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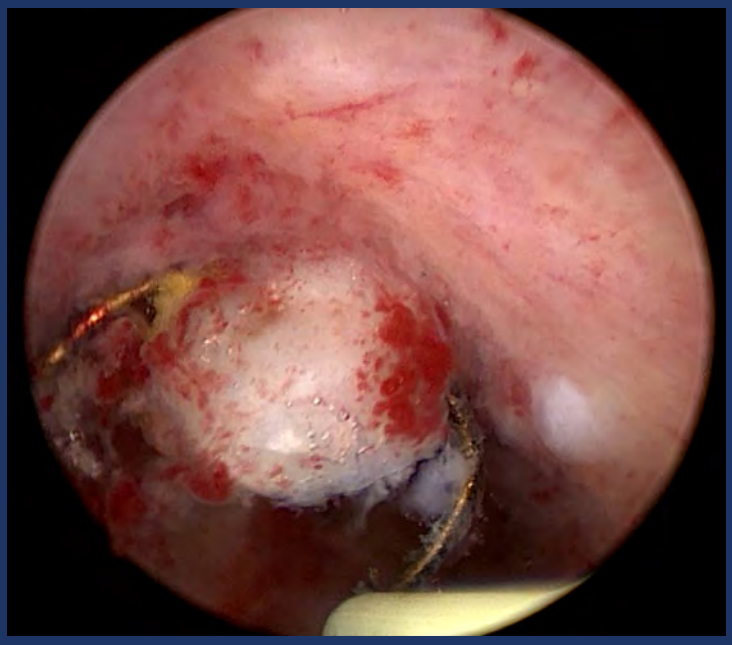

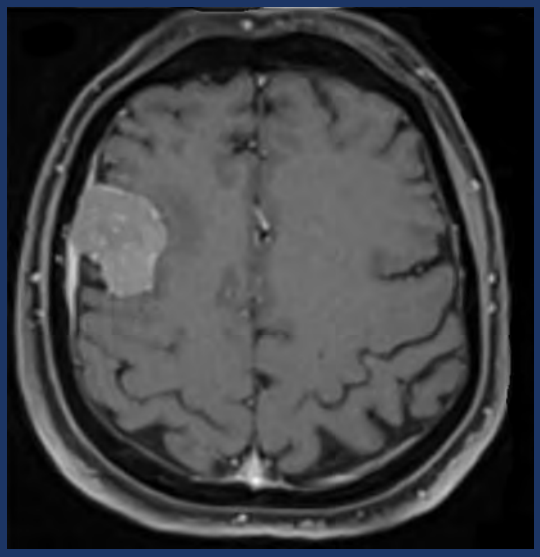

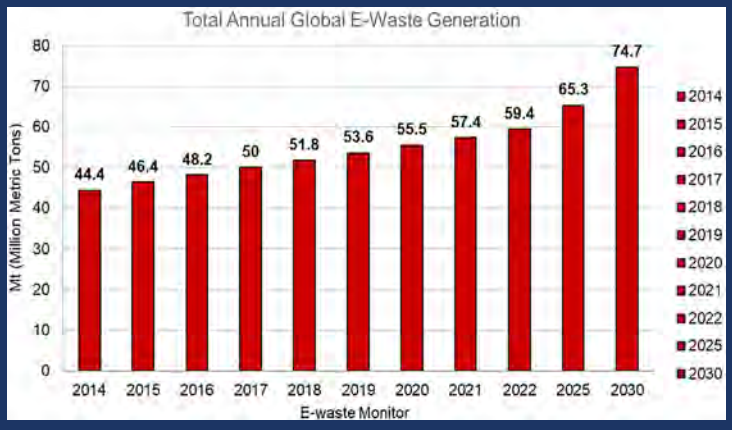

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AIMS AND SCOPE

Comprehensive Medicine is the official publication of Kanuni Sultan Süleyman Training and Research Hospital. It is published regularly, four times a year, in January, April, July and October as an electronic journal.

The journal was published by Bakırköy Obstetrics and Gynecology Hospital in 1990s as JOPP (gynecology obstetrics, pediatric and pediatric surgery) and has reached the status of 'peer-reviewed journal' in 2009. The journal was changed to İstanbul Kanuni Sultan Süleyman Tıp Dergisi in 2014 and known as Comprehensive Medicine beginning from 2023.

The language of the journal is English. It is a peer-reviewed journal and does not charge any fee from readers or authors. All published articles are open access.

The aim of Comprehensive Medicine is to provide students, who are educated in the field of medicine in all fields of medicine, and researchers to all physicians who are in the field of health and information about disease treatment and prevention methods. The journal publishes original research articles including gynecology, obstetric, pediatrics, pediatric surgery and basic medical sciences, case reports, reviews and announcements of panels and congresses. Comprehensive Medicine is to publish original researches on international level qualified, continuous and general medicine and periodically evaluated at the highest level both clinically and scientifically according to the konusunda double-blind, system for the consultant and writer. In addition to this, they include collections covering basic innovations about education, letters to the editor, and case reports.

Moreover, by conducting an objective evaluation within the framework of the ethical rules of the journal, the consultant aims to enable the reviewers to transfer their experiences to the authors, to give the author a perspective on how to write a scientific article, and to contribute to the elimination of the scientific value of the articles published in our country.

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RESEARCH ARTICLE

Fatigue and Associated Factors in Patients with Knee Osteoarthritis: A Cross-Sectional Study

Eser Kalaoğlu[1], Ömer Faruk Bucak[2], Yelda Soluk Özdemir[1], Nurdan Paker[1], Fatma Nur Kesiktaş[1]

[1]Department of Physical Therapy and Rehabilitation, İstanbul Physical Medicine Rehabilitation Training and Research Hospital, İstanbul, Türkiye
[2]Department of Physical Therapy and Rehabilitation, Başakşehir Çam and Sakura City Hospital, İstanbul, Türkiye

ABSTRACT

Objective: Fatigue is a common but underrecognized symptom in knee osteoarthritis (OA), which significantly impacts patients' quality of life. This study aimed to investigate the associations between fatigue severity and clinical variables in individuals with knee OA.

Materials and Methods: This cross-sectional study included 92 patients (mean age 64.09 ± 9.68 years; 62.0% female) clinically diagnosed with knee OA. Fatigue severity was assessed using the Fatigue Severity Scale. Additional assessments included pain intensity via the Visual Analog Scale, functional status using the Knee Injury and Osteoarthritis Outcome Score - Physical Function Shortform (KOOS-PS), and anxiety and depression levels as measured by the Hospital Anxiety and Depression Scale. Body mass index (BMI) was calculated for each participant, and radiographic severity of knee OA was determined using the Kellgren-Lawrence Classification. Spearman's rank correlation was employed for statistical analyses to determine associations between the variables.

Results: Significant positive correlations were observed between fatigue severity and BMI ($r=0.335$, $p=0.001$), pain intensity ($r=0.386$, $p<0.001$), anxiety levels ($r=0.323$, $p=0.002$), depression levels ($r=0.318$, $p=0.002$), and radiographic severity ($r=0.464$, $p<0.001$). Additionally, a significant negative correlation was found between fatigue severity and the KOOS-PS score ($r=-0.356$, $p<0.001$).

Conclusion: Fatigue in knee OA is significantly associated with radiographic severity, pain, mood disorders, functional impairment, and BMI. These findings highlight the importance of considering fatigue as a core component of OA assessment and treatment. Multidisciplinary approaches targeting these factors are recommended to improve patient outcomes.

Keywords: Anxiety, depression, fatigue, knee, osteoarthritis

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INTRODUCTION

Osteoarthritis (OA) is the most common chronic joint disorder and a major contributor to disability among the elderly.[1] Knee OA, the most prevalent subtype worldwide, is characterized by progressive cartilage degeneration, osteophyte formation, joint space narrowing, and pain, all of which collectively impair functional mobility and quality of life.[2]

The term fatigue is defined as a persistent feeling of physical and/or mental exhaustion that is not proportional to recent activity and is not relieved by rest.[3] In musculoskeletal conditions, fatigue has been conceptualized as a multifactorial symptom influenced by both peripheral and central mechanisms.[4] Although pain and physical limitations are the primary clinical concerns in OA, many patients report fatigue as a significant symptom that is often neglected in routine assessment and treatment algorithms.[5]

Most existing studies have primarily focused on inflammatory rheumatic diseases, such as rheumatoid arthritis and lupus, while fatigue in OA—particularly in its non-inflammatory degenerative forms—remains insufficiently understood.[6]

Recent biomarker studies have demonstrated that central sensitization and neuroinflammation play a significant role

Address for Correspondence: Eser Kalaoğlu, Department of Physical Therapy and Rehabilitation, İstanbul Physical Medicine Rehabilitation Training and Research Hospital, İstanbul, Türkiye
E-mail: eserkalaoglu@hotmail.com **ORCID ID:** 0000-0001-8959-6522

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in chronic pain and fatigue. However, fatigue has been found to be metabolically distinct from widespread chronic pain.[7–9] Additionally, it has been observed that central sensitization in knee OA is particularly pronounced in patients reporting high levels of clinical pain despite the absence of radiographic evidence.[10]

Psychological factors have a significant impact on functional independence in older individuals with knee OA.[11] OA pain increases fatigue and disability, leading to a depressive mood; the depressive mood, in turn, worsens fatigue and pain, further reducing functionality and creating a vicious cycle between pain and depression.[12]

Due to functional impairment, decreased muscle conditioning and physical capacity limit mobility and social participation, contributing to chronic fatigue.[3] Therefore, we consider fatigue not as an isolated symptom but as part of the complex symptomatology of knee osteoarthritis.

The aim of this study is to investigate the associations between fatigue severity and clinical variables such as pain intensity, functional status, anxiety, and depression in individuals with clinically diagnosed knee OA.

MATERIALS and METHODS

The present study was conducted as a single-centre, cross-sectional, observational study. It was performed between 15.12.2024 and 15.01.2025 at the Physical Medicine and Rehabilitation Outpatient Clinic. Ethical approval was obtained from the local ethics committee prior to the initiation of the study (approval number: 2024-77). All participants provided written informed consent prior to enrollment, and the study procedures were conducted in full accordance with the ethical principles outlined in the Declaration of Helsinki. Inclusion and exclusion criteria were established to minimize potential confounders affecting fatigue perception and to ensure homogeneity within the sample.

Inclusion Criteria

- Age between 40 and 80 years,
- Diagnosis of knee OA according to ACR clinical guidelines,
- Ability to comprehend and complete the study questionnaires independently.

Exclusion Criteria

- Prior history of knee arthroplasty or major knee surgery,
- Diagnosed fibromyalgia or chronic fatigue syndrome,
- Presence of active rheumatologic, neurological, or psychiatric disorders,
- Current use of medications that significantly alter fatigue perception (e.g., corticosteroids, antidepressants, psychostimulants),
- Decompensated cardiac, hepatic, or renal insufficiency.

Data Collection and Clinical Evaluation

Demographic and clinical characteristics were gathered using a standardized data collection form. The following variables were collated: age, gender, weight, height, and body mass index (BMI). The variables marital status, smoking history, educational attainment, and occupational status were also included. Pain duration (in months) and range of motion (ROM) of the affected knee joint were also noted. ROM was categorized as either full or restricted, based on clinical examination by a board-certified physiatrist.

Outcome Measures and Assessment Tools

All participants underwent comprehensive evaluation using validated, patient-reported outcome measures, each with established Turkish adaptations and psychometric properties.

Fatigue Severity Scale

The Turkish version of the Fatigue Severity Scale (FSS), which has been validated for both reliability and the assessment of chronic fatigue levels, was used in this study.[13] The FSS is a self-administered tool consisting of nine items, each rated on a 7-point Likert scale ("1 = strongly disagree" to "7 = strongly agree"). The average score is calculated, and according to the cutoff value established for the FSS, scores of 4 or higher indicate the presence of fatigue, with higher values reflecting more severe fatigue.[14]

Knee Injury and Osteoarthritis Outcome Score – Physical Function Shortform

The Knee Injury and Osteoarthritis Outcome Score – Physical Function Shortform (KOOS-PS) is a disease-specific instrument utilised for the evaluation of physical functional limitations associated with knee osteoarthritis (OA). The instrument comprises seven items, which are scored on a 5-point Likert scale. Scores are transformed to a 0–100 scale, with higher scores denoting better physical function. The Turkish validation study, conducted by Gul et al.[15] in 2013, established the reliability and validity of the scale.

Visual Analog Scale

The intensity of pain experienced over the preceding week was measured using a Visual Analog Scale (VAS) with a length of 10 centimeters (cm).[16] This scale was employed to ensure accurate measurement of pain intensity. The

endpoints of the scale were defined as "0 = no pain" and "10 = worst imaginable pain."

Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) is a screening tool that is employed extensively in medical populations for the identification of anxiety and depression. The tool is composed of 14 items, which are divided into two subscales: an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Each item is evaluated using a 4-point Likert scale, with subscale scores ranging from 0 to 21. The Turkish validation study, conducted by Aydemir et al.[17] in 1997, established the reliability and validity of the scale.

Radiological Assessment

Radiographic severity of OA was assessed using the Kellgren-Lawrence Classification, based on standard weight-bearing anteroposterior knee radiographs.[18] The Kellgren-Lawrence grades range from 0 (no radiographic features) to 4 (severe joint space narrowing, large osteophytes, and deformity). Radiographs were interpreted by an experienced physiatrist who was blinded to the clinical data.

Sample Size Calculation

The necessary sample size was determined by using the G*Power 3.1 program. Based on a medium correlation effect size (r=0.3), an alpha error probability of 0.05, and a statistical power of 0.90, the minimum number of participants required was determined to be 92.

Statistical Analysis

The statistical analyses were conducted using PASW Statistics for Windows, Version 18.0 (SPSS Inc., Armonk, NY). Data normality was assessed using the Lilliefors-corrected Kolmogorov-Smirnov test. Continuous variables were represented as mean±standard deviation (SD) or median with interquartile range (IQR), as indicated. Categorical data were summarized as frequencies (percentage).

Spearman's rank correlation test was used to evaluate the relationships between FSS scores and clinical parameters (VAS, KOOS-PS, HADS-A, HADS-D, BMI, pain duration, and Kellgren-Lawrence Classification grade), due to the non-normal distribution of the data. The strength of correlations was interpreted according to standard guidelines, and a p-value of <0.05 was considered statistically significant.

RESULTS

Ninety-two patients with a diagnosis of knee OA were eligible for the study. The mean age of the participants was 64.09±9.68 years, and 62% of them were female. The mean height and weight of the participants were recorded as 163.84±9.59 cm and 81.83±12.28 kg, respectively. The mean BMI of the participants was calculated to be 30.71±5.67 kg/m². Most participants were married (78.3%) and had completed only primary education (55.4%) (Table 1). In this study, 58 patients (63%) had FSS scores of 4 or higher.

Table 1. Demographic characteristics of the patients

	n	%	Mean±SD
Age (years)			64.09±9.68
Height (cm)			163.84±9.59
Weight (kg)			81.83±12.28
BMI (kg/m²)			30.71±5.67
Gender			
Female	57	62.0	
Male	35	38.0	
Marital status			
Married	72	78.3	
Single	20	21.7	
Educational level			
Primary school	51	55.4	
Secondary school	15	16.3	
High school	17	18.5	
University college	9	9.8	
Occupational status			
Employed	7	7.6	
Retired	38	41.3	
Housewife	47	51.1	
Smoking history			
Yes	76	82.6	
No	16	17.4	

The data were presented as mean±standard deviation or frequencies. SD: Standard deviation; BMI: Body mass index

Clinical assessments revealed that the scores for FSS, VAS, KOOS-PS, and HADS are summarized in Table 2. According to the Kellgren-Lawrence Classification, most participants (51.1%) had grade 2 OA, and 62% of the patients exhibited a full ROM (Table 2).

Fatigue severity showed a statistically significant positive correlation with BMI, VAS pain score, HADS-A, and HADS-D (r=0.335, p=0.001; r=0.386, p<0.001; r=0.323, p=0.002; r=0.318, p=0.002, respectively). Additionally, a statistically significant positive correlation was observed with radiographic severity based on the Kellgren–Lawrence grade (r=0.464, p<0.001). In

Table 2. Clinical features and functional assessments of the patients

	n	%	Min	Max	Median (IQR)
FSS			0.55	7.00	4.44 (3.22–5.67)
VAS			3.00	10.00	6.00 (5.00–8.00)
KOOS-PS			0.00	85.20	56.00 (51.50–66.40)
HADS anxiety			2.00	14.00	7.00 (6.00–10.00)
HADS depression			1.00	15.00	6.00 (4.00–9.00)
Duration of pain (months)			3.00	24.00	6.00 (4.00–10.00)
ROM					
Full	57	62.0			
Resricted	35	38.0			
Kellgren-Lawrence Classification					
Grade 2	47	51.1			
Grade 3	36	39.1			
Grade 4	9	9.8			

The data were presented as median (interquartile range) or frequencies. IQR: interquartile range; SD: Standard deviation; FSS: Fatigue severity scale VAS: Visual analog scale; HADS: Hospital anxiety and depression scale; ROM: Range of motion; KOOS-PS: Knee disability and osteoarthritis outcome score-physical function shortform

contrast, fatigue severity exhibited a statistically significant negative correlation with the KOOS-PS functional score (r=-0.356, p<0.001). However, no significant relationships were observed between FSS scores and patients' age, weight, or duration of pain (Table 3).

DISCUSSION

This study provides a comprehensive and clinically nuanced understanding of the multifactorial nature of fatigue in patients with knee OA. The results show that fatigue in OA is not an isolated complaint, but a multifaceted symptom closely associated with radiographic severity, pain intensity, functional activity level, mood, and BMI. This indicates that the observed statistical relationships correspond to tangible clinical differences; for instance, higher fatigue levels are associated with increased anxiety and depression that can affect daily mood and interactions, as well as a decline in physical function that impairs activities of daily living. It emphasizes the importance of recognizing fatigue as a core component of the OA symptom complex for clinical assessment and intervention.

Table 3. Correlation between fatigue severity and clinical parameters

	FSS score	
	rho	p
Age (years)	-0.139	0.186
Weight (kg)	0.023	0.831
BMI (kg/m^2)	0.335	**0.001**
Pain duration (months)	-0.014	0.897
Kellgren-Lawrence Classification	0.464	**0.000**
VAS	0.386	**0.000**
KOOS-PS	-0.356	**0.000**
HADS anxiety	0.323	**0.002**
HADS depression	0.318	**0.002**

Spearman's rank correlation. BMI: Body mass index; FSS: Fatigue severity scale; VAS: Visual analog scale; KOOS-PS: Knee disability and osteoarthritis outcome score-physical function shortform; HADS: Hospital anxiety and depression scale

One of the most striking findings in our study was the close relationship between fatigue and radiographic disease severity. Patients with more advanced structural degeneration on imaging tended to report significantly higher fatigue load. Joint degeneration not only causes nociceptive pain but also a decrease in joint function, leading to compensatory gait patterns that result in an increase in energy expenditure during locomotion.[19] We propose that this heightened energy demand contributes to fatigue.

A review of the literature reveals that pain and fatigue are often characterized as mutually reinforcing symptoms.[20, 21] Pain exacerbates fatigue through the disruption of sleep patterns, its negative impact on mood, and its limitation of physical activity. This further corroborates that fatigue is significantly shaped by the patients' pain experience. Our results show that individuals with more intense pain complaints exhibited higher levels of fatigue.

Katz et al.[22] investigated factors associated with fatigue in rheumatoid arthritis patients, using the FSS to assess fatigue severity. Their findings indicate that fatigue in rheumatoid arthritis is influenced by both disease-specific and non-specific factors, with poor sleep, depression, and obesity identified as primary predictors beyond disease activity.

The interaction between mood disorders and fatigue may be bidirectional, with factors such as pain severity, role functioning, depressive mood, self-efficacy on fatigue, worrying, helplessness, and non-restorative sleep exacerbating fatigue, while the severity of fatigue also worsens these psy-

chosocial factors, creating a self-reinforcing cycle that diminishes coping capacity and functional engagement.[23]

The results of our study in terms of physical functionality have shown that low functional capacity is consistently associated with increasing fatigue. This finding correlates with the well-known clinical course in musculoskeletal disorders, where patients experience fatigue following physical limitations.[24]

Schepens et al.[25] investigated the effects of standardized lab-based physical tasks on fatigue in older adults, both with and without OA. The study found that older adults with OA reported higher levels of fatigue following physical activity compared to their peers without the condition.

Our study highlights a significant correlation between fatigue and BMI, emphasizing the dual burden of mechanical overload in OA and systemic metabolic dysregulation. Excess weight can increase joint stress, contributing to cartilage wear and low-grade systemic inflammation, which in turn may exacerbate pain and, consequently, fatigue.[26,27] Therefore, weight management may alleviate both mechanical strain and inflammatory pathways, potentially improving pain and fatigue in OA patients.

Fatigue in OA, particularly in knee OA, has often been overlooked or underexplored in clinical research. This study distinguishes itself by evaluating fatigue through a multidimensional approach that incorporates radiographic severity, validated functional and psychological scales, and body composition metrics. Unlike previous studies that focused mainly on pain or function in isolation, we investigated the interconnected roles of somatic and psychosocial factors in determining fatigue severity. Additionally, by using face-to-face structured interviews and culturally validated Turkish versions of standardized tools, we offer a high-fidelity snapshot of real-world patient experiences. These contributions fill a critical gap in OA fatigue literature and have the potential to guide individualized, multidisciplinary treatment plans that target fatigue as a primary therapeutic concern rather than a secondary symptom.

However, several limitations should be noted. First, its cross-sectional design precludes any conclusions about causality. Second, as a single-center study, the generalizability of the findings to broader populations may be limited. Third, fatigue, being a subjective experience, may have been influenced by unmeasured confounding factors such as sleep quality, nutritional status, and social support, which were not specifically assessed. Additionally, the use of the unidimensional FSS as the sole instrument may have limited the ability to capture the multifaceted nature of fatigue, including its physical, mental, and motivational dimensions. Moreover, because ROM was evaluated categorically (as either "full" or "restricted"), and socioeconomic variables such as educational level, occupational status, and marital status were collected as categorical variables, this prevented detailed correlation analyses with fatigue.

CONCLUSION

In conclusion, fatigue in knee OA is a complex and clinically significant symptom that is intricately linked to joint pathology, pain, mood disturbances, physical impairment, and excess weight. The findings of this study highlight the importance of considering fatigue as a core domain in the evaluation and treatment of OA. Therefore, multidisciplinary treatment strategies targeting these factors are recommended; for instance, physiatrists can manage pain and improve function, psychiatrists or psychologists can address mood disorders, and dietitians can provide guidance on weight management. Future research should include longitudinal, multi-center designs to establish causal relationships, and incorporate additional potential contributors to fatigue such as sleep quality, nutritional status, and social support networks. Such comprehensive approaches would further enhance our understanding of fatigue in knee OA and refine targeted intervention strategies.

Disclosures

Ethics Committee Approval: The study was approved by the Scientific Research Ethics Committee of Istanbul Physical Therapy Rehabilitation Training and Research Hospital Ethics Committee (No: 2024-77, Date: 05/12/2024).

Informed Consent: All participants provided written informed consent prior to enrollment, and the study procedures were conducted in full accordance with the ethical principles outlined in the Declaration of Helsinki

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RESEARCH ARTICLE

Achromobacter spp.-Related Bloodstream Infections: A Review of the Literature and a Case Series

Burcu Bursal[1], İlyas Bingöl[2], Şule Çelik[3]

[1]Department of Pediatric Infectious Diseases, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[2]Department of Pediatric Intensive Care, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[3]Department of Microbiology, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: *Achromobacter spp.* are uncommon causes of bloodstream infections, typically associated with nosocomial settings and immunocompromised patients. This study aims to evaluate the clinical characteristics, antimicrobial susceptibility patterns, and outcomes of seven pediatric patients with community-acquired Achromobacter bacteremia.

Materials and Methods: A retrospective review was conducted on seven pediatric cases admitted with sepsis and positive blood cultures for *Achromobacter spp.* between 2020 and 2024. Demographic data, clinical presentation, laboratory findings, microbiologic identification, antimicrobial susceptibility results, treatment regimens, and outcomes were analyzed.

