AC	16	Cardiac and lung point-of-care ultrasound in pediatric anesthesia and critical care medicine: Uses, pitfalls, and future directions to optimize pediatric care	Paediatr Anaesth	2019
67	Sujata N	15	A randomised trial to compare the increase in intracranial pressure as correlated with the optic nerve sheath diameter during propofol versus sevoflurane-maintained anesthesia in robot-assisted laparoscopic pelvic surgery	J Rob Surg	2019

Table 1.The most-cited 100 manuscript on ultrasound in anesthesiology between 2012 and 2023 years (Cont...)

Rank	First Author	Total Citations	Title	Journal	Year
68	Oliveira KF	15	Determining the amount of training needed for competency of anesthesia trainees in ultrasonographic identification of the cricothyroid membrane	BMC Anesthesiol	2017
69	Koskinen L	15	Can intracranial pressure be measured non-invasively bedside using a two-depth Doppler-technique?	J Clin Monit Comput	2017
70	Mariano ER	15	Evaluation of a standardized program for training practicing anesthesiologists in ultrasound-guided regional anesthesia skills	Anesth Pain Med	2015
71	Rafii-Tari H	15	Panorama Ultrasound for Navigation and Guidance of Epidural Anesthesia	J Ultrasound Med	2015
72	Gupta RK	15	Improving Needle Visualization by Novice Residents During an In-Plane Ultrasound Nerve Block Simulation Using an In-Plane Multiangle Needle Guide	J Ultrasound Med	2013
73	Morparia KG	14	Respiratory variation in peak aortic velocity accurately predicts fluid responsiveness in children undergoing neurosurgery under general anesthesia	Pain Med	2018
74	Beigi, P	14	Three-Dimensional Ultrasound-Guided Real-Time Midline Epidural Needle Placement with Epiguide: A Prospective Feasibility Study	J Clin Monit Comput	2017
75	Mohammadi, SS	14	Usefulness of ultrasound view of larynx in pre-anesthetic airway assessment: A comparison with Cormack-Lehane classification during direct laryngoscopy	Ultrasound Med Biol	2016
76	Gurnaney HG	14	Anesthetic management of the first pediatric bilateral hand transplant	Can J Anesth	2016
77	Jeon Y	14	Evaluation of a simplified augmented reality device for ultrasound-guided vascular access in a vascular phantom	J Clin Anesth	2014
78	Sola C	14	Ultrasound-guided tranversus abdominis plane block for herniorrhaphy in children: What is the optimal dose of levobupivacaine?	Eur J Anaesthesiol	2014
79	You-Ten	13	Practice of ultrasound-guided palpation of neck landmarks improves accuracy of external palpation of the cricothyroid membrane	Anesth Analg	2018
80	Turkstra TP	13	Preprocedural ultrasound assessment does not improve trainee performance of spinal anesthesia for obstetrical patients: a randomized controlled trial	J Clin Anesth	2017
81	Johnson AN	13	Ultrasound-guided needle technique accuracy prospective comparison of passive magnetic tracking versus unassisted echogenic needle localization	Reg Anesth Pain Med	2017
82	Przkora R	13	Evaluation of the Head-Mounted Display for Ultrasound-Guided Peripheral Nerve Blocks in Simulated Regional Anesthesia	Pain Med	2015
83	Vial F	13	Evaluating the learning curve for the transversus abdominal plane block: a prospective observational study	Can J Anesth	2015
84	Miyashita T	13	FaceTime for teaching ultrasound-guided anesthetic procedures in remote place	J Clin Monit Comput	2014
85	Kilicaslan A	13	Differences in tip visibility and nerve block parameters between two echogenic needles during a simulation study with inexperienced anesthesia trainees	J Anesth	2014
86	Meineri M	12	Canadian recommendations for training and performance in basic perioperative point-of-care ultrasound: recommendations from a consensus of Canadian anesthesiology academic centres	Can J Anesth	2021
87	Sanders JA	12	Incorporating Perioperative Point-of-Care Ultrasound as Part of the Anesthesia Residency Curriculum	J Cardiothorac Vasc Anesth	2019
88	Sappenfield JW	12	Visualization improves supraclavicular access to the subclavian vein in a mixed reality simulator	Anesth Analg	2018
89	Alkhatib M	12	Adaptive median binary patterns for fully automatic nerves tracking in ultrasound images	Comput Methods Programs Biomed	2018
90	Luftig J	12	Ultrasound-guided retroclavicular approach infraclavicular brachial plexus block for upper extremity emergency procedures	Am J Emerg Med	2017
91	Kuang Y	12	Modelling and characterisation of a ultrasound-actuated needle for improved visibility in ultrasound-guided regional anaesthesia and tissue biopsy	Ultrasonics	2016
92	Deshpande R	12	Training the anesthesiologist in point-of-care ultrasound	Int. Anesthesiol Clin	2016
93	Woodworth GE	12	Development and Validation of an Assessment of Regional Anesthesia Ultrasound Interpretation Skills	Anesth. Pain Med	2015
94	Khedkar SM	12	Ultrasound-guided ilioinguinal and iliohypogastric nerve block, a comparison with the conventional technique: An observational study	Saudi J Anaesth	2015
95	Min JY	12	Ultrasonographic assessment of optic nerve sheath diameter during pediatric laparoscopy	Ultrasound Med Biol	2015
96	Vanderwielen BA	12	Teaching sonoanatomy to anesthesia faculty and residents: Utility of hands-on gel phantom and instructional video training models	J Clin Anesth	2015
97	Niazi AU	12	The use of an online three-dimensional model improves performance in ultrasound scanning of the spine: A randomized trial	Can J Anesth	2013
98	Leviter J	11	"Full Stomach" Despite the Wait: Point-of-care Gastric Ultrasound at the Time of Procedural Sedation in the Pediatric Emergency Department	Academic Emergency Medicine,	2019
99	Petrisor C	11	Preoperative difficult airway prediction using suprahyoid and infrahyoid ultrasonography derived measurements in anesthesiology	Medical Ultrasonography	2019
100	Woodland DC	11	Routine chest X-ray is unnecessary after ultrasound-guided central venous line placement in the operating room	Journal of Critical Care	2018

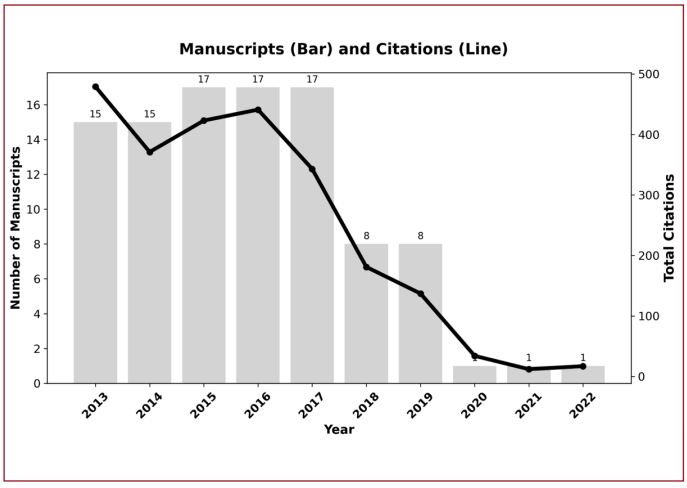

Figure 2. Publications and the cites over time

As expected, the number of articles and total citations in previous years were found to quite high. A fluctuating trend in the number of articles and total citations are also apparent in the last 10 years.

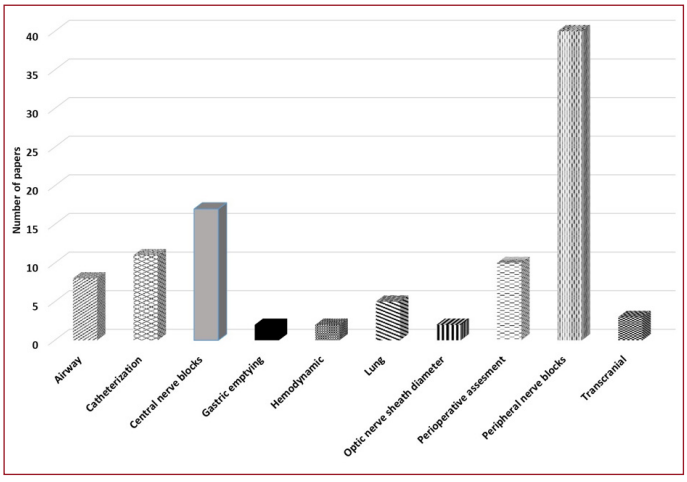

Figure 3. Evaluation of all study articles for topics

All study articles most frequently addressed the use of USG for peripheral nerve blocks, followed by central nerve blocks, catheterization, perioperative evaluation, and airway procedures (**Figure 3**). The median number of citations per year of all study articles was 2.85 (2-4.1).

The academic specialization of the first authors of 78% of the top 100 articles was anesthesiology and reanimation. In the 78 studies conducted by anesthesiology and reanimation specialists among the top 100 articles on the use of USG in anesthesiology, the most commonly addressed main topic was the use of USG for peripheral nerve blocks (n=31). On the other hand, in the six studies conducted by electrical and computer engineering experts among the top 100 articles on the use of USG in anesthesiology, the most commonly addressed main topic was the use of USG for central nerve blocks (n=5).

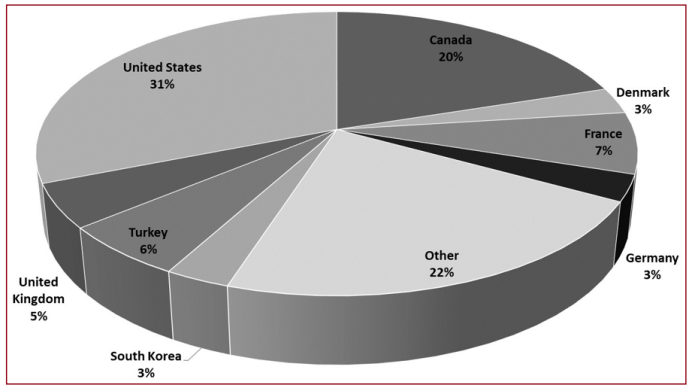

Figure 4. Country graph of the most cited articles

Additionally, it was determined that the 100 most cited articles were written from 23 different countries. It was seen that studies on these topics were mostly carried out in America (USA), followed by Canada, France, Turkey and United Kingdom (UK), respectively (**Figure 4**).

It was determined that 7 of the articles in the top 10, according to the total number of citations, also ranked among the top 10 articles in terms of the number of citations received per year (**Table 2**). The most commonly addressed main topic in the ten most cited articles per year in the field of USG and anesthesiology was the use of USG for peripheral nerve blocks (n=3), followed by the use of USG for perioperative training (n=2), preoperative fasting (n=1), gastric insufflation (n=1), arterial catheterization (n=1), transcranial function (n=1), and weaning from mechanical ventilation (n=1). It was noteworthy that Turkey was the country of origin of two of the top 10 articles with the highest number of citations per year (**Table 2**).

Among the top 10 journals with more than three of the 100 most cited articles on the use of USG in anesthesiology, it was determined that the first three journals with the highest 2021 CiteScores (10.4, 9.3, and 8.5, respectively) were Q1 and Q2 journals. Additionally, the IFs of these first three journals were 8.986, 6.627, and 5.564, respectively (**Table 3**). It was also determined that the number of publications in these quality journals with high CiteScores and IFs was lower than in other journals.

DISCUSSION

Bibliometric studies guide academicians who have just started their academic careers to areas where they can do research.[15] Before this study, there was a lack of comprehensive analysis on the most influential research in the use of ultrasonography (USG) in main anesthesiology. This bibliometric study fills that gap by identifying and analyzing the most cited articles on this topic. Our study featured 704 articles obtained as a result of the search conducted in the Scopus citation database using the keywords "ultrasonography and anesthesiology". More than half of these articles (n=482) were conducted in the last decade, that is, between 2013 and 2022. Among the all study articles on the use of USG in anesthesiology, the total

number of citations of the most cited article was 91, while the total number of citations of the least cited article was 11. The study's findings indicated that acedemicians consider the use of USG in anesthesiology interesting.

The most commonly addressed main topic in the top 100 articles in USG and anesthesiology was the use of USG for peripheral nerve blocks, followed by the use of USG for invasive procedures such as central nerve blocks, catheterization, and airway procedures.

It is noteworthy that adress in that particular study were mostly based on simulation studies. It is thought that this outcome is especially an increase parallel to the development in technology and artificial intelligence.[16,17] Since articles with older publication dates generally have higher total citation numbers, we also examined the median number of citations per year. Notably, 7 of the articles in the top 10 according to the total number of citations also ranked among the top 10 articles according to the number of citations received by year. In sum, well-designed prospective studies always attract the attention of academicians in the medical community, and the authors of such studies receive the value they deserve in world literature through the citations made to their studie.[6,8,10,18,19]

USG, a non-invasive imaging method, has recently become very popular among clinicians. In anesthesiology and reanimation departments where invasive procedures are frequently performed, using USG before surgical procedures increases the physician's success and reduces the complication rate.[1] It was determined that anesthesiologists authored 78% of the top 100 articles with the highest number of citations and that they most commonly addressed the use of USG for peripheral nerve blocks.[20,21] Notably, the physicians performing USG in the studies were not radiologists. USG imaging techniques, which were generally used only by radiologists in the past, are now widely used by anesthesiologists and other physicians. Physicians working in the fields of "anesthesiology and pain medicine" and "critical care and intensive care medicine" are especially expected to use USG when performing interventional procedures. For this reason, USG training should be given to all physicians working in anesthesiology and reanimation in our country, especially during their residency.

Table 2. The analysis of top 10 manuscript for citations per year

Citations per year	Total citations	Rank in the top 100 articles	First Author	Year	Journal	Title
17	17	53	Frykholm P	2022	IEEE Trans Biomed Eng	Pre-operative fasting in children: A guideline from the European Society of Anaesthesiology and Intensive Care
13.6	58	5	Luftig J	2018	Am J Emerg Med	Successful emergency pain control for posterior rib fractures with ultrasound-guided erector spinae plane block
11.38	91	1	Ramsingh D	2015	Anesthesiology	Impact assessment of perioperative point-of-care ultrasound training on anesthesiology residents
11.33	34	15	Dres M	2020	Anesthesiology	Usefulness of Parasternal Intercostal Muscle Ultrasound during Weaning from Mechanical Ventilation
11	77	3	Mahmood F	2016	Anesth Analg	Perioperative ultrasound training in anesthesiology: A call to action
8.5	51	8	Tiran E	2017	Ultrasound Med Biol	Transcranial Functional Ultrasound Imaging in Freely Moving Awake Mice and Anesthetized Young Rats without Contrast Agent
8.3	83	2	Marhofer D	2013	Anesthesiology	Magnetic resonance imaging analysis of the spread of local anesthetic solution after ultrasound-guided lateral thoracic paravertebral blockade: A volunteer study
7.89	71	4	Bouvet L	2014	Anesthesiology	Real-time detection of gastric insufflation related to facemask pressure-controlled ventilation using ultrasonography of the antrum and epigastric auscultation in nonparalyzed patients
7.25	29	24	Aksu C	2019	Agri	Analgesic effect of the bi-level injection erector spinae plane block after breast surgery: A randomized controlled trial
6.5	65	6	Berk D	2013	J Clin Monit Comput	Ultrasound-guided radial arterial cannulation: Long axis/in-plane versus short axis/out-of-plane approaches?

Table 3. Journals with more than three published articles from the 100 most-cited clinical studies on ultrasonography in the anesthesiology

Rank	Journal Title	Number of Manuscipt	Cite Score 2021	IF	Category/Quartile/Indexing
1	Canadian Journal of Anaesthesia	9	7.6	6.713	ANESTHESIOLOGY - SCIE(Q1)
2	Journal of Clinical Monitoring and Computing	8	3.7	1.977	ANESTHESIOLOGY - SCIE(Q4)
3	Journal of Ultrasound in Medicine	8	4.2	2.754	ACOUSTICS - SCIE(Q2) RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING - SCIE(Q3)
4	Regional Anesthesia and Pain Medicine	8	8.5	5.564	ANESTHESIOLOGY - SCIE(Q2)
5	Ultrasound in Medicine and Biology	7	5.4	3.694	ACOUSTICS - SCIE(Q1) RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING - SCIE(Q2)
6	Anesthesiology	6	10.4	8.986	ANESTHESIOLOGY - SCIE(Q1)
7	European Journal of Anaesthesiology	5	5.5	4.183	ANESTHESIOLOGY - SCIE(Q2)
8	Anesthesia and Analgesia	5	9.3	6.627	ANESTHESIOLOGY - SCIE(Q1)
9	Journal of Clinical Anesthesia	5	6.7	9.375	ANESTHESIOLOGY - SCIE(Q1)
10	Acta Anaesthesiologica Scandinavica	3	3.4	2.274	ANESTHESIOLOGY - SCIE(Q4)

The high number of citations made to an article is generally related to the proper planning and reliability of the study. Robust design of studies requires both sufficient financial budget and technical structure support. We determined that the top five countries where the top 100 articles with the highest number of citations on the use of USG in anesthesiology were conducted are economically developed and developing countries. It is gratifying that Turkey ranks fourth among these five countries. The results reveal that the majority of impactful research is authored by anesthesiologists and published in high-impact journals from developed countries. This emphasizes the importance of financial and technological support in producing high-quality studies.

Notably, 80% of the top 10 journals with more than three of the top 100 articles on the use of USG in anesthesiology were Q1 and Q2 journals and generally had a high IF. Researchers select the journals to publish their articles while designing their studies and during the manuscript's writing according to the journals' reliability and IF. Considering how difficult and laborious it is to publish articles in high-quality journals, there is no doubt that there is more trust in articles published in such journals.

The Web of Science (WOS) database provides only citations of its own journals. Additionally, the citations are detected late, approximately 1 year later. However, the Scopus database is broder as it includes open access and peer-reviewed journals. It provides wider access to readers. For this reason, this study relied solely on the Scopus database, which may have led to the exclusion of relevant articles indexed elsewhere. Citation counts can vary between databases, and this limitation might affect the comprehensiveness of the analysis. Additionally, while citation metrics are valuable, they do not fully capture an article's scientific contribution or clinical impact.

CONCLUSION

This bibliometric analysis highlights the growing importance of ultrasonography in anesthesiology, particularly for nerve blocks and vascular procedures. The most cited research, primarily authored by anesthesiologists from developed countries, underscores the influence of financial and technological resources on the quality and impact of studies. These findings emphasize the critical role of ultrasonography in enhancing clinical practice and improving patient outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of **XXXXXXXXXXXXXXXX** Ethics Committee (Date: **XXXXXXXXXX**, Decision No: 2017/99).

Informed Consent: Informed consent was obtained from the families of all children participating in the study.

Referee Evaluation Process: Externally peer-reviewed.