Results: The median age was 16 months; five patients were female. All patients were previously healthy and presented from the community. Fever was the primary symptom, with cough and poor feeding being common additional findings. Four had isolated sepsis, while three had signs of lower respiratory tract infection. Six isolates were identified as Achromobacter denitrificans and one as *A. xylosoxidans*. All isolates were susceptible to piperacillin-tazobactam and carbapenems. Initial empirical treatment with third-generation cephalosporins was modified to piperacillin-tazobactam and carbapenem upon susceptibility results. All patients recovered and were discharged in good condition, with no deaths observed.

Conclusion: Although rare, *Achromobacter spp.* can cause community-acquired sepsis in previously healthy children. Prompt identification and appropriate antimicrobial therapy guided by susceptibility testing are crucial for favorable outcomes.

Keywords: *Achromobacter spp.*, antimicrobial resistance, community-acquired infections, gram-negative bacteria, sepsis

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INTRODUCTION

Achromobacter spp. are environmental gram-negative bacteria that have emerged as opportunistic pathogens and are capable of surviving in aqueous hospital environments. While these organisms are most frequently associated with nosocomial infections such as bloodstream infections, pneumonia, and urinary tract infections, community-acquired infections are extremely rare.[1] *A. xylosoxidans* has been specifically linked to immunocompromised hosts, often with severe consequences.[2] With the increasing use of automated blood culture systems and advanced bacterial identification techniques, more cases are being identified in previously healthy individuals. This study presents a case series of seven pediatric patients with *Achromobacter spp.* bacteremia of apparent community origin.

MATERIALS and METHODS

Between 2020 and 2024, we retrospectively analyzed the medical records of patients admitted to the pediatric infectious diseases unit with a diagnosis of sepsis and a positive blood culture for *Achromobacter spp.* Inclusion criteria were: (1) age under 18 years, (2) community-acquired

Address for Correspondence: Burcu Bursal, Department of Pediatric Infectious Diseases, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
E-mail: burcubursal@hotmail.com **ORCID ID:** 0000-0002-4098-947X

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presentation, and (3) confirmed blood culture growth of *Achromobacter* species. Data collected included demographics, clinical presentation, laboratory results, antibiotic regimens, microbial identification, antimicrobial susceptibilities, hospital course, and outcomes. Microbiological identification was made by MALDI-TOF MS, and antibiotic susceptibility testing was conducted using VITEC 2 (BioMérieux) according to EUCAST.

Community-acquired infection was defined as the presence of clinical signs and positive blood cultures obtained at the time of presentation from home, without recent hospitalization (within the past 90 days), absence of central venous catheterization, and no history of known immunosuppression.

This study was approved by the University of Health Sciences, Istanbul Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee of the local committee (Date: 15.08.2025, Approval no: KAEK/2025.08.200) and was conducted in accordance with the ethical principles of the Declaration of Helsinki.

RESULTS

Two of the seven patients were male, and five were female. The median age was 9 months (range: 3 months–44 months). All children were previously healthy and presented from home. Fever was the primary complaint; associated symptoms included cough (5/7), poor feeding (4/7), and irritability (3/7). Three patients also had findings consistent with lower respiratory tract infection, while four were diagnosed with sepsis alone. One patient required high-flow oxygen therapy (Table 1).

Six patients had blood cultures showing A. denitrificans, and one patient had blood cultures showing *A. xylosoxidans*. Initial empirical treatment with third-generation cephalosporins (ceftriaxone or cefotaxime) was switched to piperacillin-tazobactam based on susceptibility results (Table 2). The average length of hospital stay was eight days. There was no mortality. All patients made a full recovery and were discharged in good health. Initial immunologic evaluations were unremarkable.

DISCUSSION

Achromobacter spp. is an infrequent pathogen in both nosocomial and community settings, with *Achromobacter* xylosoxidans being the predominant species among *Achromobacter spp*. isolates.[3] There are limited data on community-acquired infections. Pneumonia and bacteremia are the two predominant clinical manifestations of *Achromobacter spp*. infections in non-CF (Cystic Fibrosis) individuals.[4]

Case reports of *A. xylosoxidans* infections in Turkey have been documented.[5,6]

In our case series, all patients were previously healthy children from the community. Although the clinical presenta-

Table 1. Clinical and laboratory features of patients with *Achromobacter spp*. bacteremia

	Age (month)	Gender	Underlying disease& risk factors	Clinical data	WBC	NEU	LYM	PLT	CRP	PCT	Therapy and outcome
Case 1	16	F	N[a]	Sepsis, pneumonia	15000	7800	5700	371000	37	0.2	Ceftriaxone, switched to piperacillin-tazobactam (7), and discharged
Case 2	44	M	N	Pneumonia	7200	3400	3100	253000	46	0.4	Ceftriaxone, switched to piperacillin tazobactam (10), and discharged
Case 3	7	M	N	Sepsis	22000	18500	3800	534000	55	2.5	Ceftriaxone, switched to piperacillin tazobactam (10), and discharged
Case 4	9	F	N	Sepsis	41000	32000	8400	535000	181	4.5	Ceftriaxone, switched to piperacillin tazobactam (10), and discharged
Case 5	2	F	N	Sepsis	32800	18000	9500	398000	55	0.2	Ceftriaxone switch to meropenem (14) and discharged
Case 6	7	F	N	Sepsis	16200	9200	4060	945000	68	0.3	Ceftriaxone, switched to piperacillin tazobactam (10), and discharged
Case 7	42	F	N	Sepsis, pneumonia	19800	13700	3400	184000	178	2.2	

Ceftriaxone, switched to piperacillin tazobactam (10), and discharged. [a]: None, normal range: 0–5 mg/L, PCT: Procalcitonin; normal range: <0.5 µg/L. CRP: C-reactive protein; F: Female; M: Male; N:none; WBC: White blood cell; NEU: Neutrophil count; LYM: Lymphocyte count; PLT: Platelet count; PCT: Procalcitonin

Table 2. Minimum inhibitory concentrations (MICs) of *Achromobacter spp.* isolates

	Piperacillin-tazobactam	Meropenem	Amikacin	Aztreonam	Trimethoprim/ Sulfamethoxazole	Ceftazidime	Cefepime
Case 1 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)					
Case 2 MIC (µg/mL)	<=4.0 (S)	1.0 (S)	8.0 (S)	>=64.0 (R)	<=20.0 (S)		
Case 3 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)	16.0 (S)		<=20.0 (S)	2.0 (S)	16.0 (I)
Case 4 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)	8.0 (S)	>=64.0 (R)	<=20.0 (S)		16.0 (I)
Case 5 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)	8.0 (S)		<=20.0 (S)		8.0 (S)
Case 6 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)			<=20.0 (S)	>=64.0 (R)	8.0 (S)
Case 7 MIC (µg/mL)	<=4.0 (S)	<=0.25 (S)			<=20.0 (S)		

S: Sensitive; R: Resistant; I: Intermediate

tions were non-specific, they were consistent with bacterial sepsis. The management of patients with *A. xylosoxidans* bacteremia is complicated since this pathogen possesses both inherent and acquired resistance mechanisms, frequently resulting in a multidrug-resistant (MDR) phenotype.[7] Clinical isolates of *Achromobacter* have extensive multidrug resistance, albeit not universally. In addition to the production of β-lactamases and penicillin-binding proteins, numerous clinical strains of *A. xylosoxidans* possess genes that encode aminoglycoside-modifying enzymes, which provide resistance to tobramycin and gentamicin.[8]

A. xylosoxidans exhibits an atypical susceptibility profile, demonstrating resistance to aminoglycosides and most β-lactam antibiotics. Anti-pseudomonal penicillins, trimethoprim-sulfamethoxazole, and carbapenems are the chosen therapeutic agents.[1,9] Piperacillin-tazobactam and carbapenems have been shown to maintain high levels of *in vitro* activity against *Achromobacter spp.*, even among multidrug-resistant strains.[10] Our findings are in line with these reports, as all patients responded well to piperacillin-tazobactam. One patient was treated with a carbapenem. Given the organism's intrinsic resistance to aminoglycosides and fluoroquinolones, delayed treatment adjustments can compromise outcomes. This pattern of resistance has been observed consistently across pediatric and cystic fibrosis patient populations, highlighting the challenge of selecting effective empiric therapy.

While prior studies primarily documented infections in patients with comorbidities or prolonged hospitalizations, our series demonstrates that *Achromobacter spp.* can also cause significant illness in community-dwelling, previously healthy children. In the literature, some infections have been reported in healthy children.[11,12]

Shie et al.[13] assessed the features of *A. xylosoxidans* bacteremia in Taiwan and found that malignancies, central venous catheter placements, and prior major surgeries were the predominant underlying diseases.

Aisenberg et al.[14] indicated that *Achromobacter* bacteremia manifested with fever (52%), sepsis syndrome (22%), and respiratory issues (17%). A study detailing 40 cases of *A. xylosoxidans* bacteremia indicated that the predominant symptoms were fever (82%), chills (37.5%), hypotension (32.5%), and altered consciousness.[13]

A. xylosoxidans has often been isolated from environmental sources in hospital-acquired illnesses.[3] *A. xylosoxidans* was identified in deionized water within an intensive care unit, in tap water, and on the hands of two healthcare workers in a hemodialysis unit.[15]

Since the dates of positive blood cultures in our patients were not temporally clustered, an outbreak investigation was not initiated. All patients were hospitalized during the COVID-19 pandemic; however, SARS-CoV-2 was not detected in respiratory PCR tests as a causative pathogen.

The possibility of pseudo-bacteremia due to contamination during venipuncture, media preparation, or laboratory handling was considered. Nevertheless, all patients showed clinical signs consistent with true bacteremia, supported by laboratory findings such as positive blood cultures and elevated procalcitonin levels.

A lumbar puncture was performed on the 2-month-old infant diagnosed with sepsis, and cerebrospinal fluid results were not consistent with meningitis. Blood cultures for all patients were obtained at the time of initial presentation to the pediatric emergency department. None of the patients had a prior history of hospitalization.

Although previous studies have reported an increased incidence of *Achromobacter* bloodstream infections during the COVID-19 pandemic,[16] typically associated with prolonged hospitalization, broad-spectrum antibiotic use, and invasive procedures, none of our patients had underlying medical conditions, immunosuppression, or known risk factors such as central venous catheterization or mechanical ventilation.

This case series also underscores important epidemiological concerns. The occurrence of infection in children with no prior healthcare exposure suggests environmental reservoirs, such as contaminated water sources, which have been implicated in other outbreaks. These findings call for broader surveillance and environmental studies.

In terms of resistance patterns, our results mirror those in global surveillance studies, which highlight the need for local antibiograms to guide empiric choices. The ability of *Achromobacter spp.* to persist in moist environments, including hospital plumbing and devices, may also contribute to sporadic community emergence. Such an investigation is warranted when a cluster of cases emerges within a short timeframe, raising suspicion of a potential outbreak. In such scenarios, bacteriological cultures should be obtained from environmental sources, including antiseptic solutions (chlorhexidine digluconate, aqueous and alcoholic), wash basins, incubator surfaces, liquid soaps, faucets, nebulizers, and tap water. Additionally, healthcare workers' hands should be sampled by direct fingerprinting onto Petri dishes.[1]

This study has several limitations. First, it is a retrospective case series with a small sample size, which may limit the generalizability of the findings. Second, the study was conducted at a single center, potentially introducing selection bias. Finally, there was no long-term follow-up to assess for recurrence or long-term complications, which limits conclusions regarding the extended outcomes of these infections.

CONCLUSION

This case series demonstrates that *Achromobacter spp.*, despite traditionally being considered nosocomial pathogens, can cause community-acquired sepsis in healthy children. Increased clinical awareness and accurate identification are essential. For positive outcomes, timely susceptibility testing and appropriate antibiotic selection are critical.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Istanbul Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (No: KAEK/2025.08.200, Date: 15/08/2025).

Informed Consent: Informed consent was obtained from all participants.

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RESEARCH ARTICLE

Microanatomic Structure of Basillar Artery and its Perforators in Cadaver

Suna Dilbaz[1], Mehmet Yıldırım[2], Melih Üçer[3], Fahrettin Fatih Kesmezacar[2], Yunus Aydın[4]

[1]Department of Neurosurgery, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[2]İstanbul University, Cerrahpaşa Faculty of Medicine,İstanbul, Türkiye
[3]Department of Neurosurgery, Biruni University Faculty of Medicine, İstanbul, Türkiye
[4]Department of Neurosurgery, Fulya Hospital, Acıbadem Healthcare Group, İstanbul, Türkiye

ABSTRACT

Objective: The microsurgical anatomy of the posterior circulation is complex and variable. Surgeries performed close to this area are accepted to be highly risky due to important vascular and neural structures. In order to safely and securely treat pathologies in that area, understanding the microsurgical anatomy of the posterior circulation carries tremendous importance for neurosurgeons.

Materials and Methods: In order to reveal the characteristic of vertebrobasilar artery branches of people living in Turkey, we analyzed the arteries of 23 cadaveric brains (46 hemispheres) at the dissection laboratories of the Istanbul University Cerrahpasa Medical Faculty Anatomy Department. The diameter of the vertebral artery, the fusion angle of vertebral arteries, the diameter of the basilar artery were examined.

Results: 13 vertebrobasilar junctions were located across the pontomedullary sulcus, 5 were located below the pontomedullary sulcus, and 5 were above the pontomedullary sulcus. The average diameter measured 5.11 mm, the smallest being 3 mm and the largest measuring 6 mm. Out of all analyzed basilar arteries, only one revealed a fenestration. All results were compared with previous studies and were found to be coherent.

Conclusion: Damage to the vertebral artery, basilar artery or any of their branches during surgery may stay asymptomatic. However, the damage may also result in cranial nerve paralysis or go as far as coma due to ischemia. Understanding the anatomy of that area well can minimize this risk of complications and further avoid them.

Keywords: Basillar artery, microsurgical anatomy, posterior circulation

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INTRODUCTION

The posterior arterial circulation of the brain, a vital component of cerebral blood flow, is constituted by the vertebrobasilar system and its numerous branches.[1,2] This system plays a fundamental role in supplying blood to critical structures such as the medulla oblongata, pons, and midbrain, which are essential for maintaining vital bodily functions, including respiration, cardiovascular regulation, and motor control.[2] The integrity of this system is paramount, as even minor disruptions can lead to severe neurological deficits or life-threatening conditions.[3,4]

Despite its critical importance, the microsurgical anatomy of the posterior circulation remains one of the most complex and variable regions of the brain.[3,5] The intricate network of arteries, coupled with the close proximity to vital neural and vascular structures, makes surgical interventions in this area highly challenging. Even minor errors during surgical procedures can result in devastating outcomes such as ischemia, cranial nerve dysfunction, or even death. For this reason, a detailed and thorough understanding of this region is indispensable for neurosurgeons.[3,5,6]

One of the key challenges in posterior circulation surgery is addressing the significant anatomical variations commonly encountered in cerebral vascular structures. These variations, which may include differences in the branching patterns, diameters, and course of the arteries, can complicate

Address for Correspondence: Melih Üçer, Department of Neurosurgery, Biruni University Faculty of Medicine, İstanbul, Türkiye
E-mail: melihucer@hotmail.com **ORCID ID:** 0000-0002-2004-2991

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both the diagnosis and surgical approach.[3,4,7] Accurate preoperative knowledge of these variations is critical for minimizing risks and enhancing surgical outcomes.

In this study, we conducted an extensive examination of 23 human cadaveric brains to analyze the posterior vascular system in detail. Our primary focus was on the structure of the basilar artery and its perforators, given their pivotal role in supplying blood to the brainstem and cerebellum. By meticulously documenting and measuring these structures, we aimed to contribute valuable data to the existing body of literature. This study not only highlights common patterns but also underscores rare and clinically significant anatomical variations that neurosurgeons must consider during surgical planning.

By comparing our findings to existing definitions and classifications in the literature, we sought to provide an updated and comprehensive perspective on the microvascular anatomy of the posterior circulation. Our findings aim to support neurosurgeons in their efforts to safely and effectively manage pathologies in this anatomically and functionally complex region. This work underscores the critical importance of understanding the unique anatomy of each patient to tailor surgical approaches that maximize safety and efficacy.

MATERIALS and METHODS

The article and its appendices, submitted to the Bakirköy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital Ethics Committee with the file number 47773 on November 13, 2012, have been reviewed in accordance with the Regulations on Patient and Animal Rights, the Guidelines for Good Clinical Practice, and the Declaration of Helsinki, and have been approved by our Ethics Committee.

In order to reveal the characteristics of the vertebrobasilar artery branches of people living in Turkey, we analyzed the arteries of 23 cadaveric brains (46 hemispheres) at the dissection laboratories of the Anatomy Department. A mixture of 10% formaldehyde, 55% methanol, 15g sodium citrate, 15% glycerin, 5% phenol, 15% water, and 5ml eosin was injected into the arterial systems of the brains (with a pump) after being preserved in a formaldehyde pool for 6 months.

After injecting all vascular systems of the 23 brains, the brains were removed from the skull carefully using dissection methods, after lifting the calvarium. The brains, which were carefully removed from the skull, were placed in basins filled with formaldehyde-added fluid. The vertebrobasilar arteries were carefully examined after macroscopic dissection. Any brain showing pathologies was excluded from the study. After dissecting and measuring the arteries, photographs of the field were obtained to document the vascular anatomy and variations.

The dissection commenced at the vertebral arteries, followed by the basilar artery and its branches, reaching the basilar bifurcation, and revealed the vasculature.

The following details were examined: the diameter of the vertebral artery (VA), the fusion angle of vertebral arteries, the diameter of the basilar artery, its length and structure, the distance between the vertebrobasilar junction to the pontomedullary sulcus and its position, the diameters of the Anterior Inferior Cerebellar Artery (AICA), Superior Cerebellar Artery (SCA), and Posterior Cerebral Artery (PCA), the distances between the AICA and vertebrobasilar junction, as well as the SCA and basilar bifurcation, and the count of rami pontis.

RESULTS

Vertebral Artery (VA)

The union of the right and left VA leads to the formation of the vertebrobasilar junction, which occurs at the pontomedullary sulcus. In our study, 13 vertebrobasilar junctions were located across the pontomedullary sulcus, 5 were located a minimum of 3.5 mm and a maximum of 18 mm (average 6.7 mm) below the pontomedullary sulcus, and another 5 were a minimum of 2 mm and a maximum of 7.5 mm (average of 3.78 mm) above the pontomedullary sulcus. Of the ones located below the sulcus, only one was relatively closer to the medulla spinalis, measuring a distance of 18 mm from the pontomedullary sulcus and 3 mm from the medulla spinalis.

The diameters of the vertebral arteries on the right measured 6 mm as the largest, 2.6 mm as the smallest, revealing an average of 3.81 mm, and on the left, the diameters measured 6 mm as the largest, 2.5 mm as the smallest, revealing an average of 4.62 mm (Table 1). Out of the VAs, 12 (52.6%) showed equal diameters, 6 (26%) revealed a larger diameter on the right side, and 5 (21.74%) showed a larger diameter on the left. No VA fenestrations or duplications were encountered. The smallest angle of fusion between the VAs was measured as 20°, the largest 85°, resulting in an average angle of 46.609° (Table 1).

Basilar Artery

The junction of both vertebral arteries at the pontomedullary junction forms the origin of the basilar artery. It terminates after proceeding on the surface of the pons with the separation of both posterior inferior cerebellar arteries (PICA). The origins differed in several cases: 5 (21%) originated under the pontomedullary sulcus, another 5 (21%) originated above

Table 1. Diameters of Vertebral Arteries (VA) and vertebral artery fusion angles

Cadaver	Right VA diameter (mm)	Left VA diameter (mm)	VA fusion angle
1	4.5	4.5	30
2	4	4	40
3	3	5	35
4	3	3.6	50
5	4	4	40
6	3.5	3.5	45
7	6	4	20
8	5	5	45
9	2.6	2.6	50
10	3.9	3.9	70
11	3.9	3.9	40
12	4	3	55
13	3	6	60
14	5	5	65
15	3.5	3.5	37
16	5	3	40
17	3	2.5	85
18	3.5	3.5	50
19	4	4	35
20	4	3.5	50
21	3.5	4	40
22	4.5	4	45
23	4	4.5	45

Measurements include the largest, smallest, and average diameters of both right and left vertebral arteries, along with the smallest, largest, and average angles of vertebral artery fusion. Right VA Diameter (mm): Mean = 3.93, Median = 4.00, Std Dev = 0.81; Left VA Diameter (mm): Mean = 3.93, Median = 4.00, Std Dev = 0.82-; VA Fusion Angle: Mean = 46.61, Median = 45.00, Std Dev = 13.87

the sulcus, and 13 (58%) originated across the sulcus. The course of the basilar artery varied, as 14 (17%) deviated from the midline and 19 (83%) followed a straight course (Table 2).

The shortest basilar artery measured 24 mm, the longest measured 42 mm, resulting in an average length of 30.56 mm. The average diameter measured 5.11 mm, the smallest being 3 mm, and the largest measuring 6 mm (Table 2). Out of all analyzed basilar arteries, only one revealed a fenestration. No duplication was encountered. On the right side, we encountered 4–7 (average of 5) rami pontis separating from the basilar artery, and 3–8 (average of 4.78) on the left (Table 2). The basilar artery gives off large branches, such as the anterior inferior cerebellar artery, superior cerebellar artery, and posterior cerebral artery. In one case, the AICA did not arise from the basilar artery; however, it gave rise to PICA from the right, which was concluded after examining the course of the artery.

Anterior Inferior Cerebellar Artery (AICA)

The AICA is the first large branch of the basilar artery. Its distance to the vertebrobasilar junction measures a minimum of 3 mm, a maximum of 13 mm, resulting in an average of 8 mm on the right. On the left side, the distance measures at least 4 mm, at most 15 mm, which results in an average of 9.16 mm (Table 2). In around 6 (26.09%) cases, a single AICA was observed, whereas 14 (60.86%) showed double AICA, and 2 (8.69%) revealed triple AICA. Only one case (4.34%) revealed the absence of AICA.

The smallest diameter of the AICA measured 1 mm, the largest measured 2.5 mm, resulting in an average diameter of 1.39 mm on the right, whereas the left side presented the smallest diameter as 0.8 mm, the largest being 2 mm, resulting in an average diameter of 1.3 mm.

Superior Cerebellar Artery (SCA)

The SCA is the most regular branch of the basilar artery. It mostly arises adjacent to the posterior cerebral artery. The distance from the right SCA to the basilar bifurcation measures at least 0.8 mm and at most 4.3 mm, resulting in an average of 2.38 mm. On the left, the least distance to the bifurcation was measured to be 0.8 mm as well, with the longest distance measuring 3.2 mm, resulting in an average of 2.31 mm (Table 2).

In 3 cases, right and left SCA duplications were encountered. The SCAs with duplication were different; however, the duplication was always unilateral. On the right, the smallest diameter of the SCA was measured as 0.8 mm and the largest 2 mm, resulting in an average of 1.3 mm. On the left, the smallest diameter was measured as 0.75 mm, with the largest measuring 2 mm, resulting in an average of 1.30 mm (Table 2). In one case, the left SCA came off the PCA instead of the basilar artery.

Posterior Cerebral Artery (PCA)

The PCA arises from the basilar artery bifurcation and lies within the interpeduncular cistern, where it joins the posterior communicating artery. The diameter was at least 1.2 mm and at most 3.2 mm on the right, resulting in an average of 1.97 mm. On the left, the smallest diameter measured 1.2 mm, while the largest measured 3.2 mm, resulting in an average measurement of 1.93 mm (Table 2). On the left, one PCA showed to be giving off an SCA.

Table 2. Anatomical measurements and variations of the basilar artery and its main branches

Cadaver	BA diameter	BA length	Straight BA	Curved BA	Right R. pontis n	Left R. pontis n	Total R. pontis n	Right AICA-VBJ distance	Left AICA-VBJ distance	Right AICA diameter	Left AICA diameter	Right SCA-BT distance	Left SCA-BT distance	Right SCA diameter	Left SCA diameter	Right PCA diameter	Left PCA diameter
1	4.5	27	+		7	5	12	5	5	2.5	2	2.5	1.5	1.5	1.5	2.5	2
2	6	26	+		4	5	9	4–10 (2 AICA)	8	1	2	1.3	1.3	1.3	1.3	2	2
3	4	29	+		6	5	11		5		1.3	2.6	0.8	0.8	0.8	1.3	1.3
4	4	29	+		5	4	9	6	6	2	2	1.5		1.2		2	2
5	6	33	+		5	4	9	12	15	1.5	1.5	2	0.9	0.9	0.9	1.8	1.8
6	6	30	+		4	5	9	8	8	1.8	1.8	3	1.5	1.5	1.5	2	2
7	6	32	+		4	4	8	6	6	1.7	1.2	3	1.3	1.3	1.3	1.7	1.7
8	6.5	30		+	6	5	11	8	6	1		3.2	1	1.6	1	3.2	3.2
9	4	30	+		5	6	11	13	13	1.3	1.3	1.7	1	1	1	1.7	1.7
10	5	30	+		4	3	7	6	9	2	1.9	3.7	0.9	1.4	0.9	2.4	2.4
11	5	30		+	4	4	8	6		1.5		2.5	1.2	1.2	1.2	1.5	1.5
12	5	42		+	5	5	10					3	2	2	2	3	3
13	6	35	+		4	4	8		11.7		2	4.3	0.8	0.8	0.8	2.1	2.1
14	6	28	+		4	5	9	9	4	1.5	1	2.5	1.5	1.5	1.5	3	3
15	5	28	+		6	5	11	9	9	1	1	9	0.75	1	0.75	2	2
16	5	35		+	6	8	13		15		1	4	1	0.8	1.48	2	2
17	3	35	+		5	4	9	13	13	1.4	1	0.8	3	1.7	1.7	1.2	1.7
18	5	30	+		5	5	10	11	12	1	1	2	2.2	1.5	1.5	1.5	1.5
19	5	27	+		5	4	9	10	15–12 (2 AICA)	1.5	1.4	1.5	2.5	1.5	1.5	1.2	1.2
20	5	28	+		6	6	12		10		1.4	2.2	1.5	1.2	1.8	2.4	1.4
21	5	24		+	4	4	8	8	8	1	1	2	2.5	1	1	1.3	1.3
22	5	30		+	6	6	12	3	6	1	1	2	2	1.5	1.5	1.5	1.5
23	6	35		+	5	4	9	6	6	1.5	1.5	2.5	2	1.5	1.5	2	2

Included are measurements of basilar artery length and diameter, the number of pontine branches (rami pontis) on each side, distances of anterior inferior cerebellar artery (AICA) and superior cerebellar artery (SCA) from relevant anatomical landmarks, and recorded anatomical variations such as fenestrations, duplications, or absences. BA: Basilar artery; VBJ: Vertebrobasilar junction; BT: Basilar trunk; PCA: Posterior cerebral artery

DISCUSSION

The anatomy of the vertebrobasilar system is complex. Surgeries in this area are performed for aneurysms, vascular pathologies like arteriovenous malformations, tumors (astrocytomas, medulloblastomas, ependymomas, hemangioblastomas, and meningiomas), and for revascularization.[1] Understanding the anatomy ensures secure operations and helps limit possible complications for better outcomes. The anatomy also plays a significant role in understanding the mechanism of vascular diseases like aneurysms.

The basilar artery is formed at the pontomedullary sulcus by the two vertebral arteries passing through the transverse foramina of the first 6 cervical vertebrae, entering the posterior fossa via the foramen magnum.[2] In some cases, the vertebral arteries may unite before or after the pontomedullary area.[3] In our study, we found 13 (58%) of the vertebrobasilar junctions to be across the pontomedullary sulcus, 5 (21%) situated below (approximately 6.7 mm), and another 5 (21%) situated above the sulcus (approx. 3.78 mm). One of the junctions, found below the sulcus, was closer to the medulla spinalis, being situated around 18 mm away from the pontomedullary sulcus and 3 mm from the medulla spinalis.

A study by Torche et al.[4] of 20 cadavers revealed the position of the vertebrobasilar junction to be across the pontomedullary sulcus in 10 (50%) cases, above the sulcus in 7 (35%) cases, and below the sulcus in 5 (21.74%) cases. The diameter of the VA was analyzed by Yasargil et al.[5] and resulted in measurements between 0.92 and 4.09 mm. The same study also revealed a dominance of the left side in 42%, of the right in 32%, and equal calibration in 26%.

Our findings are closest to the results obtained by Pai et al.[3]. In their study, 53.3% of the VA diameters were equal, whereas 40% revealed a right dominance and 6.7% revealed a left dominance. Our study showed the diameters of the VA to be equal in 52.26%, whereas 26% were larger on the right and 21.74% had dominance of the left VA. The diameter of the VA carries clinical importance as VA aneurysms are most frequently observed on the dominant side.[4,6]

Of aneurysms found in the posterior circulation system, 6.5% are vertebrobasilar junction aneurysms. However, most commonly, VA aneurysms are situated on the PICA-VA junction, seen in 12.5% of cases. Anomalies such as duplication, fenestration, atresia, or the continuation of the VA as the basilar artery while the other VA runs as the posterior inferior cerebellar artery can be observed. However, we did not encounter any of the aforementioned anomalies. The VA fenestrating around a lower cranial nerve or being hypoplastic demonstrates a greater risk for the formation of aneurysms. Undoubtedly, knowing the anatomy of the VA well lowers the risk of damaging the vessel during surgery. Damage to the vessel may not cause any symptoms; however, it may also lead to complications such as Wallenberg syndrome (lateral medullary syndrome), coma, or death due to ischemia.

The basilar artery arises from the merging of both vertebral arteries at the pontomedullary sulcus and runs upwards through the prepontine cistern. The artery becomes more looped, gets longer, and shows a higher localization of the bifurcation as age increases.[5] In our study, we found a midline deviation of the basilar artery in 30%, while 70% revealed a straight course. However, Yasargil et al.[5] found the basilar artery to follow a straight course in 25%, whereas Grands et al.[6] revealed a straight course of the basilar artery in 74%. Numerous congenital anomalies of the basilar artery have been described. The basilar artery is formed during the 7th week of gestation as the primitive longitudinal neural arteries join. If this merge does not occur fully, fenestrations (partial or complete) may be seen.[7–10] Recently, another embryologic mechanism taking place in the 5th gestational week was found to be causing fenestrations. As persistent basivertebral anastomosis (transient bridging arteries) fail to diminish, they form vertebral or basilar artery fenestrations.[11]

Various studies have focused on this topic, with Yasargil et al.[5] revealing an occurrence of 1%. Takahashi et al.[1] examined 500 vertebral angiographies, revealing 3 cases with fenestrations. In our study, we found one (4.3%) basilar artery fenestration among 23 examined cadaveric brains. The fenestration of the basilar artery is most commonly observed at the vertebrobasilar junction. The focal defects of the tunica media of the fenestrated vessel may cause aneurysms.[12,13] The flow phenomenon at the proximal end of the fenestration, causing hemodynamic tension and increasing turbulence, may affect the formation of aneurysms.[14,15] These aneurysms are generally saccular and develop on the proximal part of the fenestration.[16–18] Understanding the complex anatomy of aneurysms and fenestrations is crucial. In order to avoid clipping a branch of the fenestrated vessel, preoperative investigation of the fenestration, apart from the aneurysm, can be helpful.[16]

A lateral suboccipital approach is advised, as aneurysms of the vertebrobasilar junction tend to lean forward.[15,16,19] Approaches such as presigmoid transpetrosal and suboccipital transcondylar also show favorable results, but they increase the risk of cerebrospinal fluid fistulas and lower cranial nerve paralysis (or palsy).[20] Other methods of treatment

include Guglielmi Detachable Coil embolization techniques.[17,21] Vertebrobasilar fenestrations are predisposing factors for vascular damage and ischemia.[11] The diameter of the basilar artery was measured in multiple studies. Our study revealed a diameter between 3 and 6 mm, resulting in an average measurement of 5.11 mm. In 1967, Wollschlager et al.[22] measured the diameters as well, showing a range between 2.7 and 4.3 mm, while Pai et al.[3] showed a diameter range of 3–7 mm in their study in 2007.

The length of the basilar artery changes with increasing age. In our study, we measured the length to be between 24 and 42 mm, resulting in an average measurement of 30.96 mm. The study conducted by Pai et al.[3] in 2007 revealed a length range between 24–35 mm, with an average of 24.9 mm. The basilar artery was observed to be giving off rami pontis alongside AICA, SCA, and PCA in our samples. However, Yasargil et al.[5] did not encounter any other long arteries arising proximal to the basilar artery in their series.

The basilar artery bifurcation is positioned at the pontomesencephalic junction. Our study showed 74% of the bifurcations to be at their expected normal location, while 26% were above the pontomesencephalic junction. However, none were located below the junction. Rhoton showed a normal position of the bifurcation in 72%, a location above the junction in 24%, and a location below the normal position in 4% in his study. For normally located basilar bifurcations, a transsylvian approach is sufficient. However, when the bifurcation is located above the dorsum sellae, aneurysms in this area cause pressure on the 3rd ventricle after reaching the mammillary bodies and must be operated on using a subtemporal approach, as retraction of the brain will be needed.

In surgeries of aneurysms with the presence of lower basilar bifurcations, special attention must be paid to the upward running of the first segment of the PCA (P1), which may complicate reaching the neck of the aneurysm. In these cases, the use of fenestrated clips may be needed. Our study showed 4–7 rami ponti coming off the basilar artery trunk on the right and 3–8 on the left side. A complication occurring during basilar trunk aneurysm surgeries is the accidental clipping of small arteries, which then causes ischemic damage due to occlusion. Anatomical knowledge of this area is essential in order to minimize these complications.

The AICA

The AICA may give up to 3 branches, but it may also be absent entirely. Yaşargil et al.[5] found the occurrence of one branch in 58%, double branches in 20%, three branches in 20%, and complete absence of AICA in 2% in their series. We found a single branch of the AICA in six patients (26.09%), double branches in 14 patients (60.86%), and three branches in 8.69% in our cadaveric brains. We observed one case of complete absence of AICA in our study (4.34%). The distance between the AICA and the vertebrobasilar junction in our study was measured between 3 and 13 mm (average of 8 mm) on the right side, and 4 and 15 mm (average of 9 mm) on the left side. Maximo Torche et al.[4] measured an average distance of 9.6 mm in 1991. Yasargil et al.[5] showed 75% of the AICA to arise from the lower 1/3 of the basilar artery, 16% from the middle portion of the basilar artery, and 9% from the junction point of the VA and the basilar artery. We observed the AICA to arise from the lower portion of the basilar artery in 65.22%, whereas 34.78% arose from the mid 1/3 portion of the basilar artery.

The AICA can be reached via retrosigmoid, mid-fossa, translabyrinthine, supra- and infratentorial presigmoid (combined) approaches. Alongside other arteries, the AICA can be damaged during interventions for cerebellopontine corner tumors, rarely seen aneurysms originating from the AICA, brainstem masses, and mid-clival chordomas. Clinical symptoms include vertigo, vomiting, tinnitus, dysarthria, ipsilateral facial paresis, hearing loss, sensory disturbance in the trigeminal area, pain in the contralateral extremity and trunk, decreased temperature sensation, and ipsilateral hemiparesis. In order to avoid these complications, the anatomy of the AICA should be well understood by surgeons.

The SCA

The SCA is the most consistent branch regarding the location of the basilar artery. It generally arises from the adjacent area of the basilar bifurcation, but may also rarely come off the PCA. Our study showed the average measured distance of 2.38 mm between the right SCA and the basilar bifurcation, whereas the left SCA was an average of 2.13 mm away from the bifurcation. Pai et al.[3] showed the right SCA to be 1.45 mm and the left SCA to be 1.33 mm away from the bifurcation in their study.

In our series, we found only one case in which the SCA came off the PCA. Wollschlager et al.[22] measured the diameter of the SCA to be 0.72–1.5 mm in their series, whereas Pai et al.[3] measured 0.5–2.5 mm in their study. We measured the diameter on the right side between 0.8 and 2 mm (average of 1.3 mm) and between 0.75 and 2 mm (average of 1.3 mm) on the left. The duplication of the SCA was described in the study of von Mitterwallner et al.[23] with an 8% occurrence on the right side and 13.3% on the left. Mani et al.[24] showed different results with a duplication rate of 28%. We encountered duplication of the SCA in 8.7% on the right and 13.04% on the left side.

The SCA can be damaged in surgical interventions for aneurysms (situated at the base or the apex of the SCA or PCA), tumors (tentorial incisura, cerebellopontine angle, clivus, upper cerebellar area), and trigeminal neuralgia (during dissection of the trigeminal nerve while decompressing), which may result in ischemia and infarctions. Postoperatively, the patient may experience headache, vomiting, dysarthria, ataxia of extremities and trunk, ipsilateral Horner syndrome, contralateral spinothalamic sensory deficit, upper motor neuron type facial paresis, and rarely, trochlear nerve paralysis.

The PCA

The PCA arises from the basilar artery bifurcation, is located within the interpeduncular cistern, where it connects to the posterior communicating artery (PComA) on the lateral aspect of the cistern. The PCA contains a total of 4 segments. However, in our study, we focused on the P1 segment only. The P1 segment begins at the commencement of the PCA and runs until the PComA, where it terminates. The average diameter of the PCA was 1.93 mm on the right side and 1.97 mm on the left side in our samples. Wollschlager et al.[22] presented their diameter measurement results as 0.65–1.78 mm. We observed one SCA arising from the P1 segment in one case. The SCA can be damaged in surgeries for basilar roof aneurysms, PCA aneurysms, and suprasellar tumors. The result of this damage may be visual field defects, contralateral sensation loss and pain, deep sensory deficit, alexia, difficulty finding words and naming (anomic aphasia), Gerstmann syndrome, memory deficits, agitation, and delirium.[25,26]

CONCLUSION

In our study, we evaluated the diameters and counts of the vertebral arteries, basilar arteries, AICA, SCA, and PCA, as well as the vertebral fusion angle, basilar artery length, count of rami pontis, the distance between the AICA and vertebrobasilar junction, the position of the vertebrobasilar bifurcation in regard to the lower border of the pons, the distance between the SCA and the basilar bifurcation, the location of the basilar bifurcation in regard to the upper border of the pons, and all variations of the branches. All results were compared with previous studies and were found to be coherent.

The results were evaluated considering the outcome of neurosurgical procedures. Damage to the VA, basilar artery, or any of their branches during surgery may remain asymptomatic. However, the damage may also result in cranial nerve paralysis or go as far as a coma due to ischemia. Understanding the anatomy of that area well can minimize the risk of complications and further avoid them.

Disclosures

Ethics Committee Approval: The study was approved by the Bakirköy Prof. Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital Ethics Committee (No: 47773, Date: 13/11/2012).

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RESEARCH ARTICLE

Evaluation of Recurrence Level of Ligation of Intersphincteric Fistula Tract (LIFT) and Laser Methods for Anal Fistula

Vahit Mutlu[1], Bülent Koca[2], Serhan Yılmaz[3], Murat Kalemoğlu[1], Kadir Yılmaz[4]

[1]Department of General Surgery, Üsküdar University, İstanbul, Türkiye
[2]Department of General Surgery, Tokat Gaziosmanpaşa University Faculty of Medicine, Tokat, Türkiye
[3]Department of General Surgery, Ankara Bilkent City Hospital, Ankara, Türkiye
[4]Department of Statistics, İstanbul Commerce University, İstanbul, Türkiye

ABSTRACT

Objective: This research aimed to evaluate the recurrence level of ligation of Intersphincteric Fistula Tract (LIFT) and Laser methods for anal fistula.

Materials and Methods: A total of 71 patients who applied to Tokat Government Hospital and İstanbul Ataşehir Memorial Hospital between 2014 and 2024 were included in the study. The patients were divided into two groups: laser (n=30) and LIFT (n=41). Gender, age, fistula type, recurrence, follow-up period, and number of operations were analyzed in the study.

Results: Gender, age, recurrence, fistula type, and number of operations differences between patient groups were statistically insignificant (p>0.05) (Table 1). The correlation between method, age, gender, number of operations, and fistula type was insignificant (p>0.05) (Table 2). Binary logistic regression analysis results for the effects of method and baseline characteristics on recurrence showed that the effect of method, age, gender, number of operations, and fistula type on recurrence was insignificant (p>0.05) (Table 3). Recurrence durations were similar between operation types, and the difference analysis was statistically insignificant (p>0.05) (Table 4).

Conclusion: There was no statistically significant difference between LIFT and laser surgery. The results we obtained show that both LIFT and laser methods give the same results in terms of treatment success.

Keywords: Anal fistula, intersphincteric fistula tract (LIFT), recurrence

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INTRODUCTION

Anal fistula is a health problem that is more common in men and has been reported in very old times; it refers to a fistula in the anorectal region.[1] Sixty-five percent of patients who have an initial perianal abscess develop recurrent or chronic anal fistula.[2] Anal fistula, which occurs with or after acute anorectal abscess, is part of the perianal sepsis spectrum.[3] Anal fistula surgery is a disease that involves chronic irritation for patients and surgeons, and due to the complexity of the anorectal anatomy, recurrence is frequently seen in treatment.[4] In addition to the disease, there is a noticeable decrease in quality of life and physical activities in anal fistula patients.[5] The ideal surgical treatment for anal fistula focuses on eliminating sepsis without disrupting the sphincters and continence mechanism.[6] For this, the operation should be performed with the least invasive intervention possible.

The Level of ligation of Intersphincteric Fistula Tract (LIFT) is a method used for anal fistula, and its use has increased in recent years. LIFT has become popular, especially in the treatment of complex anal fistula with the sphincter-spar-

Address for Correspondence: Vahit Mutlu, Department of General Surgery, Üsküdar University, İstanbul, Türkiye
E-mail: dr.vahitmutlu@gmail.com **ORCID ID:** 0000-0002-2731-6799

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ing technique, and provides surgical advantages.[7] Although there are studies reporting late complications and negative effects in the long term in previous studies on LIFT,[8] there are also clinical studies reporting reliable results.[9–14] On the other hand, studies on the validity of the method regarding recurrence are limited. Another surgical method used for anal fistula is the laser method, which again aims at minimally invasive intervention for complex anal fistulas.[15,16] However, although there are studies and clinical applications in the literature regarding the two methods, there have been no sufficient studies examining the two methods in the context of recurrence. Therefore, this study aimed to evaluate the recurrence level of ligation of Intersphincteric Fistula Tract (LIFT) and Laser methods for anal fistula.

MATERIALS and METHODS

Research Model

The study was designed retrospectively, using a descriptive screening and cross-sectional research model. In this context, both anal fistula treatment methods were compared, and then, using the relational screening model, the effects of the methods and other variables on recurrence were analyzed.

Patients

A total of 71 patients who applied to Tokat Government Hospital and İstanbul Ataşehir Memorial Hospital between 2014 and 2024 were included in the study. The patients were divided into two groups: laser (n=30) and LIFT (n=41). In patients who underwent laser application, seton application was performed, and laser treatment was performed before the fistula matured. In this context, according to the power analysis conducted in the study, it was aimed to reach 28 patient files for each method with a 95% confidence interval and a significance level of 0.05. The inclusion criteria for the patients were as follows:

- Age 18 and older,
- Having undergone anal fistula LIFT or laser surgery,
- Having complete relevant data in patient files,
- Having no negative health conditions that could affect the study results.

The exclusion criteria for the study were:

- Age younger than 18,
- Having comorbid conditions that could affect the study results,
- Missing relevant data in patient files.

Although there are no definitive guidelines for patient selection between LIFT and laser surgery, patient selection was largely based on the surgeon's judgment and the patient's physical examination. Because the study data are retrospective, the surgeon's judgment was arguably the most important selection criterion.

Data

In the study, patients' gender, age, fistula type, recurrence, follow-up period, and number of operations were analyzed.

Ethical Approval

Permission for the research was obtained from the Uskudar University Non-interventional Research Ethics Committee with the reference number 61351342/020-66, dated 31.07.2025. The research was conducted according to the Helsinki Declaration. Informed consents were taken from patients.

Statistical Analysis

Nominal and ordinal parameters were described with frequencies, whereas scale parameters were described with the mean, standard deviation, median, and ranges. Fisher's Exact test was used for normality analysis of research parameters. Mann Whitney U test was used for differences between groups due to non-normal distribution. Spearman's rho correlation was used for relationships. Binary Logistic Model was used for effect analysis due to linearization deviations.[17,18] ROC analysis was used for predictive value of follow-up duration. SPSS 25.0 for Windows was used for analysis at a 95% confidence level and a 0.05 significance p-value.

RESULTS

Gender, age, recurrence, fistula type, and number of operations differences between patient groups were statistically insignificant (p>0.05) (Table 1).

Spearman's rho correlation analysis results between recurrence and baseline characteristics of patient groups showed that the correlation between method, age, gender, number of operations, and fistula type was insignificant (p>0.05) (Table 2).

Binary logistic regression analysis results for the effects of method and baseline characteristics on recurrence showed that the effect of method, age, gender, number of operations, and fistula type on recurrence was insignificant (p>0.05) (Table 3).

Recurrence durations were similar between operation types, and the difference analysis was statistically insignificant (p>0.05) (Table 4).

Table 1. Baseline and recurrence levels of patient groups and difference analysis results

	Method				p
	Laser (n=30)		Lifting (n=41)		
	n	%	n	%	
Gender					0.603[a]
Female	8	26.7	11	26.8	
Male	22	73.3	30	73.2	
Age	40.43±14.63		39.44±13.18		0.848[b]
	36.50 (17.00–71.00)		37.00 (18.00–70.00)		
Recurrence	9	30.0	8	19.5	0.228[a]
Fistula type					0.370[a]
Intersphincteric	17	56.7	26	63.4	
Transsphincteric	13	43.3	15	36.6	
Number of operations	1.17±0.38		1.15±0.36		0.816[b]
	1.00 (1.00–2.00)		1.00 (1.00–2.00)		
Follow up duration	26.00±17.28		30.88±16.87		0.224[b]
	23.00 (4.00–62.00)		31.00 (5.00–63.00)		

[a]: Fisher's exact test; [b]: Mann Whitney U Test. SD: Standard deviation

Table 2. Spearman's rho correlation analysis between recurrence and baseline characteristics of patient groups

	r	p
Method (1=Laser, 2=Lifting)	-0.121	0.313
Age	0.056	0.640
Gender	-0.034	0.781
Number of operations	0.033	0.782
Fistula type	0.020	0.869

**: p<0.01

DISCUSSION

In this study, recurrence and possible factors were analyzed in the LIFT and laser methods used in anal fistula treatment. According to the results obtained, both methods were similar, and output differences were insignificant.

Surgical treatment of anal fistulas is an important health problem with high recurrence rates[2–4] due to the complexity of the anorectal body structure, which negatively affects the quality of life of individuals.[19–21] To provide minimally invasive procedures in the treatment of the disease, methods such as laser and LIFT have been developed. Studies on recurrence in anal fistulas establish a relationship with various factors.[22–25] Among these studies, Mei et al.[22] reported that surgical and patient-related factors are related to recurrence. Emile[23] reported that anal fistula recurrences are significant in both general surgery and colorectal surgery and are dependent on the method and treatment stage. Jordan et al.[24] reported that the internal opening factor is an important recurrence risk factor after anal fistula surgery. Malik and Nelson[25] reported that recurrence rates vary according to the method, patient demographics, and clinic. Although variables related to recurrence were shown in these studies, no sufficient studies were found examining recurrence according to method and follow-up duration.

In our study, baseline characteristics differences between patient groups were statistically insignificant. Only follow-up duration was significantly and negatively correlated with recurrence for both methods. The effect of method, age, gender, number of operations, and fistula type on recurrence was insignificant.

Limitations of the Study

The most important limitation of the study is that it is very difficult to follow up with patients with anal fistula, and recurrence patients are often underrepresented. Since both public and private sectors provide health services, patient follow-up becomes difficult. In addition, when recurrence occurs, patients often blame the health institution and surgeon, leading them to change institutions.