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

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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REFERENCES

1. Özçakar L, Ricci V, Chang KV, Mezian K, Kara M. Musculoskeletal ultrasonography: ninety-nine reasons for physiatrists. Med Ultrason. 2022;24(2):137-9.
2. Wu WT, Lin JA, Chen LR, et al. Ultrasound Imaging, Guidance, and Treatment for Shoulder-related Pain Syndrome: A Bibliometric Analysis. Pain Physician. 2022;25(9):33-45.
3. Güler T, Yurdakul FG, Önder ME, et al. Ultrasound-guided genicular nerve block versus physical therapy for chronic knee osteoarthritis: a prospective randomised study. Rheumatol Int. 2022;42(4):591-600.
4. Zhao Y, Zhang H, Song M. Clinical Observation of Ultrasound-Guided Nerve Block Anesthesia on Postoperative Pain Control of Fracture Patients. J Healthc Eng. 2022;2022:9510669.
5. https://www.scopus.com/search/form
6. Ramsingh D, Rinehart J, Kain Z, et al. Impact assessment of perioperative point-of-care ultrasound training on anesthesiology residents. Anesthesiology. 2015;123(3):670-82.
7. Woodland DC, Randall Cooper C, Farzan Rashid M, et al. Routine chest X-ray is unnecessary after ultrasound-guided central venous line placement in the operating room. J Crit Care. 2018;46:13-6.
8. Frykholm P, Disma N, Andersson H, et al. Pre-operative fasting in children: A guideline from the European Society of Anaesthesiology and Intensive Care. Eur J Anaesthesiol. 2022;39(1):4-25.
9. Bøtker MT, Vang ML, Grøfte T, Sloth E, Frederiksen CA. Routine pre-operative focused ultrasonography by anesthesiologists in patients undergoing urgent surgical procedures. Acta Anaesthesiol Scand. 2014;58(7):807-14.
10. Luftig J, Mantuani D, Herring AA, Dixon B, Clattenburg E, Nagdev A. Successful emergency pain control for posterior rib fractures with ultrasound-guided erector spinae plane block. Am J Emerg Med 2018;36(8):1391-6.
11. Mariano ER, Kim TE, Wagner MJ, et al. A randomized comparison of proximal and distal ultrasound-guided adductor canal catheter insertion sites for knee arthroplasty. J Ultrasound Med 2014;33 (9):1653-62.
12. Tran DQ, Boezaart AP, Neal JM. Beyond Ultrasound Guidance for Regional Anesthesiology. Reg Anesth Pain Med. 2017;42(5):556-63.
13. Woodworth GE, Carney PA, Cohen JM, et al. Development and Validation of an Assessment of Regional Anesthesia Ultrasound Interpretation Skills. Reg Anesth Pain Med. 2015;40(4):306-14.
14. Yu S, Tan KK, Sng BL, Li S, Sia AT. Lumbar Ultrasound Image Feature Extraction and Classification with Support Vector Machine. Ultrasound Med Biol. 2015;41(10):2677-89.
15. Bayram B, Limon Ö, Limon G, Hancı V. Bibliometric analysis of top 100 most-cited clinical studies on ultrasound in the Emergency Department. Am J Emerg Med. 2016;34(7):1210-6.
16. Farjad Sultan S, Shorten G, Iohom G. Simulators for training in ultrasound guided procedures. Med Ultrason. 2013;15(2):125-31.
17. Corvetto MA, Pedemonte JC, Varas D, Fuentes C, Altermatt FR. Simulation-based training program with deliberate practice for ultrasound-guided jugular central venous catheter placement. Acta Anaesthesiol Scand. 2017;61(9):1184-91.

18. Mahmood F, Matyal R, Skubas N, et al. Perioperative Ultrasound Training in Anesthesiology: A Call to Action. Anesth Analg. 2016;122(6):1794-804.
19. Dres M, Dubé BP, Goligher E, et al. Usefulness of Parasternal Intercostal Muscle Ultrasound during Weaning from Mechanical Ventilation. Anesthesiology. 2020;132(5):1114-25.
20. Smistad E, Lindseth F. Real-Time Automatic Artery Segmentation, Reconstruction and Registration for Ultrasound-Guided Regional Anaesthesia of the Femoral Nerve. IEEE Trans Med Imaging. 2016;35(3):752-61.
21. Nowakowski P, Bieryło A, Duniec L, Kosson D, Łazowski T. The substantial impact of ultrasound-guided regional anaesthesia on the clinical practice of peripheral nerve blocks. Anaesthesiol Intensive Ther. 2013;45(4):223-9.

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Original Article / Orijinal Araştırma

Assessment of the Use of Herbal Supplements and Attitudes of Adults Taking Medication

İlaç Kullanan Yetişkinlerde Bitkisel Destek Ürünleri Kullanımının ve Tutumların Belirlenmesi

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Abstract

Aim: The use of herbal supplements is increasing today, and these products have a significant impact on individuals' health. The aim of this study is to examine the use and reasons for using herbal supplements, as well as to determine individuals' attitudes towards these products.

Material and Method: The study was conducted with individuals aged 19-65 who use medications. A questionnaire containing questions about the participants' demographic characteristics, herbal supplement usage, and attitudes was administered by the researcher through face-to-face interviews.

Results: Of the 274 participants in the study, 10.6% use herbal supplements, with the most preferred products being ginseng, St. John's wort, and garlic (20.7%, 27.6%, and 37.9%, respectively). It was found that individuals who consume alcohol use herbal supplements 3.188 times more, and those who exercise use them 3.470 times more than those who do not (p=0.043, p=0.015, respectively). Most herbal supplement users agreed with the statement, "Herbal supplements can be used immediately when experiencing symptoms related to illness," while most non-users disagreed (p<0.001).

Conclusion: Given that the preferred herbal supplements may lead to potential interactions with medications and that individuals' attitudes towards herbal supplements vary, the importance of healthcare professionals providing individuals with accurate and comprehensive information is emphasized.

Keywords: herbal products, dietary supplements, medication, food-drug interactions

Öz

Amaç: Günümüzde bitkisel destek ürünlerinin kullanımı giderek artmaktadır ve bu ürünler bireylerin sağlık durumları üzerinde önemli bir etkiye sahiptir. Bu çalışmanın amacı, bitkisel destek ürünlerinin kullanımını ve kullanım nedenlerini inceleyerek, bireylerin bu ürünlere yönelik tutumlarını belirlemektir.

Gereç ve Yöntem: Çalışma 19-65 yaş aralığındaki ilaç kullanan bireyler ile yürütülmüştür. Bireylerin demografik özellikleri, bitkisel destek ürünü kullanım durumları ve tutumlarına yönelik sorular içeren anket formu araştırmacı tarafından yüz yüze görüşme yöntemi ile uygulanmıştır.

Bulgular: Çalışmaya katılan 274 bireyin %10,6'sı bitkisel destek ürünü kullanmaktadır ve bu ürünlerden en çok ginseng, sarı kantaron ve sarımsak ürünlerinin tercih edildiği görülmüştür (sırasıyla; %20.7, %27,6 ve %37,9). Alkol tüketenlerin tüketmeyenlere göre 3,188 kat, egzersiz yapanların yapmayanlara göre 3,470 kat daha fazla bitkisel destek ürünü kullandığı saptanmıştır (sırasıyla p=0,043, p=0,015). Bitkisel destek ürünü kullananların çoğu 'Hastalık ile ilgili bir belirti hissedildiğinde hemen bitkisel destek ürünleri kullanılabilir.' ifadesine katıldıklarını belirtirken, bitkisel destek ürünü kullanmayanların çoğu katılmadıklarını ifade etmişlerdir (p<0,001).

Sonuç: Tercih edilen bitkisel destek ürünlerinin ilaçlarla potansiyel etkileşimlere yol açabileceği ve bireylerin bitkisel ürünlere yönelik tutumlarının farklılık gösterdiği dikkate alındığında, sağlık profesyonellerinin bireyleri doğru ve kapsamlı bir şekilde bilgilendirmesinin önemi vurgulanmaktadır.

Anahtar Kelimeler: bitkisel ürün, besin destekleri, ilaç, etkileşim, besin-ilaç etkileşimleri

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INTRODUCTION

Dietary supplements are products prepared in forms such as capsules, tablets, or liquid ampoules, containing various nutrients or plant, animal, and bioactive substances, intended to support normal nutrition, with a defined daily intake dosage.[1] Herbal supplements, on the other hand, are products derived from plants and containing various components, typically used to improve health. The nomenclature surrounding herbal supplements can vary, with terms such as "botanicals," "herbal products," "herbal medicines," "herbal treatments," and "phytotherapy" being commonly used to describe these supplements.[2-3]

In contemporary society, the integration of complementary and alternative medicine into conventional healthcare practices has become increasingly prevalent. Herbal supplements, a significant component of this domain, have gained considerable attention. A recent study conducted on individuals living with chronic diseases revealed that the most prevalent (%34.9) traditional medicine method was the use of herbal products.[4] The utilization of herbal supplements is influenced by various factors, including media exposure, political climate, social environment, the nature of the disease, and educational level.[5] While many patients believe that herbal supplements are beneficial and are used as dietary supplements, some individuals express concerns that they may interact with medications and cause harm.[6] Notably, there is a growing interest in herbal supplements among individuals suffering from long-term health conditions, such as hypertension, diabetes, and chronic pain.[7]

However, the concomitant use of herbal supplements and medications has the potential to result in adverse outcomes. Herbal products may interact with medications, either enhancing or reducing their effects, or causing undesirable side effects. Specifically, the use of herbal supplements in conjunction with medications such as anticoagulants, antihypertensives, and antidepressants can lead to significant health complications.[8] Notable herbal products of common usage, such as St. John's wort, ginkgo, ginseng, kava, garlic, and echinacea, have been documented to interact with medications.[9] The absence of substantial scientific evidence regarding the efficacy and safety of numerous herbal products fosters uncertainty among users.[10] Consequently, it is essential to educate patients about the potential interactions between herbal products and medications, and to offer guidance on their proper use. The objective of this study is to assess the usage patterns of herbal supplements and to ascertain the attitudes of adults who use medications towards these products.

MATERIAL AND METHOD

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki, and approval for its conduct was obtained from the Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (Date: 01.07.2024, Decision No: 06/798). Informed consent was obtained from all participants.