Table 3. Binary logistic regression analysis for effects of method and baseline characteristics on recurrence

	OR	SE	Wald	df	p	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Age	0.003	0.021	0.023	1	0.881	1.003	0.962	1.046
Gender	-0.176	0.622	0.080	1	0.777	0.838	0.247	2.840
Method	-0.557	0.563	0.980	1	0.322	0.573	0.190	1.727
Number of operations	0.187	0.761	0.060	1	0.806	1.205	0.271	5.357
Fistula type	0.105	0.596	0.031	1	0.861	1.110	0.345	3.573
Constant	-0.485	2.168	0.050	1	0.823	0.616		

OR: Odds ratio; SE: Standard error; df: Degrees of freedom; CI: Confidence interval

Table 4. Recurrence starting durations according to operation methods

	Method		p
	Laser (n=30)	Lifting (n=41)	
Recurrence duration	26.00±17.28	30.88±16.87	0.224[a]
	23.00 (4.00–62.00)	31.00 (5.00–63.00)	

[a]: Mann Whitney U Test

Another limitation is the lack of studies comparing laser and LIFT in terms of recurrence. For this reason, sufficient comparisons could not be made in the study regarding the extent to which the findings obtained depend on the sample and can be generalized.

Contribution of the Research to Literature and Clinical Practice

The most important contribution of the research to the literature is that there have been no sufficient studies done in this field before. Therefore, this research can serve as a foundation for further studies.

CONCLUSION

According to the results obtained in our study, there was no statistically significant difference between LIFT and laser surgery. In terms of clinical applications, both methods may be selected according to the surgeon's decision and the clinical characteristics of the patients. There were differences, but they were statistically insignificant.

While there is no definitive literature on the superiority of laser versus LIFT in anal fistula treatment, LIFT surgically ligates the fistula tract, minimizing damage to the anal sphincters, aiming for faster recovery and post-treatment relief. The laser method, on the other hand, is considered less invasive. However, our results have shown that patient outcomes were similar with both methods. Therefore, when choosing a method, the surgeon and patient should select the one that best suits their needs based on cost, practicality, and comfort.

These differences may become significant with a larger sample. In addition, the results of the study can be expanded with multicenter samples that have different demographic structures. More comprehensive studies are needed to better understand the recurrence mechanism, including internal and external variables, hygiene, and sanitation.

Disclosures

Ethics Committee Approval: The study was approved by the Uskudar University Non-interventional Research Ethics Committee (No: 61351342/020-66, Date: 31/07/2025).

Informed Consent: Informed consents were taken from patients.

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RESEARCH ARTICLE

Roxadustat Efficacy in Hemodialysis Patients with Epoetin-Hyporesponsive Anemia

Cihan Uysal

Deparment of Nephrology, Ağrı Training and Research Hospital, Ağrı, Türkiye

ABSTRACT

Objective: A reduced treatment response to epoetin (EPO) therapy is a clinical challenge among hemodialysis (HD) patients. Outcomes of roxadustat in HD patients who had hyporesponse to EPO therapy were investigated.

Materials and Methods: This retrospective study analyzed adult patients undergoing long-term HD. Hyporesponsiveness to EPO was defined as a hemoglobin (Hb) level consistently below 10 g/dL despite receiving maximum EPO and having adequate iron stores for at least three months. The target Hb threshold for following roxadustat was defined as ≥11 g/dL.

Results: A total of 227 HD patients were screened, and 25 patients were enrolled. The mean age was 55.1±17.5 years. Median HD duration was 47 (19–118) months. Average Hb during the EPO treatment was 8.7±0.7 g/dL, compared to 9.8±1.3 g/dL during the roxadustat treatment. Increased Hb following roxadustat was observed in 17 patients (68.0%). Target Hb was achieved in 14 (56%) patients following roxadustat. Erythropoietin resistance index was 17.6±1.4 IU/kg/gHb in patients who responded to roxadustat, whereas it was 19.4±3.3 IU/kg/gHb in non-responders (p=0.087). The average Hb level was significantly increased during the roxadustat period (p=0.011). Lower uric acid (p=0.003) and higher Kt/V (p=0.044) were observed in patients who achieved target Hb. Pre-treatment transferrin saturation was correlated with the amount of Hb change following roxadustat (p=0.034).

Conclusion: The current study should be considered a pioneering effort, and findings support significant treatment success with roxadustat.

Keywords: hemodialysis, epoetin, roxadustat, anemia

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INTRODUCTION

Anemia is a common complication of chronic kidney disease (CKD) and is associated with poor outcomes. The underlying mechanisms of anemia associated with CKD are diverse and complex. Diminished endogenous erythropoietin production, reduced erythrocyte survival duration, functional iron deficiency, and inflammation with increased hepcidin levels are some of the causes.[1]

The frequency and severity of anemia gradually increase in the advanced stages of kidney disease, and an association between lower estimated glomerular filtration rate (eGFR) and the prevalence of anemia is observed. Furthermore, lower hemoglobin (Hb) levels are associated with an increased risk of CKD progression, cardiovascular disease, stroke, and death when adjusting for age, race, and eGFR.[2]

The severity of anemia significantly increases in patients undergoing hemodialysis. Blood transfusion requirements also increase in this population. In addition, both iron deficiency and anemia are worsened with HD procedures and frequent blood sampling.[3]

Erythropoiesis-stimulating agents are the cornerstone of renal anemia management in iron-replete HD patients. Before the availability of recombinant human erythropoietin (rHuEPO), dialysis patients frequently required blood transfusions that exposed them to the risks of iron overload, transmission of viral infections, and enhanced immune sensitization.[4]

More recently, hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs), such as roxadustat and daprodustat, have been introduced as therapeutic options for anemia in patients with CKD.[5] HIF-PHIs increase endogenous erythropoietin

Address for Correspondence: Cihan Uysal, Deparment of Nephrology, Ağrı Training and Research Hospital, Ağrı, Türkiye
E-mail: drcihanuysal@hotmail.com **ORCID ID:** 0000-0002-6214-0354

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levels by stimulating transcription of the erythropoietin gene in the kidneys and liver. Additionally, HIF-PHIs increase the amount of iron available for erythropoiesis by increasing intestinal iron absorption and decreasing iron sequestration.[6]

In the current study, we examined the efficacy of roxadustat in a specific subgroup of CKD. We reported the clinical outcomes of roxadustat use among HD patients who had an insufficient response to epoetin (EPO) treatment.

MATERIALS and METHODS

Ethical Approval

This study protocol was approved by the Agri Ibrahim Cecen University Ethics Committee (date: 28.11.2024, number: 410). This clinical investigation was carried out in accordance with the 1964 Helsinki Declaration. The data for this study, obtained from the patients' medical records, were anonymized so that the patients could not be identified. Human rights are well protected.

Study Design

This retrospective study was conducted on adult hemodialysis (HD) patients with renal anemia at the Nephrology Clinic of Ağrı Training and Research Hospital. The patient screening period spanned from January 1, 2023, to January 1, 2025, encompassing a two-year duration. The key inclusion criterion was a history of oral roxadustat treatment for at least three months due to a hyporesponse to previous EPO therapy. Roxadustat treatment response was analyzed with demographic characteristics, clinical features, and laboratory findings. Patients who had not received EPO treatment prior to roxadustat initiation, or who were administered EPO and roxadustat concurrently, were excluded from the study. Additionally, patients diagnosed with hematologic disorders or malignancies were also excluded.

Definitions

Hyporesponsiveness to EPO was defined as a Hb level consistently below 10 g/dL despite receiving the maximum EPO dosage and having adequate iron stores (ferritin >500 ng/mL) for at least three months. The maximum EPO dosage was defined as 150 IU/kg/week for EPO (alfa, beta, or zeta) and 0.75 mcg/kg/week for darbepoetin. A standard roxadustat regimen was defined for all patients according to: 70 mg orally, three times per week, following dialysis sessions.

Two timeframes were designated for evaluating anemia treatment. The "EPO period" referred to the last three months before initiating roxadustat, while the "roxadustat period" referred to the first three months after its initiation.

The target Hb threshold for renal anemia management in patients was defined as >11 g/dL. Based on their response to roxadustat, patients were categorized into two groups: (1) the responder group, in which patients achieved an Hb level of ≥11 g/dL at least once, and (2) the non-responder group, whose Hb levels remained below 11 g/dL throughout the treatment period.

The erythropoietin resistance index (ERI) is a widely used parameter for evaluating hyporesponsiveness to erythropoietin in clinical studies. ERI, expressed in IU/kg/gHb, is calculated by ERI = total EPO dose per week (IU) / body weight (kg) / hemoglobin (g/dL). An ERI value of ≥10.0 IU/kg/gHb is used as the threshold to define resistance to EPO.[7,8]

Laboratory values used in the analysis were obtained from the month in which the roxadustat therapy was initiated. Pre-dialysis samples were collected before the HD session to measure urea, creatinine, uric acid, electrolytes, bicarbonate, glucose, total protein, albumin, parathyroid hormone (PTH), complete blood count, ferritin, transferrin saturation (TSAT), iron levels, and nutritional values (folic acid and vitamin B12). Post-dialysis samples were obtained after reducing the blood pump rate to 100 mL/min for 15 seconds and subsequently stopping it. Post-dialysis urea and creatinine levels were recorded. Dialysis adequacy was assessed using both the urea reduction ratio (URR) and Kt/V, calculated using the second-generation single-pool Daugirdas formula.[9] URR was calculated as URR = (Predialysis Urea – Postdialysis Urea) / Predialysis Urea.

Statistical Analysis

Statistical analyses of the study were performed using SPSS 22.0 (SPSS Inc., Chicago, USA). The Shapiro-Wilk test was employed to assess whether numerical data followed a normal distribution. Numerical data showing a normal distribution were presented as mean±standard deviation, while non-normally distributed numerical data were presented as median (1^{st}–3^{rd} quartiles). Non-numerical (categorical) data were expressed as percentages. To compare the differences between groups, either a two-sided independent samples t-test or Mann-Whitney U test was used for continuous variables, and Pearson χ^2 analysis or Fisher's exact test was used for categorical variables. The Spearman correlation coefficient was used to explore the relationship between numerical variables. The paired t-test was used to analyze normally distributed parameters. The chi-square test was employed to assess non-numerical data. Results were evaluated at a 95% confidence interval, with significance set at $p<0.05$.

RESULTS

A total of 227 HD patients were identified, of whom 25 met the inclusion criteria and were enrolled in the study. The patients comprised 13 males (52.0%) and 12 females (48.0%). The mean age of the patients was 55.1±17.5 years, and the average body mass index (BMI) was 22.4±4.3 kg/m². The median duration of hemodialysis was 47 months (19–118). The mean URR was 75±5.6, and the median Kt/V value was 1.73±0.29. No cases of dialysis inadequacy were observed.

With respect to vascular access, 19 patients (76.0%) had an arteriovenous fistula, 5 patients (20.0%) had a tunneled dialysis catheter, and 1 patient (4.0%) had an arteriovenous graft. Baseline patient characteristics are summarized in Table 1.

Regarding EPO use, 15 patients received epoetin alfa, and 10 patients received epoetin zeta. None of the patients were treated with epoetin beta or darbepoetin. The average ERI was 18.4±2.5 IU/kg/gHb. A history of blood transfusion prior to roxadustat treatment was identified in 8 patients (32.0%). Maintenance intravenous iron supplementation was documented in 14 patients (56.0%) prior to roxadustat initiation.

The mean Hb level during the EPO treatment period was 8.7±0.7 g/dL, compared to 9.8±1.3 g/dL during the roxadustat treatment period. An increase in Hb level following roxadustat therapy was observed in 17 patients (68.0%). These results are illustrated in Figure 1.

Prior to roxadustat treatment, the median serum ferritin level was 655 ng/mL (570–914), serum iron was 49 µg/dL (41–73), TSAT percentage was 28 (26–43), folic acid was 6.3 µg/L (5.3–8.1), and vitamin B12 was 457 pg/mL (326–687). The mean MCV was 89.1±5.9 fL, the mean leukocyte count was 6.8 ±2.2 ×10³/µL, and the median platelet count was 173×10³/µL (143–205).

Target Hb level was achieved in 14 (56%) patients after roxadustat treatment. In a comparison of the two anemia treatment periods, the average Hb level was statistically significantly increased during the roxadustat period (p=0.011). The course of Hb levels according to treatment periods was demonstrated in Figure 2.

The ERI was 17.6±1.4 IU/kg/gHb in patients who responded to roxadustat and 19.4±3.3 IU/kg/gHb in non-responders. Although the average ERI was lower in patients who achieved the target Hb following roxadustat treatment, the difference was not statistically significant (p=0.082).

Patients were compared based on their response to roxadustat treatment. In the demographic analysis, there were no significant differences between the responder and non-responder groups in terms of age, duration of HD, or BMI. The proportion of female patients who achieved the target Hb level following roxadustat therapy was significantly higher than that of male patients (83.3% vs. 30.7%, p=0.008).

In the laboratory comparison, significant differences were observed between the two groups in pre-dialysis levels of urea, potassium, uric acid, and vitamin B12. Additionally, the mean Kt/V value was higher in patients who responded to

Table 1. Baseline characteristics of the patients

Parameters	Results	
	n	%
Gender		
Male	13	52
Female	12	48
Age (years)	55.1±17.5	
BMI (kg/m²)	22.4±4.3	
Hemodialysis duration (months)	47 (19–118)	
Kt/V	1.73±0.29	
URR (%)	75±5.6	
Vascular access		
AV fistula	19	76
Tunneled catheters	5	20
AV graft	1	4
CKD etiology		
Diabetes mellitus	9	36
Hypertension	7	28
Glomerulonephritis	5	20
Urological problems	2	8
Others	2	8
Blood transfusion history	8	32
Kidney transplantation history	3	12
RAS blockage use		
ARBs	6	24
ACEIs	5	20
Treatments		
Iron repletion	14	56
Vitamin D analogs	17	68
Calcimimetics	9	36
Vitamin supplements	25	100

Values are expressed as n (%), mean±standard deviation, median (1st–3rd quartiles). BMI: Body mass index; BSA: Body surface area; CKD: Chronic kidney disease; URR: Urea reduction rate; AV: Arteriovenous; ACEIs; Angiotensin converting enzyme inhibitors; ARBs: Angiotensin receptor blockers; RAS: Renin-angiotensin system

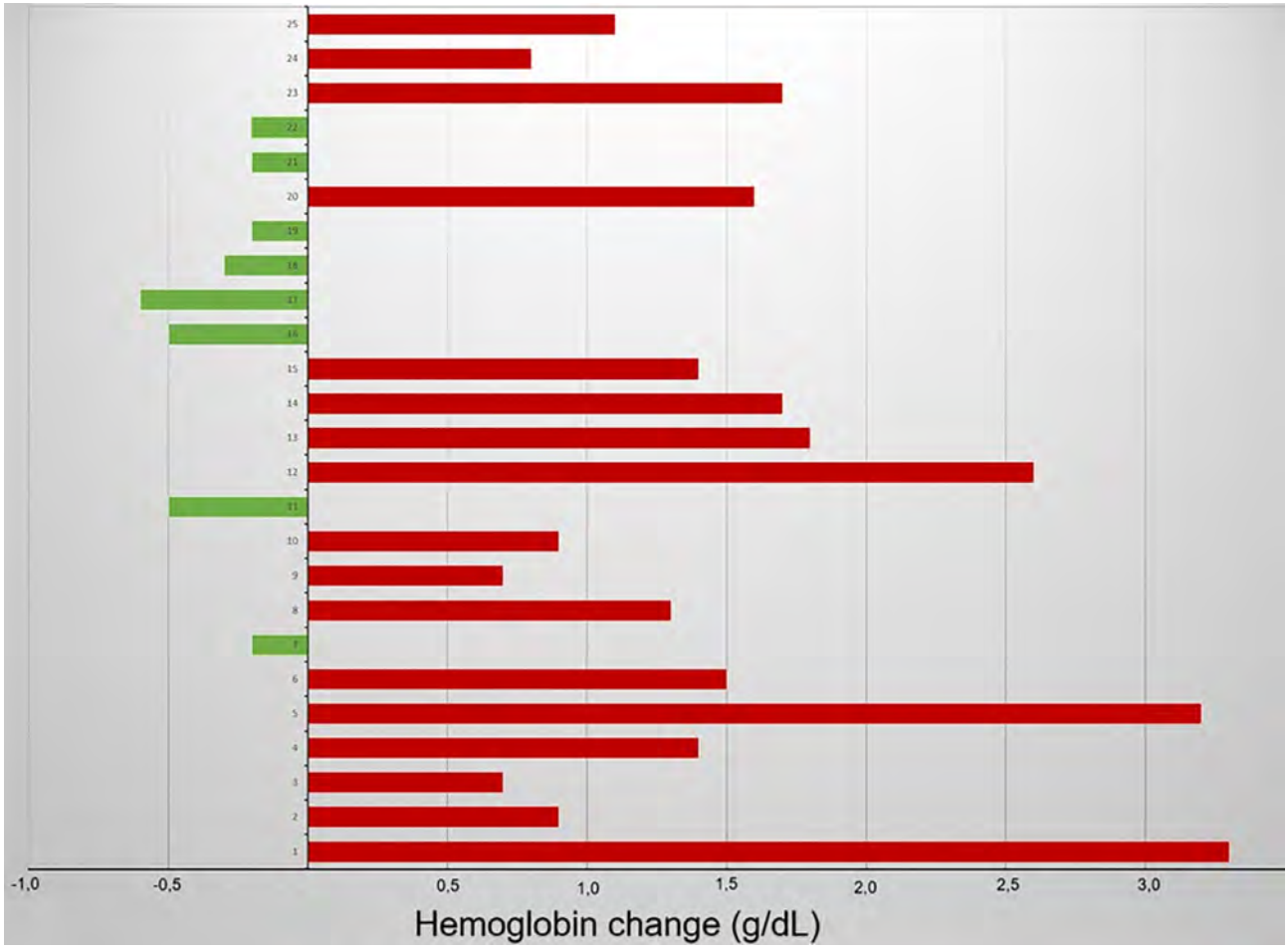

Figure 1. Quantitative hemoglobin change after roxadustat treatment for each patient

roxadustat treatment (1.83±0.3) compared to those who did not respond (1.60±0.2), with a statistically significant difference (p=0.044). In contrast, URR did not differ significantly between the groups (p=0.087). A summary of these findings is presented in Table 2.

The change in Hb levels was significantly correlated with TSAT percentage (p=0.034), as illustrated in Figure 3. However, no significant correlation was observed between Hb changes and either ferritin levels (p=0.893) or serum iron levels (p=0.306). Also, there was no correlation between ERI and change in Hb level (p=0.333). Additionally, an inverse correlation was found between Hb change and patient age (p=0.018), and this is shown in Figure 4. The increase in hemoglobin following roxadustat treatment was inversely associated with PTH levels (p=0.039), whereas no significant correlation was observed between the ERI value and PTH levels (p=0.080). Roxadustat treatment response was not associated with RAS blockage use (p=0.495).

DISCUSSION

In this study, we demonstrated the results of roxadustat treatment in HD patients who could not reach an adequate Hb level with conventional EPO treatment. We observed that 56% of the patients achieved the target Hb level (≥11 g/dL) following roxadustat treatment over a 12-week period. This rate is not negligible for an arduous patient subgroup, because all patients had persistently low Hb levels (<10 g/dL) for at least 3 months under 150 IU/kg per week EPO treatment. Also, the average ERI was 18.4±2.5 IU/kg/gHb in our cohort.

Data from both clinical and experimental studies reveal that the etiology of anemia in CKD is multifactorial; however, relative erythropoietin deficiency remains the most prominent factor. Furthermore, the positive outcomes observed in patients treated with rHuEPO strongly support the notion that erythropoietin deficiency is the primary driver of anemia in this population.[10] Several factors—including advanced age,

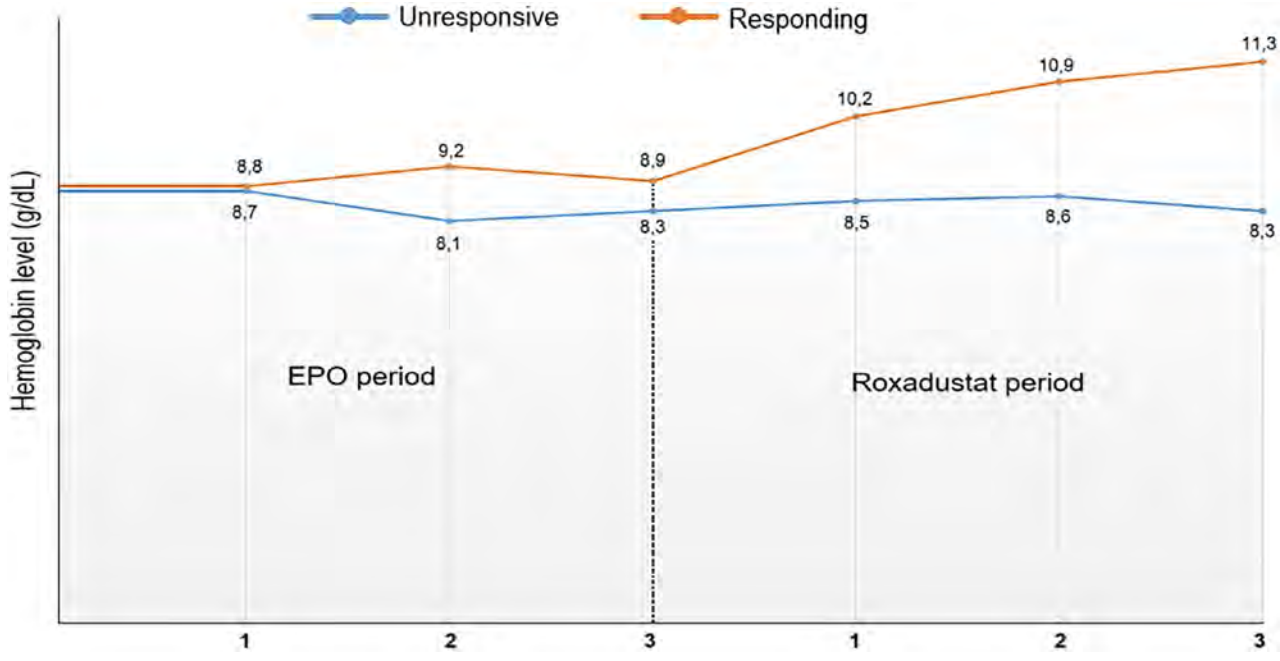

Figure 2. Comparison of the outcomes between two anemia treatment periods

higher BMI, use of renin-angiotensin system (RAS) blockers, diabetes mellitus, and severe secondary hyperparathyroidism—are associated with higher EPO dosage requirements.[11]

A reduced responsiveness to EPO therapy is a common clinical challenge among dialysis patients and is linked to increased mortality and a greater need for erythrocyte transfusions.[12] The underlying mechanisms of hyporesponsiveness to EPO are not yet fully understood. The common causes are iron deficiency, inadequate dialysis, and chronic inflammation.