Study population

This descriptive and cross-sectional study was conducted with individuals aged 19-65 in Ankara. Using a convenience sampling method, subjects who regularly used any medication were included in the study, while those diagnosed with neurological diseases (e.g. Alzheimer's disease, dementia) and those in pregnancy or lactation periods were excluded. The sample size of the study was determined to be at least 128 individuals with a 5% margin of error and 80% power using the GPower 3.1 program.

Study design

The data were collected through face-to-face interviews using a questionnaire developed by the researcher. The questionnaire included questions about the subjects' general information, their use of herbal supplements (e.g., reasons for using or not using them, where they obtained the products, and the sources recommending the product, etc.), and statements regarding attitudes toward the use of herbal supplements. The statements towards attitudes included topics such as consulting a medical professional when using herbal supplements, the perception of herbal supplements as being safer than conventional treatments, and associated concerns and were adapted from previous studies.[11,12]

Statistical analyses

The analysis of the obtained data was performed using SPSS (Statistical Package for the Social Sciences) software. Categorical variables were summarized with frequency (number) and percentage (%) values. The Chi-square test was used to evaluate relationships and differences between groups. For continuous variables, the mean ± standard deviation (SD) values were used. Binary logistic regression analysis was used to examine the factors affecting the use of herbal supplements. A significance level of $p<0.05$ was considered in all statistical analyses.

RESULTS

A total of 274 individuals participated in the study. The mean age of the participants was 47.28±15.22 years, with 64.2% being female and 35.8% being male. Most of the participants were married (71.5%) and did not smoke or consume alcohol (63.5% and 84.3%, respectively). A large majority of sample had chronic diseases (82.5%), with cardiovascular diseases (43.8%) and endocrine and metabolic disorders (34.7%) being the most common (**Table 1**).

Table 1. General characteristics of participants

	n	%
Age (years) (Mean±SD)	47.28±15.22	
Sex		
Female	176	64.2
Male	98	35.8
Educational level		
Primary School	48	17.5
Middle school	49	17.9
High school	73	26.7
Bachelor's Degree	85	31.0
Postgraduate	19	6.9
Marital status		
Single	78	28.5
Married	196	71.5
Employment status		
Unemployed	26	9.5
Employed	248	90.5
Smoking		
No	174	63.5
Yes	100	26.5
Alcohol consumption		
No	231	84.3
Yes	43	15.7
Regular exercise		
No	233	85.0
Yes	41	15.0
Presence of chronic diseases		
No	48	17.5
Yes	226	82.5
Diseases*		
Endocrinology and metabolic diseases	95	34.7
Cardiovascular diseases	120	43.8
Gastrointestinal tract diseases	24	8.8
Bone and joint diseases	29	10.6
Classification of medications used*		
Alimentary tract and metabolism	97	35.4
Cardiovascular system	143	52.1
Musculo-skeletal system	38	13.9
Nervous system	16	5.8
Respiratory system	21	7.6

* More than one answer was given.

Table 2. Data on the use of medicines and herbal supplements

	n	%
Taking the medicine with a drink other than water		
No	228	83.2
Yes	46	16.8
The type of drink the medicine is taken with		
Juice	10	21.7
Tea	28	60.9
Coffee	1	2.2
Milk and products	7	15.2
Use of herbal supplements		
No	245	89.4
Yes	29	10.6
Reason for not using herbal supplements		
Never thought about it	95	38.8
I have no information	41	16.6
Satisfied with conventional medical treatment	47	19.2
I don't believe in its effectiveness	19	7.8
It is not safe	43	17.6
Herbal supplements used*		
Aloe vera	3	10.3
Ginseng	6	20.7
St. John's Wort	8	27.6
Garlic	11	37.9
Hawthorn vinegar	1	3.4
Cinnamon	3	10.3
Black cumin	1	3.4
Purpose of use of herbal supplements		
Treating/healing the disease	2	6.9
To improve health	14	48.3
Complementary to conventional treatment	13	44.8
Source of the herbal supplement recommended		
Physician	2	6.9
Dietitian	5	17.3
Pharmacist	1	3.4
Family/friends	16	55.2
Media (social media, TV etc.)	5	17.2
Place where herbal supplements are supplied		
Herbalist	8	27.6
Pharmacy	18	62.1
Internet	3	10.3

More than one answer was given

In **Table 2**, it is shown that the majority of participants (83.2%) take their medications with water, while 60.9% of those who do not use water take their medications with tea. 10.6% of individuals use herbal supplements, with the most commonly preferred products being ginseng, St. John's wort, and garlic (20.7%, 27.6%, and 37.9%, respectively). These products are generally recommended through family/friends (55.2%) and are obtained from pharmacy (62.1%).

When examining the factors influencing the use of herbal supplements, no effect was observed for age, sex, education level, marital status, employment status, smoking status, and the presence of chronic diseases ($p>0.05$). It was found that those who consume alcohol use herbal supplements 3.188 times more than those who do not, and those who exercise use herbal supplements 3.470 times more than those who do not ($p=0.043$, $p=0.015$, respectively) (**Table 3**).

Table 3. Regression analysis of factors affecting the use of herbal supplements

	β	S.E.	p	O.R.	95% C.I.	
					Lower	Upper
Alcohol consumption	1.159	0.574	0.043	3.188	1.035	9.819
Regular exercise	1.244	0.509	0.015	3.470	1.278	9.417

β: Regression coefficient, SE: standard error, p: significance level, OR: odds ratio, CI: confidence interval

When examining participants' attitudes towards herbal supplements, a significant relationship was found between the statement " Herbal supplements can be used as soon as there is a symptom of the disease." and the use of herbal supplements ($p<0.001$). It was observed that individuals who use herbal supplements more frequently agreed with this statement, while those who do not use herbal supplements disagreed (**Table 4**).

DISCUSSION

According to the results of this study, 10.6% of adults using medication also use herbal supplements, with the most commonly preferred products being ginseng, St. John's wort, and garlic. Additionally, alcohol consumption and exercise habits have been identified as factors that increase the use of herbal supplements. It was observed that individuals who use herbal supplements are more likely to use them immediately when they experience symptoms related to diseases.

The use of herbal supplements has been steadily increasing, with a notable rise in their use for health purposes, particularly after the COVID-19 pandemic.[13] According to a report from the United States, herbal product sales, which accounted for 8.6% in 2019, surged to 17.3% in 2020, reflecting a significant growth. Among the popular herbal products are

Table 4. Attitudes of the participants according to the use of herbal supplements

Statements	1	2	3	4	5	p
	n (%)	n (%)	n (%)	n (%)	n (%)	
Herbal supplements can be used as soon as there is a symptom of the disease.						
Using herbal supplements	7 (24.1)	10 (34.5)	9 (31.0)	2 (6.9)	1 (3.4)	<0.001
Not using herbal supplements	14 (5.7)	39 (15.9)	55 (22.4)	80 (32.7)	57 (23.3)	
Total	21 (7.7)	49 (17.9)	64 (23.4)	82 (29.9)	58 (21.2)	
It is important to consult a physician before using herbal supplements.						
Using herbal supplements	6 (20.7)	16 (55.2)	4 (13.8)	3 (10.3)	-	0.176
Not using herbal supplements	100 (40.8)	96 (39.2)	23 (9.4)	17 (6.9)	9 (3.7)	
Total	106 (38.7)	112 (40.9)	27 (9.9)	20 (7.3)	9 (3.3)	
Using herbal supplements is safer than conventional treatment.						
Using herbal supplements	1 (3.4)	9 (31.0)	5 (17.2)	9 (31.0)	5 (17.2)	0.058
Not using herbal supplements	14 (5.7)	28 (11.4)	72 (29.4)	84 (34.3)	47 (19.2)	
Total	15 (5.5)	37 (13.5)	77 (28.1)	93 (33.9)	52 (19.0)	
Using herbal supplements is cheaper than conventional treatment.						
Using herbal supplements	1 (3.4)	6 (20.7)	10 (34.5)	11 (37.9)	1 (3.4)	0.655
Not using herbal supplements	18 (7.3)	45 (18.4)	75 (30.6)	80 (32.7)	27 (11.0)	
Total	19 (6.9)	51 (18.6)	85 (31.0)	91 (33.2)	28 (10.2)	
Herbal supplements are easier to use than conventional treatment.						
Using herbal supplements	5 (17.2)	12 (41.4)	5 (17.2)	6 (20.7)	1 (3.4)	0.105
Not using herbal supplements	31 (12.7)	53 (21.6)	70 (28.6)	64 (26.1)	27 (11.0)	
Total	36 (13.1)	65 (23.7)	75 (27.4)	70 (25.5)	28 (10.2)	
Herbal supplements interact with some drugs.						
Using herbal supplements	5 (17.2)	9 (31.0)	12 (41.4)	3 (10.3)	-	0.395
Not using herbal supplements	71 (29.0)	77 (31.4)	71 (29.0)	17 (6.9)	9 (3.7)	
Total	76 (27.7)	86 (31.4)	83 (30.3)	20 (7.3)	9 (3.3)	
Treatment with herbal supplements is better than conventional treatment.						
Using herbal supplements	-	8 (27.6)	9 (31.0)	8 (27.6)	4 (13.8)	0.117
Not using herbal supplements	12 (4.9)	30 (12.2)	63 (25.7)	85 (34.7)	55 (22.4)	
Total	12 (4.4)	38 (13.9)	72 (26.3)	93 (33.9)	59 (21.5)	

1:Strongly agree, 2:Agree, 3:Not sure, 4:Disagree, 5:Strongly disagree

mulberry, echinacea, ginger, mushrooms, garlic, ginkgo, and aloe vera.[14] These supplements are widely used due to their diverse health benefits. For example, ginger is known for its anti-nausea properties, garlic is effective in lowering blood pressure, and bitter melon is used to regulate blood sugar levels.[15]

Herbal supplement use is common among individuals with chronic diseases.[16,17] A study found 26.8% of hospitalized patients used herbal products, with factors like income, smoking, and disease progression influencing usage.[18] Another study showed that 63% of individuals with chronic conditions used herbal supplements, with ginger, mint, and cumin being most preferred.[19] In hemodialysis patients, 28.1% used herbal products, and married individuals were more likely to use them.[20] Similarly, in this study, 10.6% of participants used herbal supplements, with ginseng, garlic, and St. John's wort being the most common. While demographic factors had no significant impact, alcohol consumption and exercise habits were key influences on herbal product use, highlighting the role of lifestyle factors.

A study found that among cancer patients, the main reasons for using herbal products were symptom relief (35.1%) and recommendations from family/friends (64.9%).[17] Another study cited dissatisfaction with conventional treatment, past positive experiences, and family traditions as key reasons for use.[21] Similarly, this study found health improvement and use alongside conventional treatments as common reasons. Most herbal products are recommended by family and friends and purchased from pharmacies, indicating high public trust and growing popularity of herbal products as alternatives to conventional treatments.

Herbal products can interact with medications, potentially causing harmful effects. Plants like St. John's wort, ginkgo, ginseng, garlic, kava, and echinacea can alter medication effectiveness. For instance, St. John's wort can interfere with antidepressants and blood thinners, while ginkgo, ginseng, and garlic may increase bleeding risks. Kava can reduce the effectiveness of levodopa.[9] Additionally, herbal products can be hepatotoxic.[22,23] Studies show common herbal-medication interactions, like chamomile tea with cyclosporine,[18] and ginseng interacting with blood thinners.[16] In Turkey, 24.5% of preoperative patients use herbal products, highlighting the need for awareness of their potential effects.[24] This study observed similar trends, with the majority of participants using medications related to the alimentary tract, metabolism, and cardiovascular system, making them vulnerable to potential food-drug interactions. The products used in this study may have potential interactions with drugs, highlighting the importance of educating patients about the risks. Also, our study found that alcohol consumption influences the use of herbal products. Alcohol may enhance or weaken the effects of herbal products and increase medication side effects.[25] Therefore, herbal product use and drug interactions should be carefully monitored in alcohol consumers.

Individuals' attitudes towards herbal products vary. In a study with herbal users, 88.9% felt it wasn't important to inform doctors or pharmacists about their use, 73.3% considered them harmless, and 40.3% believed combining them with regular medications was unsafe.[26] In a study with the older adults, 66% felt herbal products were not risky for the general population.[27] A study with adults found 45% thought they were safe, 37.4% believed they could be used with medications, and 49.9% used them as their first choice when sick.[28] In our study, herbal product users were more likely to agree that " Herbal supplements can be used as soon as there is a symptom of the disease" while non-users disagreed. The majority of participants agreed that it is important to consult a physician before using these products and that they may interact with drugs, while they did not agree that these products are safer, cheaper, and more effective than conventional treatments. These findings suggest that herbal products are often preferred by individuals seeking quick solutions, but, unlike other studies, concerns and uncertainties about their safety and efficacy still exist.

CONCLUSION

It has been determined that preferred herbal supplements may interact with medications, leading to potential health risks. There is still uncertainty and concern among participants regarding the safety and interactions of these products. These findings highlight the need for further scientific research to ensure the safer and more effective use of herbal products and emphasize the importance of healthcare professionals providing accurate information to individuals..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (Date: 01.07.2024, Decision No: 06/798).
Informed Consent: Signed written informed consent was taken from all participants..
Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: The authors have no conflicts of interest to declare.
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REFERENCES

1. Resmi gazete. Türk gıda kodeksi takviye edici gıdalar tebliği (tebliğ no: 2013/49). Cited: 25 December 2024. Available from: https://www.mevzuat.gov.tr/mevzuat?MevzuatNo=18729&MevzuatTur=9&MevzuatTertip=5
2. Lipman TO. Herbal supplements. Curr Gastroenterol Rep. 2005;7(4):302-7.

3. Hassen G, Belete G, Carrera KG, et al. Clinical implications of herbal supplements in conventional medical practice: a US perspective. Cureus 2022;14(7):e26893
4. Bayer N, Uzuntarla Y. Kronik hastalığı olan yaşlı bireylerin akılcı ilaç kullanımı ve geleneksel tıp tutumlarının belirlenmesi: Akılcı ilaç kullanımı ve geleneksel tıp. JSOAH 2022;2(1):21-27.
5. Ritchie MR. Use of herbal supplements and nutritional supplements in the UK: what do we know about their pattern of usage?. Proc Nutr Soc. 2007;66(4):479-82.
6. Tangkiatkumjai M, Boardman H, Praditpornsilpa K, Walker DM. Reasons why Thai patients with chronic kidney disease use or do not use herbal and dietary supplements. BMC Complement Alter Med. 2014;14:1-9.
7. Tulunay M, Aypak C, Yikilkan H, Gorpelioglu S.Herbal medicine use among patients with chronic diseases. J Intercult Ethnopharmacol. 2015;4(3):217.
8. Kahraman C, Arituluk ZC, Cankaya IIT. The clinical importance of herb-drug interactions and toxicological risks of plants and herbal products. Erkekoglu P, Ogawa, T. Editors. Med Toxicol. 2020;1-31.
9. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: an updated systematic review. Drugs 2009;69(13):1777-79.
10. Bent S. Herbal Medicine in the United States: Review of Efficacy, Safety, and Regulation. J. Gen Inter Med. 2008;23(6):854-9.
11. El Khoury G, Ramadan W, Zeeni N. Herbal products and dietary supplements: a cross-sectional survey of use, attitudes, and knowledge among the Lebanese population. J Community Health 2016;41:566-73.
12. Thiab S, Barakat M, Al-Qudah RA, Abutaima R, Jamal R, Riby P. The perception of Jordanian population towards concomitant administration of food, beverages and herbs with drugs and their possible interactions: A cross-sectional study. Int J Clin Pract. 2021;75(3):e13780.
13. Ang L, Song E, Lee HW, Lee MS. Herbal medicine for the treatment of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis of randomized controlled trials. J Clin Med. 2020;9(5):1583.
14. Smith T, Kawa K, Eckl V, Morton C, Stredney R. Herbal Supplement Sales in US Increase. J Diet Suppl. 2020;17(1):95-109.
15. Sharma AK, Kapoor VK, Kaur G. Herb–drug interactions: a mechanistic approach. Drug Chem Toxicol. 2022;45(2):594-603.
16. Mohammadi S, Asghari G, Emami-Naini A, Mansourian M, Badri S. Herbal supplement use and herb–drug interactions among patients with kidney disease. JRPP 2020;9(2):61-7.
17. Kanimozhi T, Hindu K, Maheshvari Y, et al. Herbal supplement usage among cancer patients: A questionnaire-based survey. J Cancer Res Ther. 2021;17(1):136-41.
18. Goldstein LH, Elias M, Ron-Avraham G, et al. Consumption of herbal remedies and dietary supplements amongst patients hospitalized in medical wards. Br J Clin Pharmacol. 2007;64(3):373-80.
19. Albassam AA, Alenzi AN, Alhaqbani NK, et al. Beliefs, awareness, use, and factors associated with herbal supplements usage among patients with chronic diseases–A cross-sectional insight from Alkharj, Saudi Arabia. Plos one. 2024;19(1): e0295116.
20. Kara B. Herbal product use in a sample of Turkish patients undergoing haemodialysis. J. Clin. Nurs. 2009;18(15):2197-205.
21. Welz AN, Emberger-Klein A, Menrad K. Why people use herbal medicine: insights from a focus-group study in Germany. BMC Complement Alternat Med. 2018;18:1-9.
22. Lubarska M, Hałasiński P, Hryhorowicz S, et al. Liver dangers of herbal products: A case report of Ashwagandha-induced liver injury. Int J Environ Res Public Health 2023;20(5):3921.
23. Khan H, Reyes JVM, Seen T, Irefej B, Ahmad S. Herbal supplement-induced liver injury: a case report. Cureus 2023;15(1):e33663.
24. Uysal Aİ, Altıparmak B, Toker MK, Gümüş Demirbilek S. Ameliyat planlanan hastalar arasında bitkisel ürün kullanımı ve bitkisel ürünlerin nötrofil lenfosit oranına etkisi: Kesitsel araştırma. JARSS 2020;28(3):158-62.
25. Hu Z, Yang X, Ho PCL, et al. Herb-drug interactions: a literature review. Drugs 2005;65:1239-82.
26. Samojlik I, Mijatović V, Gavarić N, Krstin S, Božin B. Consumers' attitude towards the use and safety of herbal medicines and herbal dietary supplements in Serbia. Int J Clin Pharm. 2013;35:835-40.
27. Marinac JS, Buchinger CL, Godfrey LA, Wooten JM, Sun C, Willsie SK. Herbal products and dietary supplements: a survey of use, attitudes, and knowledge among older adults. JOM 2007;107(1):13-23.
28. Zaidi SF, Saeed SA, Khan MA, et al. Public knowledge, attitudes, and practices towards herbal medicines; a cross-sectional study in Western Saudi Arabia. BMC Complement Med Ther. 2022;22(1):326.

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Original Article / Orijinal Araştırma

Comparative Analysis of ERCP Results in Two Elderly Cohorts: Late Elderly and Super-Aged Patients

İki Yaşlı Kohortta ERCP Sonuçlarının Karşılaştırmalı Analizi: Yaşlı ve Süper Yaşlı Hastalar

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Abstract

Aims: Endoscopists may generally avoid performing ERCP in super-aged patients. This is because these patients often have comorbid conditions and reduced physiological function. The aim of this study was to evaluate the efficacy and safety of ERCP in the super-aged population over 85 years of age.