Table 2. Comparison of laboratory findings according to roxadustat treatment response

Parameters	Target hemoglobin response		p	Parameters	Target hemoglobin response		p
	Present (n=14)	Absent (n=11)			Present (n=14)	Absent (n=11)	
Kt/V	1.83±0.3	1.60±0.2	**0.044**	Protein (g/dL)	6.8±0.6	6.7±0.6	0.718
URR	76.9±5.8	73.1±4.8	0.087	Albumin (g/dL)	3.7±0.3	3.4±0.4	0.099
Urea (mg/dL)	110±33	148±50	**0.030**	Glucose (mg/dL)	113 (97–138)	139 (106–190)	0.250
Creatinine (mg/dL)	6.9±1.8	8.3±2.1	0.100	MCV (fL)	87.7±5.8	89.3±5.8	0.473
Uric acid (mg/dL)	5.2±0.9	6.7±1.2	**0.003**	Iron (µg/dL)	53 (43–75)	45 (37–72)	0.460
Sodium (mmol/L)	136±2.9	136±3.1	0.853	TSAT (%)	29 (27–48)	26 (22–42)	0.170
Potassium (mmol/L)	4.6±0.6	5.3±0.8	**0.039**	Ferritin (ng/mL)	647 (537–993)	780 (602–887)	0.381
Calcium (mg/dL)	9.2±0.8	8.8±0.6	0.213	Vitamin B12	352 (297–532)	680 (483–1062)	**0.021**
Phosphate (mg/dL)	5.2±1.2	5.4±1.2	0.661	Folic acid	5.6 (4.9–6.4)	5.3 (4.5–14.3)	0.874
CaXP (mg^2/dL^2)	47.±10.9	47.3±10.9	0.970	Leukocyte ($10^3/\mu L$)	6.3 (5.7–8.1)	5.6 (5.0–8.0)	0.477
PTH (pg/mL)	519 (420–893)	368 (285–721)	0.171	Platelet ($10^3/\mu L$)	189 (171–252)	155 (132–176)	0.071

Values are expressed as mean±standard deviation, median (1^{st}–3^{rd} quartiles). URR: Ure reduction rate; BMI: Body mass index; PTH: Parathyroid hormone; TSAT: Transferin saturation; MCV: Mean corposcular volume

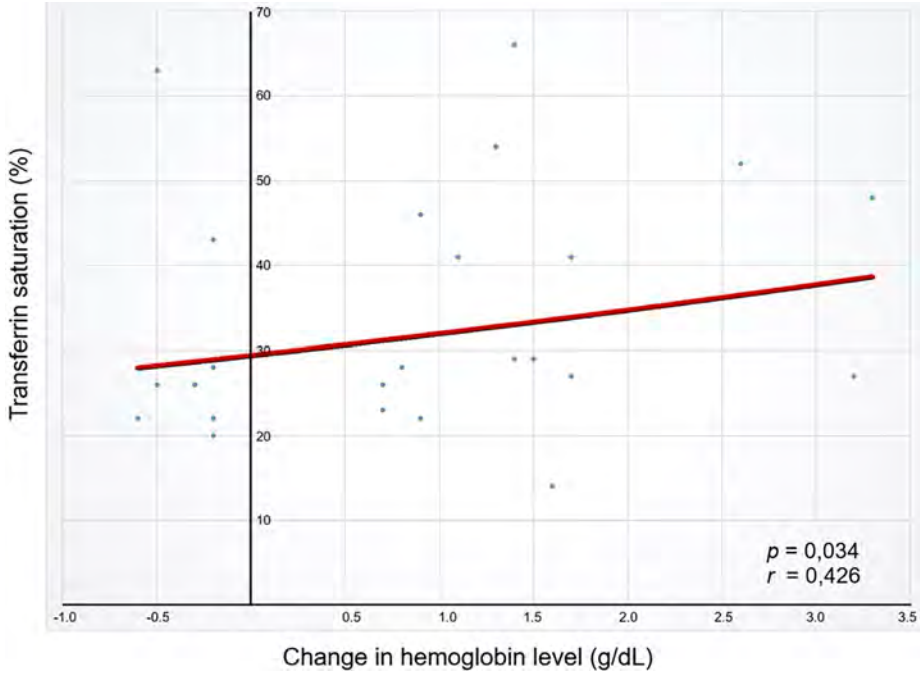

Figure 3. Spearman correlation analysis test revealed the relationship between transferrin saturation and changes in hemoglobin

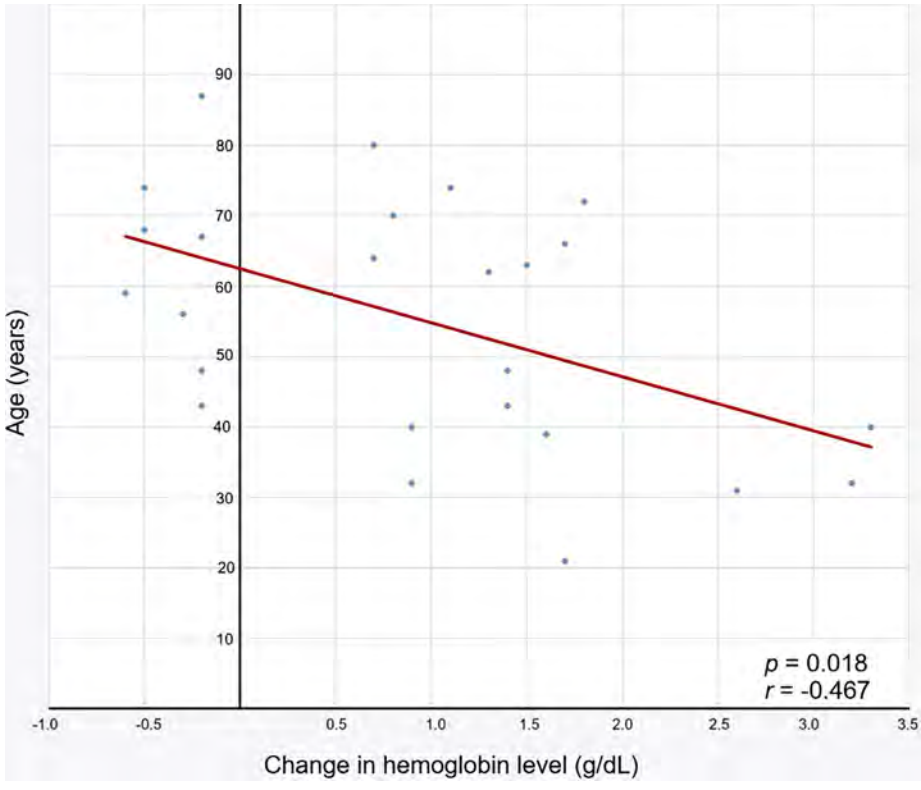

Figure 4. Spearman correlation analysis test revealed the relationship

Criteria for EPO hyporesponsiveness are not well defined. The Kidney Disease Outcomes Quality Initiative (KDOQI) suggests a criterion of inability to achieve a desired Hb concentration using a maximum dose of 450 IU/kg per week intravenous EPO or 300 IU/kg per week subcutaneous EPO.[13] According to data from the United States Renal Data System (USRDS), a study analyzing adult HD patients between 2016 and 2019 reported varying prevalence rates of EPO hyporesponsiveness depending on the definition used. When defined by a high ERI, the prevalence was 22.2%, whereas it ranged from only 2.1% to 6.0% when defined as having a Hb level below 10 g/dL for a duration of 3 to 6 months.[14] A retrospective study analyzing data from 1,934 hemodialysis patients receiving treatment for renal anemia found that the ERI was lower in patients with higher serum albumin levels and higher TSAT levels. In contrast, elevated PTH levels and the use of RAS blockers were associated with increased EPO resistance.[15] In our HD center, the prevalence of EPO hyporesponsiveness anemia was 11.0%.

We analyzed ERI regarding response to roxadustat treatment. Although the average ERI was lower in patients who achieved the target Hb, the difference was not statistically significant. Also, there was no correlation between ERI and Hb changes.

In addition, we determined several laboratory parameters which were associated with roxadustat treatment response. Lower uric acid level, lower predialysis urea level, and higher Kt/V values were observed in patients who achieved target Hb following roxadustat. Furthermore, TSAT percentage prior to treatment was correlated with the change in Hb level following roxadustat treatment.

Peritubular interstitial fibroblast-like cells are the primary source of erythropoietin production in the kidneys. The rapid induction of erythropoietin synthesis is among the earliest and most sensitive physiological responses to hypoxia. The hypoxia-inducible factors (HIFs) regulate the molecular mechanisms linking hypoxia and erythropoiesis. The transcriptional activity of HIFs is primarily managed by their degradation rate, which is controlled by oxygen-sensing enzymes known as prolyl hydroxylase. Under hypoxic conditions, the activity of prolyl hydroxylase enzymes decreases, leading to the accumulation of HIF-α subunits and enhanced HIF transcriptional activity. This, in turn, stimulates the expression of erythropoietin, erythropoietin receptors, and proteins that facilitate intestinal iron absorption and the recycling of iron from macrophage iron stores.[6,16–19]

Recognizing the crucial roles of the HIF-prolyl hydroxylase pathway in regulating erythropoiesis has paved the way for new therapeutic strategies in the management of renal anemia. Roxadustat is a member of oral HIF-PHI. Additionally, roxadustat is now safely used worldwide in the management of anemia in kidney diseases as an alternative to EPO therapy.

Chen et al.[5] evaluated the efficacy of roxadustat in comparison to epoetin alfa in 305 long-term dialysis patients. The study found that roxadustat led to a greater increase in Hb levels from baseline compared to EPO alfa. Additionally, roxadustat was more effective in increasing transferrin and serum iron levels, while also attenuating the decrease in transferrin saturation when compared to EPO alfa. Furthermore, roxadustat was associated with a mean reduction in hepcidin of 30.2 ng/mL, compared to a reduction of only 2.3 ng/mL in the epoetin alfa group. As a result, the authors concluded that oral roxadustat was noninferior to EPO alfa in the anemia treatment.

Although peritoneal dialysis patients generally tend to have higher Hb levels and require lower EPO doses, roxadustat proved effective in the treatment of anemia in these patients, showing non-inferiority to EPO treatment.[20] Additionally, roxadustat improved Hb levels without compromising renal function in kidney transplant recipients with post-transplant anemia.[21] Furthermore, red blood cell (RBC) survival time was significantly longer in HD patients treated with roxadustat (75.5 days) compared to those treated with rHuEPO (65.0 days).[22]

Xu et al.[23] investigated the effect of roxadustat on erythropoietin-hyporesponsive anemia in patients undergoing chronic hemodialysis. The addition of low-dose roxadustat (50 to 70 mg, three times per week) to EPO treatment resulted in an increase in Hb levels after 12 weeks. The mean Hb level rose from 7.7 g/dL to 9.2 g/dL following roxadustat treatment. The Hb response rate was observed to increase by 72%. In our HD center, the roxadustat response rate was 56% in a similar population.

Daprodustat is another member of the HIF-PHI class, and its efficacy was investigated as an anemia treatment in HD patients who were hyporesponsive to rHuEPO. A total of 15 participants were enrolled, with 7 (47%) completing the 16-week treatment regimen. At the 16-week mark, 2 of the 7 subjects (29%) experienced an increase of >1 g/dL in Hb from baseline.[24] In our HD center, 12 patients (48%) experienced an increase of >1 g/dL in Hb from baseline after roxadustat.

When considered in the context of previous research, our findings are consistent with those reported in the literature. One of the key findings of this study is the absence of a statistically significant association between the response to roxadustat treatment and the ERI value. Moreover, in terms of patient numbers, although our sample size may appear small, similar numbers have been reported in studies in the literature conducted on comparable patient groups (HD patients with EPO hyporesponsiveness).

The most important reported adverse effects of roxadustat include thrombotic events (2.9%), liver damage (3.9%), thyroid dysfunction, and hyperkalemia.[25] In our HD center, all patients well tolerated oral roxadustat treatment. No treatment-related complications were observed in the patients throughout the study period.

One of the key limitations of this study is the relatively small sample size, which is attributable to the study being conducted at a single center. Additionally, multiple dosing regimens of roxadustat were not administered, as the retrospective nature of the study limited such variations in treatment. Furthermore, pre-treatment hepcidin levels were not analyzed, which could have offered valuable insights into the potential association between baseline hepcidin status and treatment response. These factors may have limited the depth of interpretation and generalizability of the findings.

CONCLUSION

In conclusion, the current study can be considered a pioneering effort. We aimed to share our experience with this novel treatment option in a challenging patient population. Our findings demonstrate significant treatment success with roxadustat. We believe that our results will provide valuable guidance to clinicians in the management of renal anemia.

Disclosures

Ethics Committee Approval: The study was approved by the Agri Ibrahim Cecen University Ethics Committee (No: 410, Date: 28/11/2024).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The author have no conflict of interest to declare.

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RESEARCH ARTICLE

Preoperative Challenges in Diagnosing Meningioma-like Dural-based Lesions: A Retrospective Dual-center Study

Abdurrahim Tekin[1], Engin Can[1], Ozan Başkurt[2]

[1]Department of Neurosurgery, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[2]Department of Neurosurgery, Memorial Bahçelievler Hospital, İstanbul, Türkiye

ABSTRACT

Objective: This study aimed to evaluate the prevalence of meningioma-like dural-based lesions that were histopathologically diagnosed as non-meningioma tumors, characterize their underlying pathologies, and assess clinical–radiological correlations to improve diagnostic accuracy and patient management.

Materials and Methods: A retrospective dual-center study was conducted, including 210 patients with dural-based lesions resembling meningiomas on MRI between January 2020 and December 2025. Imaging features, histopathological diagnoses, and clinical data were analyzed. Statistical comparisons were performed using univariate and multivariate analyses.

Results: Among the 210 patients, 12.8% (n=27) of lesions initially suspected as meningiomas were histopathologically confirmed as non-meningioma tumors. Metastatic lesions were the most common mimics (63%), followed by high-grade glial tumors (14%), lymphomas (11%), schwannomas (7%), low-grade glial tumors (7%), and primitive neuroectodermal tumors (4%). Homogeneous contrast enhancement and dural tail signs were observed in both meningiomas and their mimics, complicating preoperative diagnosis. Advanced imaging techniques and histopathological examination were critical for accurate differentiation.

Conclusion: A significant proportion of dural-based lesions resembling meningiomas are non-meningioma tumors, with metastatic and high-grade glial neoplasms being the most prevalent. Careful evaluation of imaging features and a multidisciplinary approach, including advanced imaging and histopathological confirmation, are essential for accurate diagnosis and optimal patient management.

Keywords: Differential diagnosis, dural-based lesions, histopathology, intracranial tumors, meningioma, meningioma mimics, MRI

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INTRODUCTION

Meningiomas are among the most common primary intracranial tumors in adults, accounting for 20–30% of brain tumors.[1] These tumors arise from arachnoid cap cells, are typically dural-based, well-circumscribed, slow-growing, and most often benign in nature. Radiologically, meningiomas usually appear isointense on T1-weighted magnetic resonance imaging (MRI), hyperintense on T2-weighted MRI, and tend to enhance homogeneously after contrast administration. In addition, the "dural tail" sign—thickening of the dura surrounding the tumor following contrast enhancement—represents a characteristic imaging feature of meningiomas.[2–4] However, these classic radiological features may overlap with other intracranial pathologies. Metastatic lesions, high-grade superficially located glial tumors, lymphomas, solitary fibrous tumors (SFTs), hemangiopericytomas (HPCs), neurosarcoidosis, and granulomatous infections are among various dural-based lesions that may exhibit radiological findings similar to meningiomas.[5–10] These similarities can lead to misdiagnosis in the preoperative evaluation process and may cause significant clinical challenges in terms of surgical planning and patient counseling.

Address for Correspondence: Abdurrahim Tekin, Department of Neurosurgery, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
E-mail: tekinabdurrahim@gmail.com **ORCID ID:** 0000-0001-5401-1547

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Although advanced imaging techniques (DTI, MR spectroscopy, PET-MR, and perfusion MRI) contribute to the differential diagnosis, in some cases a definitive diagnosis is only possible through histopathological examination.[11–13] Therefore, it is of great importance that every dural-based lesion is evaluated in detail and that the limitations of imaging techniques be kept in mind.

The purpose of this study was to determine the proportion of cases that exhibited classical MRI features of meningioma but were subsequently diagnosed with different histopathological entities, to characterize the non-meningioma pathologies identified, and to evaluate clinical–radiological correlations. The aim was thereby to increase awareness of differential diagnosis among surgeons and radiologists and to improve patient management strategies.

MATERIALS and METHODS

This retrospective, dual-center study included data from 658 patients who underwent surgery for intracranial masses between January 2020 and December 2025 at the Neurosurgery Departments of Kanuni Sultan Süleyman Training and Research Hospital and Memorial Bahçelievler Hospital. The imaging studies of all cases were reviewed to identify features suggestive of meningioma-like lesions. A total of 210 patients who demonstrated dural enhancement resembling the "dural tail" phenomenon adjacent to an extra-axial neoplasm on contrast-enhanced T1-weighted imaging were included in the analysis. For each patient, basic demographic data—including age at surgery, sex, and histopathological diagnosis—were collected from the hospital database.

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Kanuni Sultan Süleyman Training and Research (Approval No: 2025.09.238; Date: 25.09.2025). The requirement for written informed consent was waived due to the retrospective design of the study.

Image Assessment

Imaging was performed using 1.5T scanners, and T1, T2, FLAIR, and gadolinium-enhanced T1 sequences were evaluated. The lesions were assessed in terms of parameters such as size, location, signal characteristics, contrast enhancement pattern, presence of edema, dural tail sign, and bone invasion.

Histopathological Assessment

Pathological examination was performed using hematoxylin–eosin (H&E) staining, and, when necessary, immunohistochemical markers (GFAP, EMA, Ki-67, IDH1-R132H, ATRX, and CD34) were utilized. Glial tumors were graded according to the 2021 World Health Organization (WHO) Classification. In cases of metastatic lesions, the primary focus was identified based on clinical evaluation and systemic screening results.

Data Analysis

The radiological characteristics of the lesions, including size, location, contrast enhancement patterns, signal homogeneity, presence of edema, and bone invasion, were analyzed in detail. Radiological assessments were performed in a blinded manner by an independent radiologist.

Statistical Analysis

A standard descriptive analysis was performed. Where applicable, 95% confidence intervals were calculated using the binomial exact method.

RESULTS

A total of 210 patients with dural-based radiological imaging findings were included in our study. The prevalence of meningioma mimics was found to be 12.8%. The mean patient age was 45.1±20.4 years, and 59.3% of the patients (n=16/27) were female.

According to their locations, the lesions were distributed as follows: parietal region (n=10/27; 37%), frontal region (n=7/27; 26%), temporal region (n=5/27; 19%), posterior fossa (n=3/27; 11%), and occipital region (n=2/27; 7%).

Based on their anatomical classification, the lesions were categorized as convexity (n=17/27; 63%), parasagittal/parafalcine (n=5/27; 19%), skull base (n=2/27; 7%), cerebellopontine (n=2/27; 7%), and spheno-orbital (n=1/27; 4%) (Table 1).

The majority of meningioma-like dural-based masses were metastases (17/27; 63%), comprising 6 breast, 5 lung, 2 gastric, 1 malignant melanoma, 1 papillary thyroid, 1 prostate, and 1 chondrosarcoma. These were followed by lymphomas (3/27; 11%), high-grade glial tumors (4/27; 15%), low-grade glial tumors (2/27; 7%), schwannomas (2/27; 7%), and primitive neuroectodermal tumor (1/27; 4%).

In preoperative MRI imaging of patients with a pathological diagnosis of metastasis, homogeneous contrast enhancement was observed in 10 patients (10/17; 59%), and dural tail-like dural thickening was present in 6 patients (6/17; 35%). In preoperative MRI imaging of patients with a non-metastatic pathological diagnosis, homogeneous contrast enhancement was observed in 8 patients (8/10; 80%),

Table 1. Demographic and anatomical characteristics of patients with non-meningioma dural-based lesions

Variable	Non-meningioma lesions (n=27)	
	n	%
Age (years), mean±SD	45.1±20.4	
Sex, female/male	16/11	
Lesion location		
Parietal region	10	37
Frontal region	7	26
Temporal region	5	19
Posterior fossa	3	11
Occipital region	2	7
Anatomical classification		
Convexity	17	63
Parasagittal/parafalcine	5	19
Skull base	2	7
Cerebellopontine	2	7
Spheno-orbital	1	4

Data are presented as mean±standard deviation or n (%). SD: Standard deviation

Table 2. Radiological and histopathological characteristics of non-meningioma dural-based lesions

Parameter	Non-meningioma lesions (n=27)	
	n	%
Histopathological diagnosis		
Metastasis	17	63
High-grade glial tumor	4	14
Lymphoma	3	11
Schwannoma	2	7
Low-grade glial tumor	2	7
PNET	1	4
MRI characteristics		
Homogeneous enhancement	16	59
Dural tail sign	10	37
Bone invasion	4	15
Peritumoral edema	14	52
Irregular margins	12	44
Multiple lesions	6	22

Percentages are calculated based on the non-meningioma subgroup.
PNET: Primitive neuroectodermal tumor; MRI: Magnetic resonance imaging

dural tail-like dural thickening was present in 4 patients (4/10; 40%), and bone involvement was observed in 2 patients (2/10; 20%) (Table 2). Representative preoperative MRI images of a 37-year-old female patient with invasive ductal breast carcinoma are shown (Figs. 1, 2).

DISCUSSION

This study demonstrates that a significant portion of dural-based contrast-enhancing lesions resembling meningiomas on preoperative MRI are histopathologically non-meningioma tumors. The prevalence of meningioma-like lesions in our series was 12.8%, which is higher than the 7.2% reported by Yamaki et al.[11] This discrepancy may be attributed to our broader inclusion criteria encompassing all dural-based contrast-enhancing lesions, thereby reflecting a wider clinical spectrum.

Metastatic tumors represented the most common meningioma-like masses in our series, accounting for 63% of cases, which aligns with the predominance of breast and lung metastases described by Alali et al.[14] regarding dural invasion and meningioma-like appearance. Moreover, the ability of metastases to exhibit homogeneous contrast enhancement and dural tail signs in 44% of patients further complicates differential diagnosis.[15]

While Alali et al.[14] proposed a diagnostic scoring system to distinguish dural metastases from meningiomas based on imaging criteria, our dual-center design with histopathological confirmation provides real-world validation of these challenges, emphasizing the practical limitations of imaging-based differentiation. As noted by Laidlaw et al.,[16] such radiologic overlap can lead to significant diagnostic pitfalls during preoperative evaluation and surgical decision-making.

In our study, glioblastomas and other high-grade glial tumors were observed in 14% of dural-based masses. This rate is consistent with observations by Romano et al.,[17] who reported that superficially located glial tumors can contact the dura and mimic meningiomas. The potential for high-grade glial tumors, such as glioblastomas, to be mistaken for meningiomas is critically important for prognosis and treatment planning. The large sample size, dual-center design, and histopathological confirmation in our study support these observations, highlighting the importance of careful imaging evaluation and a multidisciplinary approach in clinical practice.

In practice, this multidisciplinary workflow can be implemented through regular joint reviews among radiologists, neurosurgeons, and pathologists for atypical dural lesions. Establishing standardized imaging checklists for meningioma mimics, ensuring histopathological confirmation in

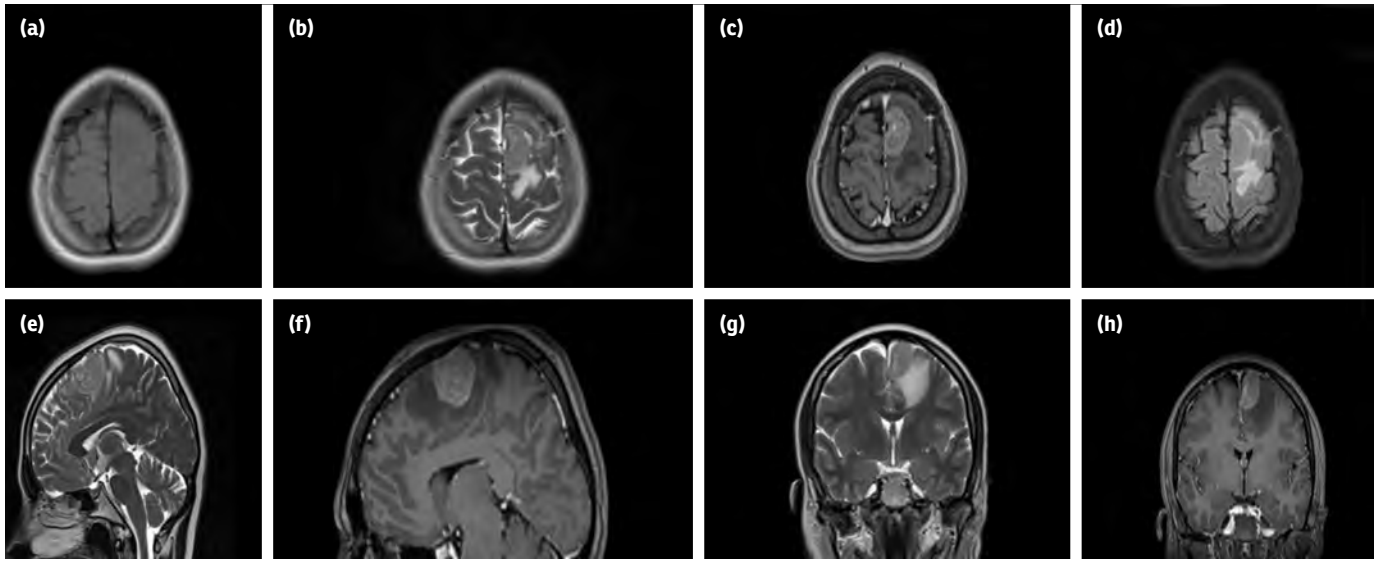

Figure 1. MRI characteristics of a dural-based metastatic lesion mimicking meningioma in a 37-year-old female patient with a history of invasive ductal breast carcinoma. **(a)** Axial T1-weighted image showing an isointense dural-based lesion. **(b)** Axial T2-weighted image demonstrating mild hyperintensity. **(c)** Contrast-enhanced T1-weighted axial image revealing homogeneous enhancement. **(d)** Axial FLAIR image showing perilesional edema. **(e)** Sagittal T2-weighted section displaying dural attachment. **(f)** Sagittal contrast-enhanced T1-weighted image showing a prominent dural tail sign. **(g)** Coronal T2-weighted image illustrating hyperintensity and dural continuity. **(h)** Coronal contrast-enhanced T1-weighted image confirming homogeneous enhancement

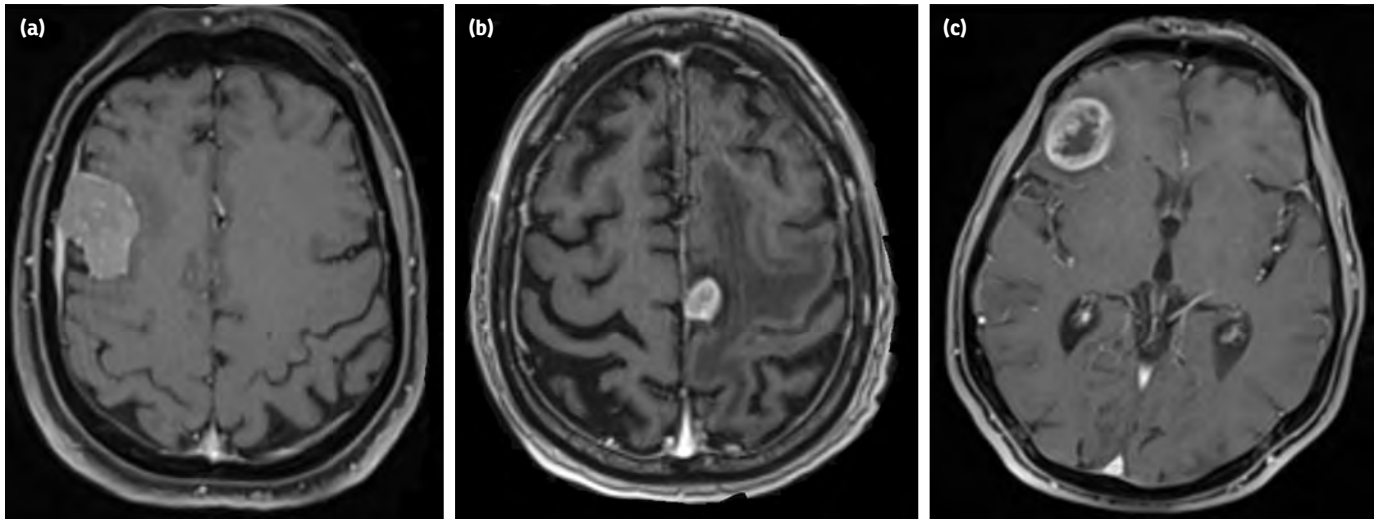

Figure 2. Representative MRI images of dural-based lesions mimicking meningioma. **(a)** Typical convexity meningioma showing a well-defined extra-axial mass with homogeneous contrast enhancement and a broad dural attachment. **(b)** Adenocarcinoma metastasis exhibiting focal dural involvement and intense enhancement, resembling meningioma on preoperative MRI. **(c)** Glioblastoma presenting with irregular ring enhancement, perilesional edema, and indistinct dural interface, mimicking meningioma radiologically

ambiguous cases, and conducting systemic screening when metastasis is suspected may further improve diagnostic accuracy and patient outcomes.

Lymphomas were represented by three cases in our series. As reported by Karschnia et al.,[18] primary central nervous system lymphomas can rarely present on the dural surface

and be mistaken for meningiomas. In our series, cases preoperatively diagnosed as meningiomas but histopathologically confirmed as lymphomas were identified. This finding underscores the indispensable role of biopsy in establishing a definitive diagnosis.

Schwannomas and low-grade glial tumors constituted a smaller group (7%) in our study. Additionally, a single case of primitive neuroectodermal tumor was identified. Although rare, these tumors can mimic meningiomas.

Our study demonstrates that many lesions resembling meningiomas, particularly metastatic and glial neoplasms, receive different histopathological diagnoses. Therefore, MRI findings alone are insufficient. Careful evaluation of parameters such as contrast enhancement patterns, signal homogeneity, presence of edema, and bone involvement can enhance diagnostic accuracy. Additionally, advanced imaging techniques such as MR spectroscopy, diffusion tensor imaging, and PET-MR may provide potential contributions to distinguishing meningiomas from their mimics. However, real-world clinical adoption remains limited by availability, protocol variability, and lack of standardization. A pragmatic approach would prioritize MR spectroscopy and perfusion MRI when conventional features are equivocal, reserving PET-MR for cases with suspected receptor-positive meningioma or systemic disease.[5,19,20]

Strengths and Limitations of the Study

The strengths of this study include its dual-center design, large patient cohort, and histopathological confirmation of all cases. However, the retrospective design introduces certain limitations. In particular, the heterogeneous patient population and the lack of advanced imaging modalities in all cases were limiting factors in differential diagnosis. Incomplete follow-up data in some patients may have affected the longitudinal assessment of outcomes. In addition, the inclusion of surgically treated cases may have introduced patient selection bias, potentially inflating the proportion of aggressive or symptomatic pathologies. Heterogeneity in MRI scanner models and acquisition parameters across the two centers could also have influenced image interpretation and feature visibility. Finally, the distribution of histopathological subtypes was imbalanced, which may limit the precision of subgroup comparisons and the generalizability of our findings.

CONCLUSION

This study shows that a significant portion of dural-based contrast-enhancing lesions resembling meningiomas are histopathologically non-meningioma tumors. In our series, the prevalence of non-meningioma pathologies was 12.8%, with metastatic tumors and high-grade glial neoplasms being the most common. Many of these tumors exhibit classic meningioma features, such as homogeneous contrast enhancement and dural tail-like signs, which pose significant challenges in preoperative diagnosis. Adopting a multidisciplinary approach, particularly for metastatic and high-grade glial tumors, will improve patient management and contribute to accurate surgical planning and prognosis determination.

Future prospective multicenter studies are warranted to validate and expand upon these findings using standardized MRI protocols across sites. Such studies should incorporate quantitative scoring systems and perform external validation to assess diagnostic performance in independent cohorts. Evaluating clinical impact—such as changes in preoperative decision-making, time-to-treatment, and cost-effectiveness—will clarify how advanced imaging augments routine practice.

Disclosures

Ethics Committee Approval: The study was approved by the Kanuni Sultan Süleyman Training and Research Hospital Ethics Committee (No: 2025.09.238, Date: 25/09/2025).

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RESEARCH ARTICLE

Evaluation of Pain and Quality of Life in Patients with Pelvic Congestion Syndrome Treated with Endovascular Plug Embolization

Fatma Tuğba İlal Mert[1], Gözde Altun[2]

[1]Department of Cardiovascular Surgery, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[2]Department of Anesthesiology and Reanimation, İstanbul University-Cerrahpaşa, Institute of Cardiology, İstanbul, Türkiye

ABSTRACT

Objective: Pelvic congestion syndrome (PCS) is usually encountered in female patients of reproductive age. Medical and endovascular interventions are used in the treatment. This study aimed to evaluate the effects of endovascular plug embolization on pain and quality of life in patients diagnosed with PCS.

Materials and Methods: In this retrospective study, 36 patients diagnosed with PCS and who underwent embolization of ovarian veins with the plug method between June 2023 and March 2024 were analyzed. All information such as age, BMI (body mass index), site and side of pain, medical treatments, comorbidities, time between onset of pain and endovascular intervention, accompanying symptoms, positions in which pain increased, and clinics consulted during the diagnostic process were recorded. NRS-11 (Numeric Rating Scale-11) and SF-12 (Short Form-12) scores were recorded before, and one and three months after, the endovascular procedure.

Results: The mean age of the patients was 39.5±8.2 years, and the mean duration of pain was 49.6±32.28 months. Compared to the pre-procedural baseline, the NRS score significantly decreased from 9.3 to 2.06, indicating substantial pain relief. The MCS-12 (Mental Component Summary-12) scores increased from 27.5 to 32.4, reflecting an improvement in patients' mental quality of life. Similarly, PCS-12 (Physical Component Summary-12) scores rose from 26.2 to 47.5, demonstrating enhanced physical quality of life. At the 3-month follow-up, statistical analysis of NRS and SF-12 scores confirmed a significant reduction in pain and an increase in quality of life ($p<0.001$).

Conclusion: Endovascular plug embolization is an effective and safe method in patients with PCS. Endovascular plug embolization in patients with PCS resulted in significant pain reduction and notable improvement in both mental and physical quality of life within three months post-procedure.

Keywords: Chronic pain, pelvic congestion syndrome, pelvic pain, plug embolization

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INTRODUCTION

Pelvic congestion syndrome (PCS) is predominantly observed in women of reproductive age and is characterized by abdominal and pelvic pain, accompanied by a sensation of fullness in the perineal and vulvar regions. Patients often report dysmenorrhea, dyspareunia, postcoital pain, urinary discomfort, and, less commonly, hematuria. Low back and hip pain may also be present. The pain typically worsens when standing and improves when lying down. PCS represents one of the causes of chronic pelvic pain (CPP), with symptoms persisting for more than six months and occurring independently of the menstrual cycle. Although the precise etiopathogenesis of PCS remains unclear, it is recognized that ovarian vein dilation is a hallmark of the condition. Disorders associated with abnormalities in the pelvic venous system, such as those observed in PCS, are currently classified under the broader category of "pelvic venous disorders."[1–3] There is currently no universally established diagnostic standard for PCS. Al-

Address for Correspondence: Gözde Altun, Department of Anesthesiology and Reanimation, İstanbul University-Cerrahpaşa, Institute of Cardiology, İstanbul, Türkiye
E-mail: gozde.altun@iuc.edu.tr **ORCID ID:** 0000-0002-6025-944X

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though clinical suspicion can guide initial assessment, catheter-based venography remains the definitive diagnostic modality. For situations in which non-invasive evaluation is preferred, a key ultrasonographic criterion is the presence of ovarian vein dilatation greater than 6 mm, detectable via either transvaginal or transabdominal ultrasonography. This finding is considered one of the most reliable indicators of PCS in imaging studies.[1,4,5]

Significant advancements have occurred in the management of PCS in recent years. Since the 1980s, therapeutic strategies have evolved widely, encompassing both pharmacological and surgical approaches. In the early 2000s, laparoscopic interventions became less favored due to potential complications, including nerve injury and hemorrhage. Currently, minimally invasive procedures are considered the standard of care. Endovascular techniques, such as sclerosing agents, foam sclerotherapy, and plug or coil embolization–either used individually or in combination—are commonly employed. Evidence indicates that these approaches are both highly effective and associated with low rates of adverse events.[6–8] Despite advancements in treatment, PCS patients frequently experience delayed diagnosis, often after multiple consultations in urology and gynecology clinics. This delay may result in unnecessary interventions, prolonged pain, and increased economic and productivity losses. Chronic pain associated with delayed recognition also contributes to both physical and psychological impairments. Endovascular plug embolization represents a minimally invasive intervention that allows same-day discharge, yet literature on its use remains limited compared to coil embolization.[9]

This study aimed to evaluate the effects of endovascular plug embolization on pain and quality of life in patients diagnosed with PCS.

MATERIALS and METHODS

The ethics committee approval from the University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital (KAEK/2024.03.52, 27/03/2024) was obtained for the study. The study was conducted in accordance with the Declaration of Helsinki. The study was registered in clinicaltrials.gov with the number NCT06553014.

Our study is single-center and retrospective. We did not perform a formal sample size calculation prior to data collection. Our sample size (n=36) was determined by the number of cases within the defined time period and the service capacity of our institution. We presented our findings with p-values; we interpreted our analysis as exploratory/hypothesis-generating in nature. We included all consecutive patients who underwent endovascular "plug" embolization for PCS at our institution between June 2023 and March 2024 and who met the eligibility criteria.

Patients older than 18 years who presented with abdominopelvic pain with an numeric rating scale-11 (NRS-11) score of ≥5 lasting for more than six months and who had ovarian vein dilatation greater than 6 mm on transvaginal or transabdominal ultrasonography (USG) were included in the study.

Patients with leiomyoma, pelvic inflammatory disease, endometriosis, postoperative adhesions, a history of urologic or gynecologic surgery, end-stage renal disease, allergy to drugs used during the endovascular plug procedure, May-Thurner syndrome, Nutcracker syndrome, a history of abdominopelvic trauma or malignancy, a history of radiotherapy or chemotherapy, or known psychiatric illness were excluded. Additionally, patients who were pregnant or breastfeeding, or those diagnosed with fibromyalgia, lumbar disc herniation, scoliosis, facet syndrome, sacroiliac dysfunction, genitourinary, or gastrointestinal diseases were also excluded. Patients with missing data or those who refused to participate in the study were not included in the analysis.

The study included 36 patients who met the inclusion and exclusion criteria. The flow diagram of the patients included in the study is presented as Figure 1.

All ultrasonographies were performed by the same radiologist with at least 10 years of experience. A single ultrasound device (Esaote, Mylab X7, Genova, Italy) was used in this study.

Demographic and clinical information about the patients and the procedure was recorded in the database: Age, body

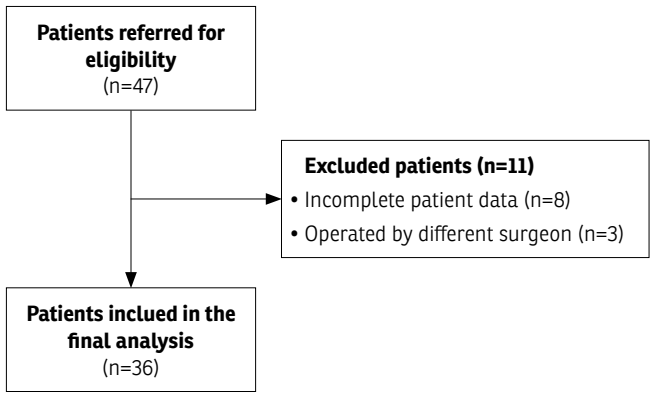

Figure 1. Flow chart of the patients

mass index (BMI), site of pain (perineum, vulva, labia majora/minor, hypogastrium, inguinal region, hip, lower back, leg) and side, past medical treatments, comorbidities, the time between the onset of pain and endovascular intervention, accompanying symptoms (feeling of heaviness in the perineum, swelling in the labia majora, dysuria, hematuria, dyspareunia, postcoital pain, dysmenorrhea, frequent urination), information on the position in which the pain increases (lying/standing/sitting), presence or absence of varicose veins in the lower extremity, need for a repeat procedure, vein entered during endovascular intervention, vein embolized, type of embolotherapy, duration of procedure (minutes), cumulative radiation exposure during the procedure (mGy-cm²). Complications (vessel perforation/hematoma/phlebitis/embolism/migration/dyspnea/panic attack/allergic reaction/infection) were recorded and evaluated according to the Society of Interventional Radiology (SIR) classification. In treatment planning for PCS, established guidelines and consensus statements from the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) and the Society of Interventional Radiology (SIR) were carefully considered and incorporated.

The NRS-11 and short form-12 (SF-12) scores were used to assess pain and functionality before, 1, and 3 months after the endovascular procedure, and the results were recorded. The patients' NRS-11 and SF-12 scores, as documented during their 1st- and 3rd-month postprocedural follow-up examinations conducted by the same physician, were reviewed and recorded.

Intervention

All patients were taken to the procedure room and monitored with a 5-lead electrocardiogram (ECG), pulse oximetry, and blood pressure. Intravenous access was established in the forearm. The procedure was performed as an outpatient procedure with moderate sedation using midazolam 0.02–0.07 mg/kg (Zolamid ampul, 5 mg/ml, Vemilaç, Türkiye), fentanyl 1–2 µg/kg (Talinat ampul, 0.5 mg/10 ml, Vemilaç, Türkiye), and local anesthesia (5.0–10.0 mL of 0.5% lidocaine solution, Lidon ampul, 100 mg/5 ml, Onfarma, Türkiye). Venous access was obtained by ultrasound-guided right internal jugular or right femoral vein access with a 6F introducer sheath. First, the left renal vein was selectively catheterized with 5F macro-catheters advanced over a 0.035 hydrophilic wire. Venography was performed to evaluate ovarian vein reflux and to rule out hemodynamically significant renal vein compression. A venography image was obtained under the Valsalva maneuver. If left ovarian vein reflux was evident, the left ovarian vein was selectively catheterized, and venography was performed to visualize it from the renal vein separation to the most distal part (Fig. 2). Left ovarian embolization was performed after confirmation of valve regurgitation, filling of the pelvic venous reservoir, and elimination of contrast stagnation within the reservoir. The embolization material to be used was determined according to the diameter and width of the venous structure. Plugs ranging in size from 10 mm to 18 mm, selected according to the diameter of the vein, were delivered with a micro-delivery catheter, and the plugs placed into the lumen from the most distal to the proximal were allowed to open in the lumen (Fig. 3). Intermittent venography was performed to ensure adequate placement of plugs, and the absence of distal filling was clearly demonstrated. Subsequently, catheterization of the internal iliac veins and digital subtraction venography via a balloon occlusion catheter was performed. In this way, the remaining filling of the pelvic

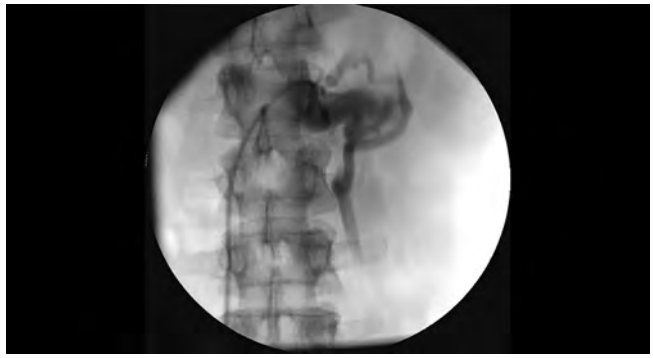

Figure 2. Contrast injection through the left renal vein following right femoral venous catheterization demonstrates distal reflux

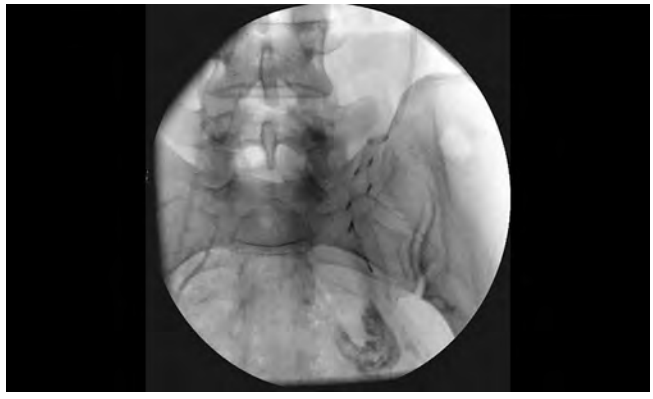

Figure 3. Plug embolization procedure performed in the left ovarian vein

Figure 4. Following plug embolization, contrast injection demonstrates no distal reflux into the left ovarian vein

reservoir was evaluated, and the need for additional embolization was determined (Fig. 4). None of the patients included in our study underwent embolization to a vein other than the ovarian vein. After the procedure, patients were monitored for 2 hours. Patients who did not develop any complications were discharged from the hospital on the same day with the necessary recommendations.

Pain and Quality of Life Assessment

1. Numeric Rating Scale-11 (NRS-11): It is a numerical scale in which patients rate their pain between 0 (no pain at all) and 10 (the most severe pain they have ever felt in their life).[10]

2. Short Form-12 (SF-12): It is a scale by which patients' quality of life is evaluated. Short Form-12 is a shortened version of Short Form-36. In SF-12, the patient's general health status, physical and mental status, quality of life, and social activities are questioned. This scale has mental component summary (MCS-12) and physical component summary (PCS-12) components. It is scored between 0 and 100. A high score is associated with a good general health status.[11,12] (Table 1).

Statistical Analysis

All analyses were performed using IBM SPSS Statistics v22 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as counts (%). Continuous variables were examined for distribution characteristics using Q–Q plots and Shapiro–Wilk tests; findings were reported as mean ± SD and median (min–max). For NRS-11, PCS-12, MCS-12, and SF-12, the primary within-subject factor was time, consisting of three levels (pre-treatment, 1 month, 3 months). A one-way repeated-measures ANOVA was performed for each outcome; the sphericity assumption was assessed using the Mauchly test. Effect sizes were reported as partial η^2 for the omnibus time effect. In cases of sphericity violation, Greenhouse–Geisser ($\varepsilon \leq 0.75$) or Huynh–Feldt ($\varepsilon > 0.75$) corrections were applied to degrees of freedom. When normality or outlier checks showed significant deviation, results were confirmed using the nonparametric Friedman test. For pairwise comparisons between time points, the Bonferroni-corrected test was used under parametric conditions. All tests were two-tailed, and the statistical significance level was set at α=0.05. The internal consistency of the SF-12 is ideally assessed at the item level using Cronbach's alpha. In this retrospective dataset, the SF-12 was only archived as summary scores (PCS-12, MCS-12), so α could not be calculated at the item level. In this context, the alpha values reported in published validity-reliability studies for the SF-12 (Turkish validation)[11] were used as a reference, and this limitation of our study was noted.

RESULTS

The study included 36 patients. The mean and median ages of the patients were 39.5±8.2 and 38 years, while the mean and median BMI values were 25.27±2.78 and 24.9, respectively. The mean procedure time was 27 minutes, with an average cumulative radiation dose of 4567 mGy·cm² measured during fluoroscopy (Table 2).

Chronic diseases were present in 25% of the patients. A history of medical treatment was present in 22.2% of the patients (Table 2).

The distribution of pain, accompanying symptoms, positions exacerbating pain, and menstrual cycle disturbances–including dysmenorrhea–were found to vary significantly among patients. Furthermore, patients had a history of consultations across multiple medical specialties prior to undergoing the procedure (Table 2). Varicose veins in the lower extremities were present in 77.8% of the patients, and hemorrhoids were present in 2.8%. Complications developed in 22.2% of patients (Table 2).