Material and Method: This study was retrospectively designed in a single tertiary care centre. Patients over 75 years of age with naive papillae who underwent ERCP between February 2019 and June 2022 were included in the study. Among the patients in the study, patients over 85 years of age were defined as super-aged, and patients aged 75-84 years were defined as late-elderly. The procedural data, efficacy and procedure-related adverse events of ERCP were compared between the two groups.

Results: A total of 260 patients were included, with 200 (76.9%) in the late elderly group and 60 (23.1%) in the super-aged group, of whom 37 were over 90 years old. According to the results of the analyses, only age and Charlson score showed a significant difference ($p<0.001$) between the demographic variables. There was no significant difference between the two groups in terms of procedural success, cannulation time, difficult cannulation, cannulation techniques and other procedural data. Cardiopulmonary complications were significantly more frequent in the super-aged group (8.3% versus 2%, $p=0.033$). The length of hospital stay was also found to be higher in the super-aged group compared to the late elderly group ($p=0.005$).

Conclusion: Our study demonstrated that ERCP is a safe and effective procedure in super-aged patients, with no significant difference in ERCP related adverse events between late elderly groups. However, cardiopulmonary complications warrant caution and may lead to longer, more complex hospitalizations for super-aged patients undergoing ERCP.

Keywords: ERCP, adverse events, pancreatitis, super-aged patients

Öz

Amaç: Endoskopistler, genellikle süper yaşlı (85 yaş ve üzeri) hastalarda ERCP yapmaktan kaçınmaktadır. Bunun nedeni, bu hastaların sıklıkla komorbiditelere sahip olması ve fizyolojik rezervlerinin azalmasıdır. Bu çalışmanın amacı, 85 yaş üstü süper yaşlı popülasyonda ERCP'nin etkinliğini ve güvenliğini değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif çalışma, üçüncü basamak bir sağlık merkezinde gerçekleştirildi. Şubat 2019 ile Haziran 2022 tarihleri arasında naive papillae ile ERCP uygulanan 75 yaş ve üstü hastalar çalışmaya dahil edildi. Hastalar, süper yaşlı (≥85 yaş) ve geç yaşlı (75–84 yaş) olarak sınıflandırıldı. Gruplar arasında işlem verileri, etkinlik ve ERCP'ye bağlı advers olaylar karşılaştırıldı.

Bulgular: Çalışmaya toplam 260 hasta dahil edildi: 200'ü (%76,9) geç yaşlı, 60'ı (%23,1) süper yaşlı grubunda yer aldı; bu gruptaki 37 hasta 90 yaşın üzerindeydi. Süper yaşlı grubunda yaş ve Charlson skoru anlamlı derecede daha yüksekti ($p<0,001$). İşlemsel başarı, kanülasyon süresi, zor kanülasyon oranları ve kullanılan teknikler açısından gruplar arasında anlamlı bir fark yoktu. Ancak, süper yaşlı grupta kardiyopulmoner komplikasyonlar daha sık görüldü (%8,3 vs. %2, $p=0,033$) ve bu hastaların hastanede kalış süreleri daha uzundu ($p=0,005$).

Sonuç: ERCP, süper yaşlı hastalar için güvenli ve etkili bir prosedür olarak görülmüştür ve geç yaşlı gruplar arasında ERCP'ye bağlı advers olaylar açısından anlamlı bir fark bulunmamıştır. Bununla birlikte, süper yaşlı hastalarda kardiyopulmoner komplikasyon riskinin artması, dikkatli bir ön değerlendirme ve yönetim gerektirmektedir.

Anahtar Kelimeler: ERCP, olumsuz olaylar, pankreatit, süper yaşlı hastalar

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INTRODUCTION

Endoscopic retrograde cholangiopancreatography (ERCP) is now a common procedure for the treatment of many conditions affecting the pancreas and bile ducts. The global increase in life expectancy in recent years has also led to a gradual rise in the proportion of the elderly population. In 2010, an estimated 8% of the global population was aged 65 and over. This proportion is projected to rise to 16% of the world's population by 2050.[1] With the growing elderly population, it is crucial to understand the specific challenges that various medical interventions pose for this age group. In particular, developments in endoscopic techniques and instrumentation are expected to lead to a gradual increase in the use of ERCP in the elderly population.

ERCP is thought to have a higher risk of side effects than other gastrointestinal endoscopic procedures.[2] Recently, studies investigating the efficacy and safety of ERCP in the elderly population have been increasing in the literature. The age ranges of the populations compared in these studies vary. Although some have taken 80 years of age as cut off in comparison,[3,4] fewer studies have investigated the efficacy of ERCP procedures in the super-aged population over 85 years of age.[5,6] In current clinical practice, endoscopists may generally avoid performing ERCP in super-aged patients. This is because these patients often have comorbid conditions and reduced physiological function.

The aim of this study was to evaluate the efficacy and safety of ERCP in the super-aged population over 85 years of age. By comparing ERCP-related adverse events and technical success between super-aged patients over 85 years of age and late elderly patients aged 75-84 years, we wanted to shed light on whether age is a limiting factor for ERCP.

MATERIAL AND METHOD

Study design and Patients

Ethical approval was obtained from the local ethics committee (Date: 22.12.2021, Decision No: E2-21-1153) and the study was conducted in accordance with the guidelines of the Declaration of Helsinki.

This study was retrospectively designed in a single tertiary care centre. Patients over 75 years of age with naive papillae who underwent ERCP between February 2019 and June 2022 were included in the study. A retrospective analysis of data from consecutive elderly patients undergoing ERCP was performed using electronic medical records and the endoscopy database. Patients with surgically altered anatomy (such as Billroth II gastrectomy or Roux-en-Y anastomosis), individuals who received percutaneous biliary drainage prior to ERCP, individuals under 75 years of age, and those who had previously undergone sphincterotomy were excluded from the study. Additionally, patients with incomplete records and missing data were also excluded.

ERCP procedures

Endoscopic retrograde cholangiopancreatography (ERCP) was performed in cases where common bile duct stones (CBDS) or sludge were identified by imaging techniques, including abdominal ultrasound (USG), magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS) or computed tomography (CT). In this study, all patients underwent USG and additional imaging was only used if the USG results were inconclusive or raised suspicion. All ERCP procedures were conducted using a lateral scope (TJF 190; Olympus Optical, Tokyo, Japan) by an experienced endoscopist who performs over 800 therapeutic ERCPs annually. Patients were sedated with propofol and midazolam by an anesthesiologist. Standard biliary cannulation was performed with a guide wire and sphincterotome. In cases where selective biliary cannulation was unsuccessful, alternative methods such as double guidewire and precut techniques were used. After the procedure, all patients were followed up with clinical, laboratory and imaging modalities if necessary.

Definitons

In geriatric literature, people aged 65 and over are generally classified as elderly. Current classifications further divide this group into three sub-categories: "young-old" (65-74 years), "middle-old" (75-84 years) and "oldest-old" (85 years and older).[7] This refined categorisation allows for more precise health strategies that address the different needs of each age group. Among the patients in the study, patients over 85 years of age were defined as süper-aged, and patients aged 75-84 years were defined as late elderly.[8] Successful cannulation was defined as the successful deep biliary cannulation. In cases where deep biliary cannulation could not be achieved during the initial session, a repeat ERCP was performed 48 hours later. Patients who failed to achieve deep biliary cannulation after the second attempt were classified as having failed cannulation. Cannulation time referred to the duration from the first visualization of the papilla until deep cannulation was achieved. Total procedure time was measured from the initiation to the completion of the procedure. As per a recently published guideline, difficult cannulation was characterized by an inability to achieve biliary cannulation within five minutes or by two or more inadvertent pancreatic cannulations.[9] ERCP-related complications were defined following the 2017 guidelines of the American Society for Gastrointestinal Endoscopy.[10] Additionally, cardiopulmonary complications, ICU admission, and mortality occurring during or after the procedure were considered adverse events (AE). In our study, cardiopulmonary complications were defined as the occurrence of hypotension, hypoxia, respiratory arrest, or cardiac arrest during the procedure, resulting in its interruption.

Statistical analysis

In our study, the data were analysed using SPSS 27 (Armonk, NY: IBM Corp) software. Mean, standard deviation, median (Q1-Q3), frequency and percentage values were used for descriptive statistics. Normality assessment was performed by Kolmogorov

Smirnov test. Chi-square (Pearson, Yates' corrected, Fisher's Exact and likelihood ratio) tests were used to analyse the relationship between nominal variables. Mann Whitney U test was used to analyse numerical variables according to groups. The significance level was set as 0.05 for all tests.

RESULTS

A total of 1,238 ERCP patients were retrospectively reviewed and 260 patients were included in the study, including 200 patients (76.9%) in the late elderly group and 60 patients (23.1%) in the super-aged group. Of these, 37 patients were over 90 years old. Although the groups were stratified by age, the overall mean age of the patients was 81.7±5.7 years (range: 75-104), with 38.8% of the sample being male. The majority of patients (83.8%) had no history of cholecystectomy and the most common indication for ERCP was related to common bile duct disease (83.8%). Hypertension was the most common comorbidity, observed in 72.3% of cases, while orthopaedic disorders were the least common (5%). The baseline characteristics of the patients are summarised in **Table 1**.