Time-dependent within-subject effects were significant for all outcomes (ANOVA with repeated measures, GG-corrected), and large effect sizes were found for pain and overall quality of life, and moderate effect sizes for mental health: partial η^2=0.959 (NRS-11), 0.835 (PCS-12), 0.798 (SF-12 total), and 0.211 (MCS-12). Pairwise comparisons confirmed this pattern: the NRS-11 score was 9.36±0.83 before treatment, 2.51±1.87 at 1 month, and 2.06±1.51 at 3 months (pre vs 1 month $p<0.001$, pre vs 3 months $p<0.001$, 1 vs 3 months $p=0.04$). PCS-12 increased at 1 and 3 months compared to baseline and showed an additional increase between 1 and 3

Table 1. Short Form-12 parameters

Scales	Item no	Contents	Response categories
Physical Component Summary (PCS-12)	1	General health	Excellent/very good/good/fair/poor
	2	Moderate activities	Limited a lot/limited a little/not limited at all
	3	Climb several flights of stairs	Limited a lot/limited a little/not limited at all
	4	Accomplished less (physical)	All of the time/most of the time/some of the time/ a little of the time/none of the time
	5	Limited in kind of work	All of the time/most of the time/some of the time/ a little of the time/none of the time
	8	Pain—interference	Not at all/a little bit/moderately/quite a bit/ extremely
Mental Component Summary (MCS-12)	6	Accomplished less (emotional)	All of the time/most of the time/some of the time/ a little of the time/none of the time
	7	Did work less carefully	All of the time/most of the time/some of the time/ a little of the time/none of the time
	9	Calm and peaceful	All of the time/most of the time/some of the time/ a little of the time/none of the time
	10	Energy or vitality	All of the time/most of the time/some of the time/ a little of the time/none of the time
	11	Downhearted and blue	All of the time/most of the time/some of the time/ a little of the time/none of the time
	12	Social limitations	All of the time/most of the time/some of the time/ a little of the time/none of the time

months (all p<0.001, 1 vs. 3 months p=0.002). MCS-12 showed a delayed but significant improvement (omnibus p=0.002): pre vs. 1st month p=0.11, pre vs. 3rd month p=0.003, 1st vs. 3rd month p=0.001. The SF-12 total score showed a steady increase compared to baseline in both follow-ups and in the 1–3 month comparison, all p<0.001 (Table 3).

While the mean NRS score was 9.36 before the procedure, it was 2.5 at the end of the 1st month and 2.06 at the end of the 3rd month (Fig. 5).

While the mean MCS-12 score was 27.5 before the procedure, it was 30.33 at the end of the first month and 32.42 at the end of the third month (Fig. 6).

While the mean PCS-12 score was 26.22 before the procedure, it was 44.61 at the end of the 1st month and 47.56 at the end of the 3rd month (Fig. 7).

DISCUSSION

In our study, we examined the demographic characteristics of PCS patients, the type and anatomical localization of their pain, and the effects of plug embolization on pain levels and quality of life. The study demonstrated a significant reduction in pain intensity and a marked improvement in quality of life, as evidenced by decreased NRS and increased SF-12 (PCS and MCS) scores at the 1st and 3rd months after the procedure. The mean NRS score decreased from 9.36 pre-procedure to 2.06 at the 3rd month, while PCS-12 and MCS-12 scores improved substantially over the same period. The procedure was performed safely with a short mean duration (27 minutes) and a low complication rate (22.2%), indicating both clinical effectiveness and procedural safety.

PCS is an important cause of CPP in middle-aged premenopausal women. Although multiple pregnancies or changes in estrogen hormone levels have been thought to be involved in its etiopathogenesis, the cause has not been fully elucidated.[13] In our study, 86.1% of the patients were multiparous, and the mean age was 38 years. The relationship of PCS with menstruation has not been shown.[14] In our study, 63.9% of the patients had normal menstrual cycles. Patients with menorrhagia, metrorrhagia, or dysmenorrhea were in the minority.

Embolization was first performed in the treatment of PCS in 1993.[3,15] First, sclerotherapy was applied, and then coil embolization was performed. Sclerosing agents such as polidocanol and sodium tetradecyl sulfate are available.

Table 2. Sociodemographic data and clinical features of the patients (n=36)

Descriptive data	Mean±SD	Median (min-max)
Age (year)	39.5±8.2	38 (23–59)
BMI (kg/m^2)	25.27±2.78	24.9 (20–33.2)
Duration of pain (months)	49.6±32.28	36 (6–132)
Duration of fluoroscopy (minutes)	27.3±8.2	27 (10–44)
Radiation exposure (mGy-cm^2) (Cumulative)	4413.2±1441.5	4567 (1956–7660)

	n	%
Chronic diseases +	10	27.8
Type of chronic disease		
Anemia	3	8.3
Asthma	1	2.8
DM	1	2.8
FMF	1	2.8
Gastritis	1	2.8
HT	1	2.8
Hypothyroidism	2	5.6
Medical treatment +	8	22.2
Type of medical treatment		
Antihypertensive	1	2.8
Bronchodilator	1	2.8
Iron	2	5.6
Insulin	1	2.8
Colchicine	1	2.8
Levothyroxine	2	5.6
Site of pain		
Vagina	20	55.6
Groin	28	77.8
Hip	23	63.9
Back	15	41.7
Lower abdomen	16	44.4
Anus	9	25
Perineum	14	38.9

	n	%
Site of pain		
Lumbar region	17	47.2
Vulva	9	25
Position increasing pain		
Lying down	4	11.1
Standing	36	100
Sitting	11	30.6
Symptoms associated with pain		
Dyspareunia	28	80
Urgency	11	31.4
Postcoital pain	31	88.6
Dysuria	2	5.6
Clinic visited		
Gynecology	35	97.2
Urology	20	55.6
Cardiovascular	13	36.1
Gastroenterology	2	5.6
Varicose vein at the lower extremity	28	77.8
Menstruation		
Dysmenorrhea	2	5.6
Menometrorrhaga	2	5.6
Menorrhagia	4	11.1
Normal	23	63.9
Post-menauposal	5	13.9
Hemorrhoids+	19	52.8
Parity		
Multiparous	31	86.1
Uniparous	5	13.9
Complication during procedure+	8	22.2
Complications related with the procedure		
Dyspnea	2	5.6
Panic attack	5	13.9
Vasovagal reflex	1	2.8

SD: Standard deviation; BMI: Body mass index; DM: Diabetes mellitus; FMF: Familial mediterranean fever; HT: Hypertension

Polidocanol is available in foam and liquid forms, but the foam form is thought to be more effective. Ethanolamine is thought to create a large foam area in the vascular intima. Inflammation in the endothelium and the release of neuromediators result in fibrosis and occlusion in venous vessels.[14,16] Studies on the agents used have shown that most methods have similar efficacy and safety, high treatment success (>90%), and low complication rates.[17–19] In our study, only the plug embolization method was used, and the NRS scores of the patients decreased from 9.3 before the procedure to 2.03 at the end of the third month. With the plug method, 100% of the patients had a 50% or more reduction in NRS scores. This result shows that the procedure was successful.

Table 3. Comparison of the NRS-11 and SF-12 Scores at different time intervals

	Pre-procedure (pre) Mean±SD	1st month Mean±SD	3rd month Mean±SD	p†	p†† Pre vs 1st month, Pre vs 3rd month, 1st month vs 3rd month
NRS-11	9.36±0.83	2.5±1.87	2.06±1.51	**<0.001**	**<0.001 <0.001 0.04**
MCS-12	27.5±4.82	30.33±8.22	32.42±8.24	**0.002**	0.11 **0.003 0.001**
PCS-12	26.22±7.64	44.61±3.69	47.56±1.89	**<0.001**	**<0.001 <0.001 0.002**

†: Repeated ANOVA test; ††: Post Hoc-Bonferroni test. SF-12: Short form-12; SD: Standard deviation; NRS-11: Numeric rating scale-11; MCS-12: Mental component summary-12; PCS-12: Physical component summary-12

In the study by De Gregorio et al.,[20] the plug method was compared with the plug+polydocanol combination, and both treatment methods were found to be 100% effective. In the same study, it was observed that embolization with different methods provided significant improvement in pain scores determined by VAS (visual analog scale) at the 12-month follow-up in patients with PCS. Therefore, it was concluded that embolization was a highly effective treatment method. While the mean fluoroscopy time in this group was 25.4 minutes, it was found to be 34 minutes in patients who underwent plug+polidocanol foam sclerotherapy. In total, the mean fluoroscopy time was calculated as 27.3 minutes. The decrease in the duration of the procedure, the absence of major complications during the procedure, and the significant improvement in patient complaints in the follow-up of the patients reveal the effectiveness of plug embolization.

In a review by Hansrani et al.[21] evaluating 13 studies, the pain level in patients was evaluated with the VAS score, and it was concluded that the endovascular method was highly effective. In our study, SF-12 was used, and quality of life was evaluated in detail. To the best of our knowledge, our study is the first study in this patient group in which a detailed mental and physical evaluation was performed together with pain scores. In this study, the plug method was used

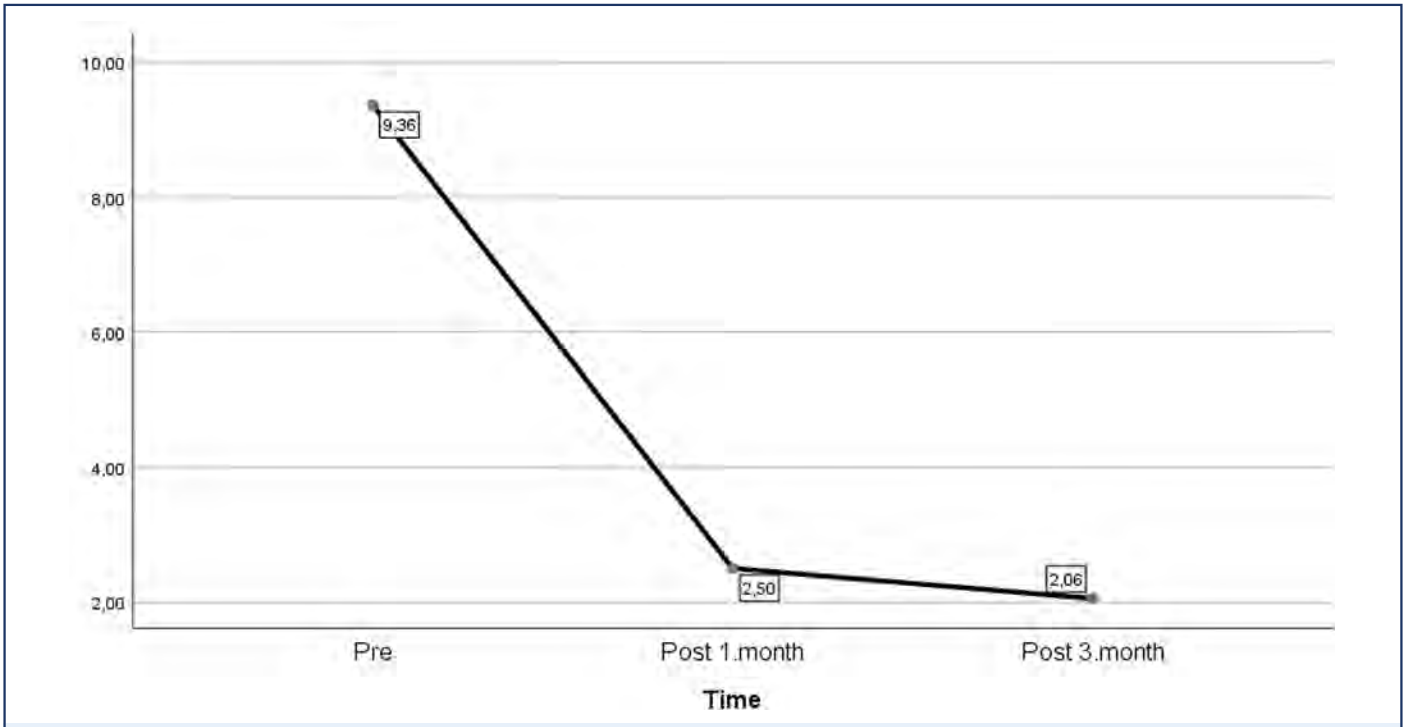

Figure 5. Graph demonstrating the change in the NRS-11 Scores at different time intervals

NRS-11: Numeric rating scale-11

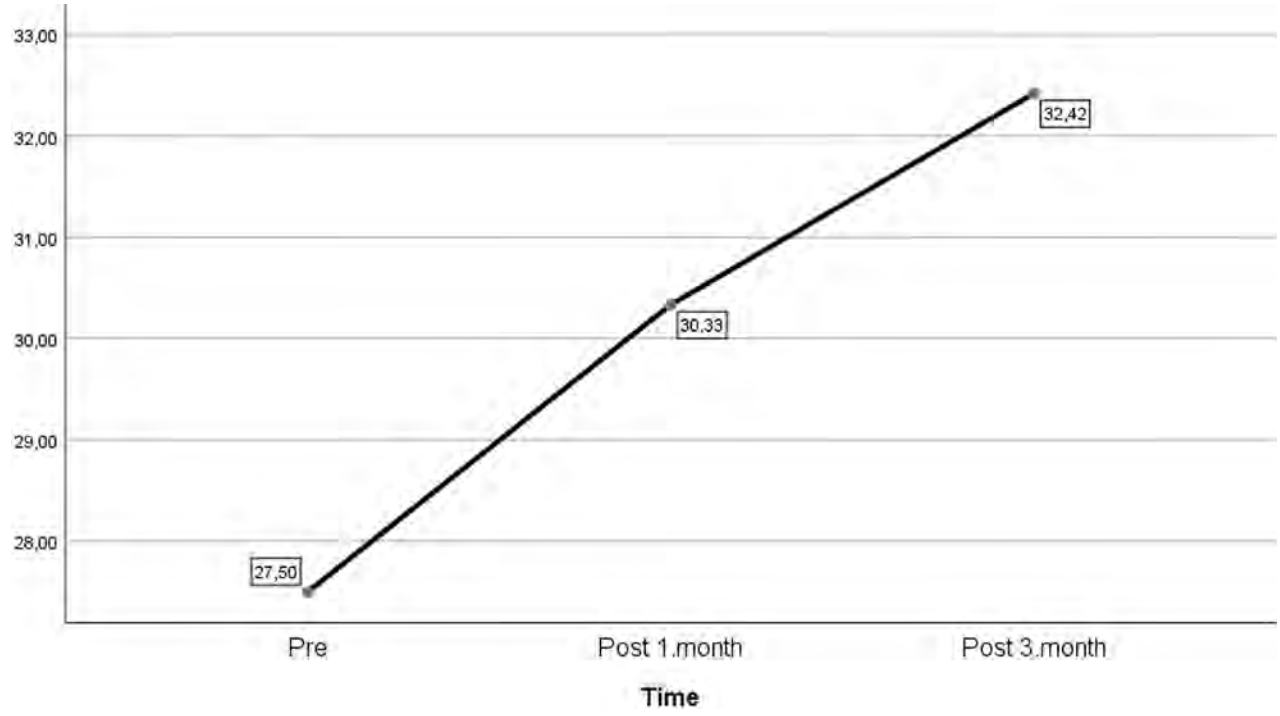

Figure 6. Graph demonstrating the change in the MCS-12 Scores at different time intervals

MCS-12: Mental component summary-12

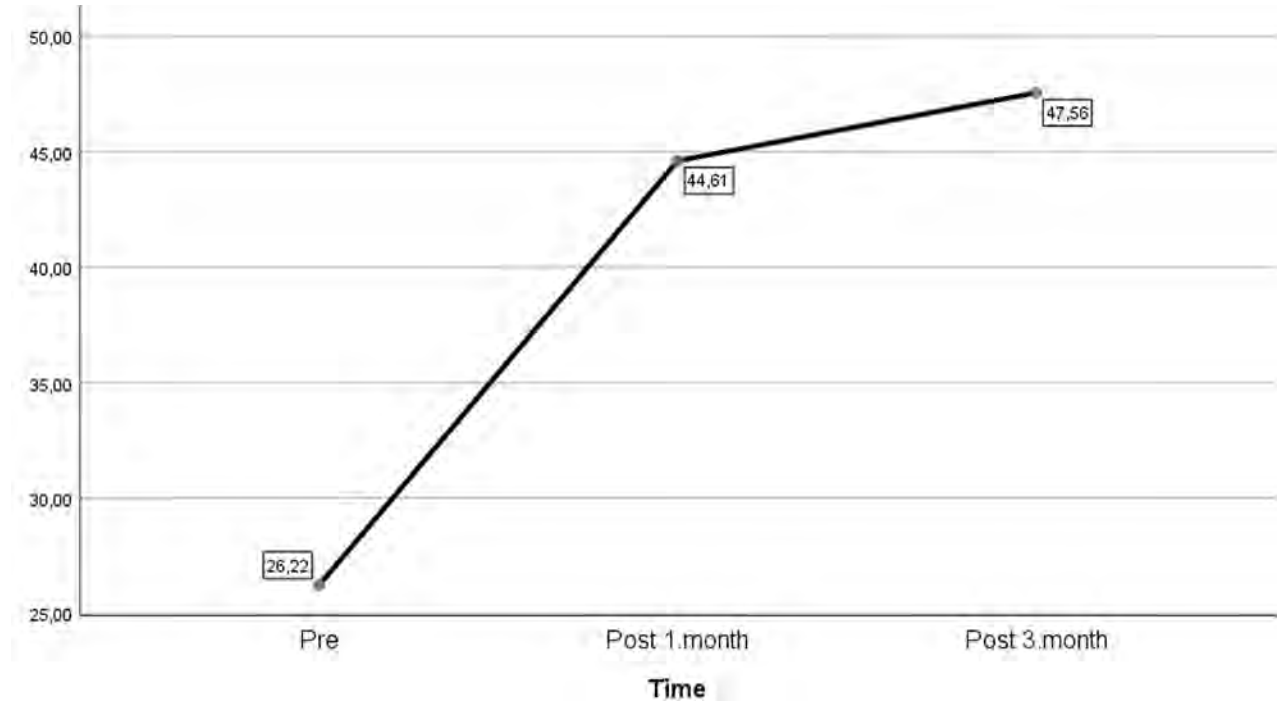

Figure 7. Graph demonstrating the change in the PCS-12 Scores at different time intervals

PCS-12: Physical component summary-12

in interventional treatment, and there was a significant improvement in NRS scores at 3 months after treatment.

In a review, Brown et al.[22] reported that diagnostic difficulties in PCS patients caused serious health problems and socioeconomic damage. In our study, the mean duration from the time the patients were diagnosed with PCS until interventional treatment was applied was 36 months. We believe that diagnostic difficulties prolong the management process.

In this study, complications encountered during the procedure were graded according to SIR classification.[9,23] During the procedure, panic attacks developed in 5 patients, short-term dyspnea in 2 patients, and vasovagal reflex in 1 patient. All complications were grade A, according to SIR. There were no complications related to the interventional technique and medications administered during and after the procedure. It is known that sedation reduces the risk of procedure-related complications in patients undergoing day-case procedures.[24,25] We suggest that this fact should be taken into consideration in terms of reducing complications.

In our study, only 1 patient had a rheumatologic disease. Comorbidities such as hypertension, asthma, and DM were also negligible. In the literature, there is insufficient data on the association of chronic diseases with PCS, which is a cause of CPP. Our data do not support the idea of an association. The presence of varicose veins in the lower extremities is thought to be a risk factor for PCS.[26] In our study, it was observed that 77.8% of the patients had varicose veins in the lower extremities.

In our study, all patients with PCS had pain that increased with standing. In addition, most of the patients had postcoital pain, dyspareunia, groin pain, and, less frequently, urgency and dysuria. Our patient group consisted of middle-aged women with a normal body mass index, most of whom were multiparous. There were no female patients who had never given birth. More than half of the patients had radiating pain in the hips and lower back. This finding is also noteworthy.

In a study by Laborda et al.,[27] patients with PCS were followed up for 60 months after coil embolization, and there was a significant regression in VAS scores. In our study, significant improvement was observed at the end of the third month in the MCS-12 and PCS-12 scores, which are subcomponents of the SF-12 evaluating the physical, mental, and social status and quality of life of the patients. The increase in SF-12 scores at 3 months compared to 1 month after the procedure suggests that the improvement continued over time.

Limitations

The main limitations of our study include its retrospective design, the relatively short duration of patient follow-up, the inability to perform direct comparisons with other interventional treatments for PCS, and the absence of objective post-procedural imaging to verify treatment efficacy. These limitations may affect the generalizability and robustness of our findings. Also, this study has a small sample size. Our limited sample size and failure to perform an a priori sample size calculation may increase the probability of Type II error, particularly in secondary endpoints and subgroup comparisons, and may limit the sensitivity of our estimates. Although including all eligible consecutive cases during the study period supports external validity, we are cautious about generalizability to different patient profiles and care settings. To validate our findings and refine our effect estimates, we recommend prospective, pre-planned, power-based studies with larger samples and longer follow-up periods, as well as comparisons with alternative embolization techniques.

CONCLUSION

Plug embolization appears to be a safe, effective, and durable treatment for pelvic congestion syndrome, providing significant relief from chronic pelvic pain and improving quality of life. Mean NRS scores in our cohort fell from 9.3 before the procedure to 2.03 at 3 months, with all patients achieving a ≥50% reduction in pain. Similarly, substantial improvement was shown in PCS-12 and MCS-12 scores, in keeping with improved physical and mental well-being. Such findings are in keeping with the literature regarding sclerotherapy and coil embolization but emphasize that plug embolization in isolation can achieve comparable or better results. Given the often very prolonged time to diagnosis in PCS, early recognition and timely intervention are important. Plug embolization therefore represents a reliable, minimally invasive approach to the management of PCS, bringing about considerable symptom benefit and improved quality of life in patients.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital Ethics Committee (No: KAEK/2024.03.52, Date: 27/03/2024).

Informed Consent: Informed consent was obtained from all participants.

Conflict of Interest Statement: The authors have no competing interests to declare.

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RESEARCH ARTICLE

Evaluation of the Quality of English Videos on YouTube as a Source of Information About Preimplantation Genetic Diagnosis

Teymur Bornaun

Department of Obstetrics and Gynecology, University of Health Sciences, İstanbul Bağcılar Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: The aim of the study is to evaluate the quality and functionality of videos on PGD on YouTube.

Materials and Methods: One hundred videos were evaluated; the date of upload, duration, the person who uploaded the video, and the number of comments, views, likes, and dislikes were recorded. Video Power Index (VPI), modified DISCERN scale, Journal of the American Medical Association (JAMA), and Global Quality Scale (GQS) were used in the evaluation. Videos were divided into three groups: University/Professional Organisations (UOO), Medical Advertising/Profit-Oriented Companies (MPC), and Independent Users (IU).

Results: A significant difference was found between the groups in the modified DISCERN parameter (p 0.042). In modified DISCERN scores, the IU group was significantly lower than the other groups. While no difference was detected in the JAMA parameter (p=0.155), the difference between the groups was found to be significant in the GQS parameter (p=0.002). The IU group had the lowest GQS score.

Conclusion: We think that it would be more beneficial if the videos published on the internet, especially YouTube, are prepared by experts by utilising reliable sources of information, current literature, and scoring systems.

Keywords: Preimplantation diagnosis, YouTube, *in vitro* fertilization, embryology

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INTRODUCTION

In the contemporary digital age, YouTube has emerged as a multifaceted platform that not only entertains and educates but also influences public understanding and perceptions of complex scientific and medical subjects.[1] YouTube plays an important role in education, offering many benefits to both students and educators. It does this in many ways, including access to diverse content, visual and engaging learning, accessibility and flexibility, supplemental learning, global learning community, and skill development. In addition, low-cost access, feedback, and assessment make YouTube the preferred choice for education.[2,3]

In addition to its educational uses, it is becoming one of the main sources of information and research for the diagnosis and treatment of diseases that patients are particularly curious about.[4] It provides a space for researchers, medical professionals, and educators to share their expertise, thereby influencing public perception and awareness of these cutting-edge technologies. However, the dynamic nature of YouTube can also present challenges, as information can vary in accuracy, completeness, and reliability.[1,3]

One such important issue is preimplantation genetic diagnosis (PGD), a reproductive technology with significant ethical, societal, and medical implications. PGD involves the screen-

Address for Correspondence: Teymur Bornaun, Department of Obstetrics and Gynecology, University of Health Sciences, İstanbul Bağcılar Training and Research Hospital, İstanbul, Türkiye
E-mail: teymurbornaun1@gmail.com **ORCID ID:** 0009-0007-8081-8003

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ing of embryos prior to implantation, allowing the selection of embryos without certain genetic disorders or chromosomal abnormalities.[5] Nowadays, the increasing number of *in vitro* fertilization treatments and the search for a healthy baby, especially by parents with genetic diseases, have increased the importance of PGD.[6]

By using PGD in conjunction with *in vitro* fertilization (IVF), parents can reduce the chance of passing on inherited disorders to their offspring by screening embryos for genetic abnormalities prior to implantation. The process involves removing one or more cells from early-stage embryos and subjecting them to genetic analysis.[7] This technique has attracted attention for its potential to reduce the incidence of genetic disorders in families. However, a lack of knowledge and experience of preimplantation genetic diagnosis among prospective parents has been identified as a barrier to access to this reproductive option, so there is a need to evaluate sources of information.[8]

As a leading video-sharing platform, YouTube plays a key role in disseminating information about various scientific and medical advances, including PGD. By analysing a selection of YouTube videos, this study aims to evaluate the accuracy of the information presented, identify common narratives or misconceptions, and assess the potential impact of these videos on public opinion and decision-making regarding reproductive choices. In addition, this research aims to shed light on the role of YouTube as a medium for scientific communication, highlighting the need for reliable and accessible information in a field as complex as reproductive genetics.