Table 1. Baseline characteristics of the study

Variables	Statistics
Age	81.7±5.7
Gender (Female)	159 (61.2)
History of cholecystectomy	42 (16.2)
Charlson score	4 (4-5)
Indication of ERCP	
Common bile ducts	218 (83.8)
Malignant biliary structure	22 (8.5)
Others	20 (7.7)
Comorbidities	
HT	188 (72.3)
DM	77 (29.6)
Cardiac diseases	78 (30)
COPD/ Asthma	27 (10.4)
CKD	19 (7.3)
Orthopaedic diseases	13 (5)
Neurological diseases	33 (12.7)
Antiaggregant/anticoagulant medication use	
Antiaggregant	
Single	79 (30.4)
Dual	2 (0.8)
Anticoagulant	22 (8.5)
Laboratory data's	
Tbil	2.5 (1.15-4.3)
GGT	272.5 (123-523.5)
WBC	8.89 (6.71-12.2)
CRP	29.6 (7.25-89.7)
Radiological data's	
Common bile duct dilatation on USG	6 (2.3)
Common bile duct stone or sludge	179 (68.8)

ERCP, Endoscopic retrograde cholangiopancreatography; HT, Hypertension; DM, Diabetes mellitus; COPD, Chronic obstructive pulmonary disease; CKD, Chronic kidney disease; Tbil, Total bilirubin; GGT, Gama-glutamyl transferase; WBC, White blood cell; CRP, C-reactive protein; USG, Ultrasonography

Patients in both groups were compared according to demographic, comorbid diseases, antiaggregant/anticoagulant use, laboratory and radiological data (**Table 2**). According to the results of the analyses, only age and Charlson score showed a significant difference (p<0.001) between the variables. Although cardiac and neurological comorbidities were observed at high rates in the super-aged group, they did not reach a statistically significant level (p=0.077 and p=0.086, respectively). Similarly, although antiaggregant and anticoagulant use was more frequent in the super-aged group compared to the late elderly group, no significant result was found (p=0.293 and p=0.200, respectively).

Table 2. Comparison of demographic, laboratory and radiological data between groups

Variables	Late elderly Group	Super-aged Group	p
	Statistics		
Age	79.1±2.9	90.5±3.6	<0.001
Gender (Female)	121 (60.5)	38 (63.3)	0.693
History of cholecystectomy	32 (16)	10 (16.7)	0.902
Charlson score	4 (4-5)	5 (4-5)	<0.001
Indication of ERCP			
Common bile ducts	167 (83.5)	51 (85)	
Malignant biliary structure	17 (8.5)	5 (8,3)	0.952
Others	16 (8)	4 (6.7)	
Comorbidities			
HT	141 (70.5)	47 (78.3)	0.234
DM	64 (32)	13 (21.7)	0.124
Cardiac diseases	54 (27)	24 (40)	0.077
COPD/ Asthma	18 (9)	9 (15)	0.274
CKD	12 (6)	7 (11.7)	0.158
Orthopaedic diseases	8 (4)	5 (8.3)	0.185
Neurological diseases	21 (10.5)	12 (20)	0.086
Antiaggregant/anticoagulant medication use			
Antiaggregant			
Single	59 (29.5)	22 (36.7)	0.293
Anticoagulant	14 (7)	8 (13.3)	0.200
Laboratory data's			
Tbil	2.5 (1.2-4.3)	2.3 (1-4.3)	0.586
GGT	278 (147.5-544)	260.5 (60.5-449)	0.118
WBC	8.9 (6.7-11.8)	9.9 (6.8-13.4)	0.212
CRP	29.1 (7.6-86.5)	46.9 (5.9-116)	0.631
Radiological data's			
Common bile duct dilatation on USG	5 (2.5)	1 (1.7)	1.000
Common bile duct stone or sludge	140 (70)	39 (65)	0.463

HT, Hypertension; DM, Diabetes mellitus; COPD, Chronic obstructive pulmonary disease; CKD, Chronic kidney disease;

When both groups were compared in terms of procedure-related data (**Table 3**), it was found that all variables showed a similar distribution. The higher rates of cannulation success in the first session (93.3% and 91%) and cannulation time less than 5 minutes (77.6% vs. 68.7%) in the super-aged group were noteworthy (p=0.597 and p=0.423, respectively). However, there was no significant difference between the two groups in terms of procedural success, cannulation time, difficult cannulation, cannulation techniques and other procedural data.

Table 3. Comparison of procedural data between groups

Variables	Late elderly Group	Super-aged Group	p
	Statistics		
Successful cannulation in the first session	180 (91)	56 (93.3)	0.597
Overall cannulation success	193 (98.5)	57 (95)	0.701
Difficult cannulation	66 (33)	17 (28.3)	0.496
Cannulation time			
<5 minutes	136 (68.7)	45 (77.6)	
5-10 minutes	23 (11.6)	5 (8.6)	0.423
10> minutes	39 (19.7)	8 (13.8)	
Total procedure time	27 (23-33)	27 (24-33)	0.913
Presence of PAD	52 (26)	18 (30)	0.54
Cannulation technique			
Wire-guided cannulation	151 (75.5)	45 (75)	
Double guidewire technique	34 (17)	11 (18.3)	0.764
Precut techniques	8 (4)	1 (1.7)	
Failed	7 (3.5)	3 (5)	
Sphincterotomy	192 (96)	60 (100)	0.204
Stone removal (Balloon or basket)	140 (70)	39 (65)	0.463
Plastic stent placement	137 (68.5)	40 (66.7)	0.789
Covered metal stent placement	2 (1)	2 (3.3)	!
EBD	5 (2.5)	1 (1.7)	1.000

!: Not calculated; PAD, Periampullary diverticulum; EBD, Endoscopic biliary dilatation.

When both groups were compared in terms of adverse events after ERCP (**Table 4**), it is noteworthy that all adverse effects except pancreatitis (14.5% vs. 8.3%) were more common in the super-aged group but did not reach a significant level. However, cardiopulmonary complications were significantly more frequent in the super-aged group (p=0.033). The length of hospital stay was also found to be higher in the super-aged group compared to the late elderly group (p=0.005).

Table 4. Comparison of both groups in terms of adverse events

Variables	Late elderly Group	Super-aged Group	p
	Statistics		
Pancreatitis	29 (14.5)	5 (8.3)	0.306
Bleeding	10 (5)	4 (6.7)	0.744
Perforation	2 (1)	2 (3.3)	0.229
Cardiopulmonary complications	4 (2)	5 (8.3)	0.033
ICU admission	11 (5.5)	6 (10)	0.236
Mortality	7 (3.5)	3 (5)	0.701
LHS	7 (5-12)	11 (6.5-15)	0.005

ICU, intensive care unit; LHS, Length of Hospital Stay

DISCUSSION

This study showed that the efficacy and safety of ERCP in patients over 85 years of age were similar to late elderly patient groups. In terms of adverse effects after ERCP, cardiopulmonary complications during or after the procedure were significantly higher in the super-aged group. In addition, the length of hospitalisation was significantly higher in the super-aged patients, which is among the other important findings of the study.

Research on the therapeutic effectiveness of ERCP in elderly patients has gained significant attention, largely due to the high incidence of pancreaticobiliary disease and the elevated risk of surgical complications associated with aging. Numerous studies across different countries and populations have examined the safety and success of therapeutic ERCP in older adults.[6,11] In recent years, many articles have been published in the literature stating that ERCP is effective and safe in elderly patients over 65 years of age.[12,13]

Previous studies have reported technical success rates for cannulation ranging from 80.5% to 100%.[14,15] In one study, the success rate of cannulation in elderly patients was significantly lower than in the control group.[16] However, it is often suggested that there is no significant difference between the older groups and the control groups in terms of cannulation success rates.[3,4,15,17] In this study, no significant difference in cannulation success was observed between the two elderly cohorts. Additionally, the cannulation success rate in both groups was over 95%. A recently published study also reported a cannulation success rate exceeding 95% in a cohort of patients aged over 90 years.[17] In our study, there were no significant differences between the groups in terms of cannulation time, procedure duration, difficult cannulation, or the cannulation techniques used during the procedure. A study investigating the efficacy and safety of ERCP in patients over 80 years of age also found no differences between groups regarding cannulation techniques, difficult cannulation, or cannulation time.[18] However, another study reported that total procedure time was longer in patients over 80 years old compared to the 65–80 age group.[3] Both studies noted a higher prevalence of periampullary diverticula (PAD) in patients over 80.[3,18] Unlike these studies, no difference in PAD prevalence was found between the groups in our study, which may be due to the closer age ranges of the two cohorts.

Multiple studies have demonstrated the safety of ERCP in elderly patients, showing no significant difference in the incidence of ERCP-related adverse events.[3,4,18] Similarly, in our study, patients aged ≥85 years did not exhibit a higher rate of overall adverse events compared to late elderly patients. Post-ERCP pancreatitis (PEP) was the most common adverse event observed, with elderly patients showing a lower incidence of pancreatitis. This reduction may be attributed to factors such as pancreatic fibrosis, atrophy, and decreased pancreatic enzyme secretion in older adults. Rates of ERCP-related perforation and bleeding were comparable across age groups, although elderly patients experienced a higher incidence of bleeding, likely related to the frequent use of antithrombotic medications. However, with the exception of cardiopulmonary complications, no significant differences in ERCP-related adverse events were observed between the groups. Cardiopulmonary complications were more frequent in the super-aged group, likely due to decreased cardiac and lung function associated with aging. These complications predominantly

arose during the procedure and were often related to anesthesia. Additionally, the length of hospital stay (LHS) was significantly longer in the super-aged group compared to the late elderly group. A similar study also found that LHS was notably longer for patients over 80 years of age compared to those under 80.[19] This may be attributed to the extended time needed for pre-procedural anesthesia preparation and the increased need for support and care in the postoperative period for super-aged patients. There was no difference in mortality between the two groups. In the late elderly group, one patient died due to sepsis associated with surgery for perforation and prolonged intensive care. All other patients who died succumbed to cardiopulmonary failure during or after the procedure.

Limitations

This study has several limitations. The first was its single-center design and retrospective nature. Another important limitation is that the study was conducted in a tertiary referral ERCP centre. This may have led to bias in choosing to include more complex cases.

CONCLUSION

Our study demonstrated that ERCP is a safe and effective procedure in super-old patients, with no significant difference in ERCP-related adverse effects between elderly groups. However, caution is advised regarding cardiopulmonary complications in this patient population, and it is important to keep in mind that hospital stays may be longer in super-aged patients. Healthcare providers should anticipate that the hospitalization period for super-aged patients undergoing ERCP may be extended and involve more complex care requirements.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bilkent City Hospital Local Ethics Committee (Date: 22.12.2021 Decision No: E2-21-1153).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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REFERENCES

1. World Health Organization; National Institute on Aging; National Institutes of Health. Global Health and Aging. NIH Publication No. 11-7737. Published 2011.
2. Andriulli A, Loperfido S, Napolitano G, et al. Incidence rates of post-ERCP complications: a systematic survey of prospective studies. Am J Gastroenterol. 2007;102(8):1781-8.
3. Yıldırım AE, Öztürk ZA, Konduk BT, et al. The safety and efficacy of ERCP in octogenarians: a comparison of two geriatric age cohorts. Acta Gastroenterol Belg. 2017;80(2):263-70.
4. Han SJ, Lee TH, Kang BI, et al. Efficacy and Safety of Therapeutic Endoscopic Retrograde Cholangiopancreatography in the Elderly Over 80 Years. Dig Dis Sci. 2016;61(7):2094-3101.
5. Takahashi K, Tsuyuguchi T, Sugiyama H, et al. Risk factors of adverse events in endoscopic retrograde cholangiopancreatography for patients aged ≥85 years. Geriatr Gerontol Int. 2018;18(7):1038-45.
6. Mazzola P, Spedale V. Commentary: Risk factors for complications in elderly patients aged 85 years and over undergoing endoscopic biliary stone removal. Front Surg. 2023;10:1139745.
7. Ouchi Y, Rakugi H, Arai H, et al. Joint Committee of Japan Gerontological Society (JGLS) and Japan Geriatrics Society (JGS) on the definition and classification of the elderly. Redefining the elderly as aged 75 years and older: Proposal from the Joint Committee of Japan Gerontological Society and the Japan Geriatrics Society. Geriatr Gerontol Int. 2017;17(7):1045-7.
8. Kazumori H, Fukuda K, Onishi K, Ohno Y. Urgent Endoscopic Retrograde Cholangiopancreatography Treatment Useful for Acute Cholangitis Caused by Bile Duct Stones in Patients Aged 90 Years and Older. Gerontology. 2024;30:1-9.
9. Testoni PA, Mariani A, Aabakken L, et al. Papillary cannulation and sphincterotomy techniques at ERCP: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy. 2016;48(7):657-83.
10. ASGE Standards of Practice Committee, Chandrasekhara V, Khashab MA, et al. Adverse events associated with ERCP. Gastrointest Endosc. 2017;85(1):32-47.
11. Yun DY, Han J, Oh JS, Park KW, Shin IH, Kim HG. Is endoscopic retrograde cholangiopancreatography safe in patients 90 years of age and older? Gut Liver. 2014;8(5):552-6.
12. Ergin E, Oruç N, Ersöz G, Tekeşin O, Özütemiz Ö. Prognosis and risk factors of ERCP pancreatitis in elderly. Sci Rep. 2021;11(1):15930. Erratum in: Sci Rep. 2021;11(1):17769.
13. Sugimoto S, Hattori A, Maegawa Y, et al. Long-term Outcomes of Therapeutic Endoscopic Retrograde Cholangiopancreatography for Choledocholithiasis in Patients ≥90 Years Old: A Multicenter Retrospective Study. Intern Med. 2021;60(13):1989-97.
14. Pericleous S, Smith LI, Karim MA, Middleton N, Musbahi A, Ali A. Endoscopic retrograde cholangiopancreatography in Ayrshire, Scotland: a comparison of two age cohorts. Scott Med J. 2015;60(2):95-100.
15. Hu L, Sun X, Hao J, et al. Long-term follow-up of therapeutic ERCP in 78 patients aged 90 years or older. Sci Rep. 2014;4:4918.
16. Mohammad Alizadeh AH, Afzali ES, Shahnazi A, Sanati A, Mirsattari D, Zali MR. Utility and safety of ERCP in the elderly: a comparative study in iran. Diagn Ther Endosc. 2012;2012:439320.
17. Colmenero Gargari AE, Melgar Somoza FE, Vera J, Micames CG. ERCP in patients over 90 years old: Safety and efficacy comparison with a younger cohort. Endosc Int Open. 2023;11(9):893-8.
18. Tabak F, Wang HS, Li QP, et al. Endoscopic retrograde cholangiopancreatography in elderly patients: Difficult cannulation and adverse events. World J Clin Cases. 2020;8(14):2988-99.
19. Chan KS, Mohan R, Low JK, Junnarkar SP, Huey CWT, Shelat VG. Elderly patients (≥80 years) with acute calculous cholangitis have similar outcomes as non-elderly patients (<80 years): Propensity score-matched analysis. World J Hepatol. 2021;13(4):456-71.

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Letter to the Editor/ Editöre Mektup

Sharing the Same Site with Neurosurgeons: The Bispectral Index Sensor

Beyin Cerrahları ile Aynı Alanı Paylaşmak: Bispektral İndeks Sensörü

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Dear Editor,

Electroencephalographic monitoring with the bispectral index (BIS) is a method for assessing level of consciousness and depth of anesthesia. Incidence of accidental awareness during anesthesia can be prevented with BIS monitoring. BIS can provide optimal anesthetic consumption, reduced time to extubation, early recovery from anesthesia and discharge from both the operating room and post anesthetic care unit, low incidence of nause and vomiting, cognitive impairment and delirium, as well.[1]

The manufacturer's recommended placement of BIS sensor for monitoring depth of anesthesia usually conflicts with the surgical site. Neurosurgeons and anesthesiologists have to share the same anatomic area, where BIS sensor is placed between the forehead and eyebrows. Wet clothes due to blood and irrigation fluids in the surgical site, mechanical and magnetic interference of surgical equipments like mayfield pins placement, neuro-navigation and electrocautery prevent the proper use of BIS sensor. There is a decrease and interruption in signal quality. Even drapping may be ineffective for protecting the sensor.

Alternative placements of BIS sensor have been applied and the correlation between the frontal placement have been evaluated. Nasal dorsum and under the eye is an appropriate site for monitoring. Nelson et al., determined slightly more variability when compared with the standard positioning, but this variability was not found clinically significant.[2] It has been shown that an alternative position across the mandible can be availably used. Shiraishi et al. found a good correlation between frontal and occipital BIS placements. Post auricular sensor placement was also found as a practical alternative.[3] Overall, a cross-sectional study was conducted comparing BIS scores derived from frontal and supralabial electrode placement. Supralabial placement was found as an alternative place.[4] On the other hand, false elevation of BIS may be possible due to electromyographic (EMG) activity, use of surgical devices, and electrocardiogram (ECG) artifacts.[5]

According to the literature, we mostly use nasal dorsum placement when the surgical skin insicion is close to the forehead (**Figure 1**).

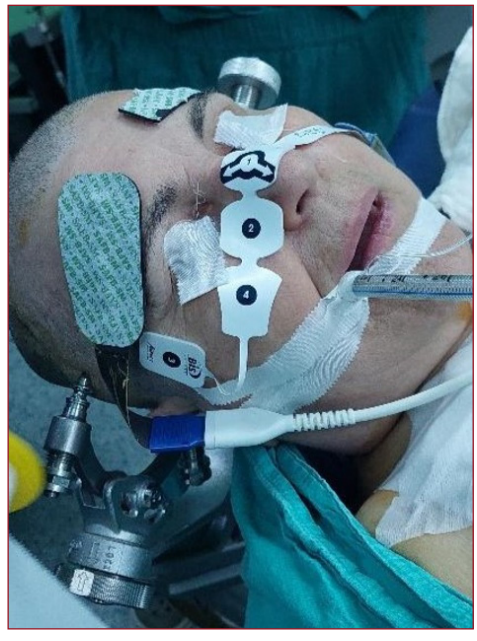

Figure 1. Placement of the bispectral index sensor on the nasal dorsum

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This provides better surgical satisfaction by staying away from the surgical field. The reliability of the sensor may decrease when the sensor is far from the standart placement site. So, causion should be taken due to interferences that may affect BIS scores.

In summary, an alternative positioning of BIS can be easily used without a clinically significant variability. Anaesthesiologists should consider different placements when using BIS monitoring during neurosurgical procedures especially close to frontal site.

Keywords: Bispectral index, neurosurgeons, alternative placement, nasal dorsum

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REFERENCES

1. Lewis SR, Pritchard MW, Fawcett LJ, Punjasawadwong Y. Bispectral index for improving intraoperative awareness and early postoperative recovery in adults. Cochrane Database Syst Rev 2019;9:CD003843.
2. Nelson P, Nelson JA, Chen AJ, Kofke WA. An alternative position for the BIS-Vista montage in frontal approach neurosurgical cases. J Neurosurg Anesthesiol 2013;25:135-42.
3. Akavipat P, Hungsawanich N, Jansin R. Alternative placement of bispectral index electrode for monitoring depth of anesthesia during neurosurgery. Acta Med. Okayama 2014;68(3):151-5.
4. Dubey JK, Goel N, Chawla R, Gupta M, Bhardwaj M. Supralabial site: an alternative site for bispectral index monitoring: a cross-sectional study. J Neuroanaesthesiol Crit Care 2022;9:149–54.
5. Kim YS, Lim BG, Lee IO. False elevation of bispectral index with a mandibular position in a patient undergoing craniotomy. J Neurosurg Anesthesiol 2014;26(3):265-7.