MATERIALS and METHODS

Users of YouTube can watch, like, share, comment on, and upload videos on the platform. The review process began with the YouTube search history being cleared. The 'Relevance' filter option and 'preimplantation genetic diagnosis' as search terms were entered into the search bar. The study excluded commercial videos; non-visual, non-audio, non-English videos; and videos lasting longer than an hour or less than one minute. Videos with any of these reasons were excluded from the research. Out of two or more repeat videos, only the first one was included.[9,10] More than 90% of YouTube users only watch the first 60 videos in their search results to find the information they need. In our analysis, the first 100 videos were taken into account with the assumption that visitors would not view more than 100 videos in the search results. Based on previous studies, the top 100 videos were watched between 06/04/2023 and 08/06/2023. Fifteen videos were less than 1 minute. Three videos were longer than 1 hour. Five videos were not in English. Fourteen videos were exactly the same.[11] Out of these 100 videos, 63 videos were analysed by two histology and embryology specialist medical doctors (doctors who successfully specialised in histology and embryology after the medical specialisation examination).

On June 8, 2023, the following information was recorded: video names, source URLs, views, duration since upload (including finish date), and number of likes, dislikes, and comments. Ethical approval is not required as our study did not involve human subjects and included videos open to the public.

The videos were considered in three groups. The first group was evaluated as University/Occupational Organizations (UOO), the second group was Medical Ad/Profit-Oriented Companies (MPC), and the third group was evaluated as Independent Users (IU).

Video Popularity

The Video Power Index (VPI), which measures the popularity of videos, was calculated using the following formula: Like rate = [likes × 100 / (likes + dislikes)] and view rate (number of views/day); VPI=[(like rate × view rate) / 100].[12]

Quality Assessment

The DISCERN scoring system is a scale used to evaluate the quality of written information, developed by Charnock et al.[13] We used the modified DISCERN scale, which Singh et al.[9] constructed by shortening the original scale. Information and visual media were evaluated with a five-question modified DISCERN scale that assesses the reliability, clarity, and impartiality of the content. The videos were evaluated in terms of quality according to the total score, by giving 0 or 1 point according to the answers to the questions. Very low quality is indicated by one point, poor quality by two, medium quality by three, good quality by four, and very good quality by five points.[14,15]

One of the most popular scoring methods for evaluating medical information from websites is the Journal of the American Medical Association (JAMA) scoring system. Silberg et al.[16] proposed the Journal of the American Medical Association (JAMA) benchmarking criterion for evaluating the information dependability of videos. A total JAMA score is calculated by assigning points to each of the four basic standards, which include authorship, clearly stated and properly cited sources, currency of information, and disclo-

Table 1. Quality assessment scoring systems

Modified DISCERN scoring system	**Yes**	**No**
Are the aims clear and achieved?	1 Point	0 Point
Are reliable sources of information used?	1 Point	0 Point
Is the information presented balanced and unbiased?	1 Point	0 Point
Are additional sources of information listed for viewers?	1 Point	0 Point
Are areas of uncertainty mentioned?	1 Point	0 Point
The JAMA scoring system		
Section	**Yes**	**No**
Attribution		
References and sources for all content should be listed clearly, and all relevant copyright information should be noted.	1 Point	0 Point
Authorship		
Authors and contributors, their affiliations and relevant credentials should be provided.	1 Point	0 Point
Disclosure		
Website "ownership" should be prominently and fully disclosed, as should any sponsorship, advertising, underwriting, commercial funding arrangements or support, or potential conflicts of interest	1 Point	0 Point
Currency		
Dates when content was posted and updated should be indicated.	1 Point	0 Point
Global quality scale (GQS) criteria		
Description of quality	**Grade**	
Poor quality and unlikely to be of use for education.	1	
Poor quality and of limited use to education because some information is present	2	
Suboptimal quality and flow; somewhat useful to education; important topics are missing; some information is present	3	
Good quality and flow; useful to education because most important topics are covered	4	
Excellent quality and flow; highly useful to education.	5	

sure of potential conflicts of interest. A score of zero indicates the lowest accuracy and reliability, while a score of four indicates the highest accuracy and reliability.

The Global Quality Scale (GQS) is a 1–5 scale that evaluates the overall information quality, flow, and educational relevance of content. A high score indicates good quality and useful information. There are three quality levels: (1–2) low, (3) medium, and (4–5) high educational quality.[9,17,18] Videos are categorized as "useful" (GQS >3) or "not useful" (GQS ≤3) in GQS assessments. "Useful videos" are defined as those that can be suggested as qualitative learning materials and that reasonably add to patients' knowledge.[12]

The suggested YouTube videos were watched by two specialists in histology and embryology at the same time. Modified DISCERN, JAMA, and GQS rating systems were used to assign ratings to the videos (Table 1).

Statistical Analysis

The data were analyzed using IBM SPSS version 21. Data were analyzed using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY, USA). The distribution of the data was examined with the Shapiro–Wilk test, and it was observed that none of the data followed a normal distribution. The median values of the modified DISCERN, JAMA, and GQS scores were calculated. Since these data did not show a normal distribution, group differences were determined using the Kruskal–Wallis test. Differences between groups were considered significant for p-values < 0.05. As all data did not follow a normal distribution, correlations between parameters were analyzed using the Spearman correlation test. Correlation values between 0 and 1 were interpreted such that values close to 1 indicated a high correlation, and those close to 0 indicated a low correlation. Accordingly, correlations

Table 2. Descriptive analysis of modified DISCERN, JAMA and GQS

	University/occupational organizations	Medical ad/profit-oriented companies	Independent users	p
N	41	13	9	
Modified DISCERN				
Mean±SD	2.512±1.186	2.385±1.044	1.444±1.509	0.042
Median (min-max)	2 (1–5)	2 (1–4)	1 (0–5)	
Rank	34.573	33.423	18.222	
JAMA				
Mean±SD	3.122±0.458	2.923±0.641	2.667±0.866	0.155
Median (min-max)	3 (2–4)	3 (2–4)	3 (1–4)	
Rank	34.427	29.231	24.944	
GQS				
Mean±SD	2.731±1.225	2.462±0.877	1.222±0.667	0.002
Median (min-max)	3 (1–5)	3 (1–4)	1 (1–3)	
Rank	35.829	33.231	12.778	

GQS: Global quality scale; JAMA: Journal of the American Medical Association; SD: Standard deviation

between 1 and 0.80 were classified as very high, 0.8–0.6 as high, 0.6–0.4 as moderate, 0.4–0.2 as low, and 0.2–0 as weak.

RESULTS

Video names, video source links, number of views, time since the video was uploaded (including end date), and number of likes, dislikes, and comments were recorded. The quality and reliability of the videos were evaluated using the GQS and modified DISCERN tool, respectively.[19]

In the modified DISCERN parameter, the mean and median values were as follows: for the University/Occupational Organization group, the mean was 2.512±1.186 and the median was 2 (min 1–max 5); for the Medical Ad/Profit-Oriented Companies group, the mean was 2.385±1.044 and the median was 2 (min 1–max 4); and for the Independent User group, the mean was 1.444±1.509 and the median was 1 (min 0 – max 5) (Table 2). The Kruskal–Wallis test conducted to determine group differences revealed a significant difference between groups for the DISCERN parameter (p=0.042). No significant difference was found for the JAMA parameter (p=0.155), while a significant difference was observed for the GQS parameter (p=0.002) (Table 2). According to the p-values obtained as a result of the Kruskal–Wallis test in the data in Table 3, there is no difference between the groups in all parameters (p>0.05) (Table 3).

In the correlation analysis presented in Table 4, the results show a moderate positive correlation between modified DISCERN and Length (r=0.449, p<0.001) and JAMA (r=0.554, p<0.001), while there is a high positive correlation between modified DISCERN and GQS (r=0.639, p<0.001). There is also a moderate positive correlation between GQS and JAMA (r=0.400, p<0.001) and between GQS and Length (r=0.449, p<0.001). The positive correlations with the Length parameter indicate that the duration of the video has a significant enhancing effect on quality. On the other hand, a negative low correlation between Length and Days since upload (r=-0.389, p<0.01) suggests that as the upload date becomes more distant, the duration significantly decreases. A positive low correlation between video length and comments (r=0.266, p=0.05) indicates that as the duration increases, the number of comments may also increase. The number of views shows a high positive correlation with comments (r=0.604, p<0.001) and dislikes (r=0.629, p=0.001), and a very high correlation with the number of likes (r=0.802, p<0.001) and VPI (r=0.956, p<0.001). The increase in views is strongly associated with significant increases in the parameters of comments, likes, and dislikes. A negative low but significant correlation was found between the video upload time and dislikes (r=-0.271, p<0.05). A strong positive correlation was observed between the number of comments and views (r=0.604, p<0.001), likes (r=0.753, p<0.001), dislikes (r=0.670, p<0.001), and VPI (r=0.667, p<0.001).

Although there is a high correlation between VPI and the number of likes and views due to their inclusion in the calculation, the significant positive correlation between VPI and comments (r=0.667, p<0.001) indicates that videos with higher like rates and view counts receive more comments. Contrary

Table 3. Descriptive analysis of other parameters

Descriptives	N	Mean	SD	p
Length (Second)				
Universities/Occupational organizations	41	435.902	601.169	0.171
Medical Ad/profit-oriented companies	13	207.462	63.803	
Independent users	9	894.889	1028.786	
Views				
Universities/Occupational organizations	41	7341.024	12769.682	0.352
Medical Ad/profit-oriented companies	13	9405.308	14395.086	
Independent users	9	7538.889	8793.711	
Days since upload				
Universities/Occupational organizations	41	2510.659	1196.679	0.627
Medical Ad/Profit-oriented companies	13	2323.385	999.828	
Independent users	9	2211.667	654.742	
Comments				
Universities/Occupational organizations	41	3.195	7.163	0.189
Medical Ad/Profit-oriented companies	13	2.077	3.818	
Independent users	9	7.111	12.544	
Likes				
Universities/Occupational organizations	41	39.415	77.583	0.099
Medical ad/Profit-oriented companies	13	63.846	127.019	
Independent users	9	58.000	64.506	
Dislikes				
Universities/Occupational organizations	41	1.780	4.704	0.226
Medical ad/Profit-oriented companies	13	3.077	5.823	
Independent users	9	4.778	7.645	
VPI				
Universities/Occupational organizations	41	3.860	8.515	0.377
Medical ad/Profit-Oriented companies	13	4.660	7.191	
Independent Users	9	3.697	4.594	

SD: Standard deviation; VPI: Video Power Index

to expectations, video upload time did not have a significant correlation with any parameters other than dislikes ($r=-0.271$, $p<0.05$) and length ($r=0.389$, $p<0.01$). It was observed that whether the videos are up to date or not does not have a significant impact on viewers. Furthermore, no significant correlation was found between the scores of health professionals and the preferences of viewers. This suggests that viewers do not consider the quality of the video content, whereas health professionals assign higher scores to longer videos that contain more information and content, in contrast to viewers.

DISCUSSION

PGD, a method used to increase IVF success rates or to reduce the risk of having a child with a single gene or chromosomal condition in high-risk, carrier couples, allows the genetic status of the embryo to be evaluated, and pregnancy can be achieved by transferring embryos with intact genetic material. Biopsy of the developing embryo before transfer is an invasive procedure that allows for genetic evaluation of the embryo.[20] Selecting unaffected embryos improves implantation and live birth rates per embryo.[21]

YouTube is a popular tool for information retrieval, with over 2.1 billion monthly active users worldwide and over 122 million daily users. Examining the information on this platform is essential, especially for an illness that is frequently misunderstood and has the potential to significantly affect quality of life. On this social media network, a lot of doctors, whether they are employed by hospitals or operate independent-

Table 4. Correlation of the parameters

	Modified DISCERN	JAMA	GQS	Length (Second)	Views	Days since upload	Comments	Likes	Dislikes	VPI
Modified DISCERN	–	0.554	0.639	0.449	0.184	-0.076	0.143	0.171	0.058	0.179
		<0.001	<0.001	<0.001	0.150	0.555	0.264	0.181	0.649	0.160
JAMA	0.554	–	0.400	0.211	-0.028	-0.059	-0.022	-0.070	-0.059	-0.028
	<0.001		<0.001	0.097	0.827	0.647	0.863	0.587	0.644	0.828
GQS	0.639	0.400	–	0.342	0.154	-0.157	0.013	0.144	0.058	0.187
	<0.001	<0.001		<0.01	0.229	0.220	0.918	0.261	0.650	0.143
Length (Second)	0.449	0.211	0.342	–	0.089	-0.389	0.266	0.246	0.198	0.161
	<0.001	0.097	<0.01		0.486	<0.01	0.05	0.052	0.120	0.206
Views	0.184	-0.028	0.154	0.089	–	0.001	0.604	0.802	0.629	0.956
	0.150	0.827	0.229	0.486		0.992	<0.001	<0.001	0.001	<0.001
Days since upload	-0.076	-0.059	-0.157	-0.389	0.001	–	-0.241	-0.245	-0.271	-0.246
	0.555	0.647	0.220	<0.01	0.992		0.057	0.053	<0.05	0.052
Comments	0.143	-0.022	0.013	0.266	0.604	-0.241	–	0.753	0.670	0.667
	0.264	0.863	0.918	<0.05	<0.001	0.057		<0.001	<0.001	<0.001
Likes	0.171	-0.070	0.144	0.246	0.802	-0.245	0.753	–	0.722	0.847
	0.181	0.587	0.261	0.052	<0.001	0.053	<0.001		<0.001	<0.001
Dislikes	0.058	-0.059	0.058	0.198	0.629	-0.271	0.670	0.722	–	0.667
	0.649	0.644	0.650	0.120	<0.001	<0.05	<0.001	<0.001		<0.001
VPI	0.179	-0.028	0.187	0.161	0.956	-0.246	0.667	0.847	0.667	1.000
	0.160	0.828	0.143	0.206	<0.001	0.052	<0.001	<0.001	<0.001	

The upper value shows the correlation value and the lower value shows the p value. Between 1-0,80 shows very high correlation, 0.8-0.6 shows high correlation, 0.6-0.4 shows moderate correlation, 0.4-0.2 shows low correlation and 0.2-0 shows weak correlation. VPI: Video power index, GQS: Global quality scale, JAMA: Journal of the American Medical Association

ly, share their professional advice. These recommendations could be objective and purely focused on informing the public, with no ulterior objectives, or they could be biased and meant to draw attention to the relevant medical institutions.[22]

The widespread accessibility of YouTube makes it a valuable resource for patients seeking information about medical conditions. The accuracy and reliability of these videos and the information they contain can sometimes be a cause for concern.[23–25]

According to a 2018 national health survey, 33% of patients used YouTube for medical education. In addition to text resources, YouTube's video format is a powerful educational tool for both patients and healthcare professionals.[26,27]

This study aimed to evaluate the quality and reliability of PGD-related information available on YouTube.

In the studies conducted, the scales used in the evaluation of written scientific materials such as modified DISCERN and JAMA are also used in studies related to videos on the internet. Azer et al.[28] suggested the development of an appropriate method and scales for the evaluation of visual publications such as videos. GQS was used for non-specific evaluation of the educational quality of videos.[18] VPI measures the overall performance and impact of the video on various platforms. It takes into account factors such as the number of views, engagement metrics (likes, shares, comments), social media influence, and overall reach. VPI helps to assess the popularity and effectiveness of a video.[23–25,29]

Şahin et al.[30] investigated YouTube as an information source in retinopathy of prematurity. They used VPI value, GQS, and modified DISCERN scale in their study, and as a result, they found that the videos added by independent users were of lower quality than those added by health professionals. In our study, although the VPI value was not statistically significant between the groups, the videos uploaded by independent users in the GQS and modified DISCERN evaluations were statistically significantly lower than the other groups. Our study supports the findings of Şahin et al.[30] and shows the importance of the source of videos containing medical information on YouTube.

In our study, JAMA and modified DISCERN scores were found to be moderately correlated, and these scores were found to be high in the UOO and MPC groups. Thus, we have again observed that information reliability is higher in individuals and institutions with medical education or working in the health field.

Erdem et al.[31] showed that JAMA and GQS values were low in the evaluation of kyphosis-related videos on YouTube. Stogowski et al.[32] also conducted a video review of anterior lumbar interbody fusion and concluded that the average modified DISCERN score and overall quality remained low. Unal-Ulutatar et al.[33] found that 73% of the videos were useful in their study using the words "systemic sclerosis" and "scleroderma". Ng et al.[34] also emphasized the availability of reliable and high-quality YouTube videos with useful information about systemic lupus erythematosus. The inconsistencies in the results of these studies may be due to differences in the areas studied.

Our study showed that the YouTube videos evaluated were not as useful to patients as desired, and that the lowest scores among the groups belonged to independent users. The quality and reliability of health videos shared on YouTube are generally average or below average. In a study by Osman et al.[27] on the quality of health information on YouTube, the mean modified DISCERN score of the videos analysed was 2.36, and the mean GQS score was 2.68.

In a different study, Kizilet et al.[15] determined the mean values of the videos about labiaplasty to be 2.29 on the modified DISCERN scale and 2.75 on the GQS scale. In our investigation, the UOO group's mean modified DISCERN value was 2.52, the MPC group's was 2.38, and the IU group's was 1.44. The mean GQS values in the UOO group were 2.73, 2.46 in the MPC group, and 1.22 in the IU group, all of which were consistent with previous investigations.

In a study conducted by Mylavarapu et al.,[35] the quality of videos was evaluated based on the identity of the uploader. The findings indicated that videos uploaded by medical professionals, specifically doctors and hospitals, exhibited the highest quality. The researchers discovered that videos published by sources other than medical professionals, healthcare organisations, hospitals, and news agencies exhibited a higher VPI than videos published by these entities. In contrast, Çelik et al.[36] observed that videos published by medical professionals exhibited a higher VPI in their investigation of rotator cuff repair. The results of our study indicate that there was no statistically significant difference between VPI values. However, the IU group exhibited lower values than the other groups, which supports the findings of Çelik et al.[36]

The majority of YouTube users are not medical professionals; therefore, they may not have comprehended what doctors or healthcare professionals were attempting to convey in the videos they uploaded, or what they were told did not meet their expectations.

Similar findings were reported by Ferhatoğlu et al.,[37] who found a negative relationship between video popularity and video quality ratings. Biggs et al.[38] discovered that shorter videos are watched more than longer videos. In our study, shorter videos were generally watched more, but the modified DISCERN score tended to increase as video length increased.

According to the Nicholl et al.[39] study, 62% of parents preferred trustworthy information, 61% chose correct information, and 65% preferred up-to-date information.

Songur et al.[40] discovered that the GQS and JAMA scores were poor, and the DISCERN evaluation was moderate in their video investigation on retinal detachment. They emphasized that even though there are a good number of videos on the topic on YouTube, they are of poor quality and not very helpful as a source.

In our opinion, the inconsistencies in the results of the studies may be due to differences in the areas under investigation.

One of the major limitations of our study is that only English videos were watched, and the number of videos in the groups was not equal. Another limitation is that we examined specific videos between specific dates on YouTube, a social site where new videos are constantly uploaded and status changes such as likes and comments are visible. Different people rate videos using GQS, which might lead to variation in interpretation and scoring.

CONCLUSION

Today, the internet is one of the most important sources of medical information. Our study highlighted the importance of medical information provided through YouTube, a social media platform. Users searching for information about PGD on YouTube may encounter inadequate, inaccurate, and sometimes misleading information. Particularly for patients and students seeking information, the information provided in the videos should be accurate, reliable, and sufficient. These videos also guide patients in making decisions about their health, which have both financial and moral consequences. Particularly in IVF treatment, the aim is to take home a healthy baby, and patients carry both a financial and moral burden in relation to both IVF treatment and the decision to undergo PGD.

We may not be able to control and correct all the information that is publicly available on the internet, especially

on social media, but we should at least be aware of how patients are accessing the right information and how it is influencing their decisions.

When we looked at most of the videos we saw, we found that the uploaders were universities or academic institutions, and the video quality was inadequate. We recommend that videos uploaded to platforms such as YouTube, where videos are uploaded for educational and informational purposes—especially in the field of medicine—should be accurate, sufficient, understandable, and reliable, without keeping the video duration too long, and should be prepared by knowledgeable people working in the field of health; we recommend that they comply with quality scores such as modified DISCERN, JAMA, and GQS. We also think that our study will guide new researchers in evaluating videos on different medical topics.

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RESEARCH ARTICLE

Oral Hygiene in Focus: A Comparative Study Between Children with Rheumatic Disease and Their Healthy Peers

Büşra Başer Taşkın[1], Gülşah Kavrul Kayaalp[1], Selen Duygu Arık[1], Ayşenur Doğru Kılınç[1], Bengisu Menentoğlu[1], Ahmet Taşkın[2], Özlem Akgün[1], Nuray Aktay Ayaz[1]

[1]Division of Pediatric Rheumatology, Department of Pediatrics, İstanbul University Faculty of Medicine, İstanbul, Türkiye
[2]Division of Pediatric Neurology, Department of Pediatrics, İstanbul Medipol University, İstanbul, Türkiye

ABSTRACT

Objective: This study investigates the oral health status and hygiene practices of children with rheumatic diseases compared to healthy peers. It emphasizes the need to integrate dental care into managing these chronic conditions.

Materials and Methods: Children under 18 years of age with rheumatic diseases were recruited from a pediatric rheumatology clinic. Demographic, diagnostic, and treatment data were collected, and a survey administered via Google Forms assessed general information, oral hygiene practices, and education.

Results: The study included 303 participants: 150 with rheumatic diseases and 153 healthy controls. The results indicated that while dental visit frequency was similar between groups, children with rheumatic diseases were more likely to use manual toothbrushes (93.3% vs. 75.2%) and non-fluoride toothpaste. Both groups showed limited knowledge about toothpaste ingredients, but patients demonstrated slightly less awareness. Many participants had not attended oral hygiene workshops, although there was significant interest in further education.

Conclusion: The findings show differences in oral hygiene between children with rheumatic diseases and healthy controls, highlighting the need for targeted care and better rheumatologist-dentist collaboration.

Keywords: Dental health education, oral hygiene, rheumatology, toothbrushing

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INTRODUCTION

Pediatric rheumatic diseases (PedRDs) are conditions affecting the joints, muscles, and connective tissues. They mainly include autoinflammatory diseases, juvenile idiopathic arthritis (JIA), connective tissue diseases, and vasculitis, which each have their own set of symptoms and treatment approaches. The treatment plans usually comprise a combination of anti-inflammatory agents and conventional, biological, or targeted synthetic disease-modifying antirheumatic drugs. Regular follow-ups with a pediatric rheumatology healthcare team are of utmost importance for monitoring the disease and making the required arrangements during follow-up. Recent studies have increasingly emphasized the importance of multidisciplinary management in pediatric rheumatology, highlighting how systemic inflammation may influence oral health and vice versa.[1,2]

Upon in-depth evaluation of children with chronic diseases, physicians are now aware of many issues that can improve patients' well-being, such as regular exercise, a healthy diet, and avoiding smoking. Although oral hygiene constitutes an important part of overall well-being in children, it remains an understudied topic in pediatric rheumatology. Oral hygiene involves dental and periodontal health, which are interconnected in a two-way relationship with overall

Address for Correspondence: Nuray Aktay Ayaz, Division of Pediatric Rheumatology, Department of Pediatrics, İstanbul University Faculty of Medicine, İstanbul, Türkiye
E-mail: nurayaktay@gmail.com **ORCID ID:** 0000-0003-3594-7387

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systemic health. The oral cavity harbors the second-largest microbiota in the human body, following the gut. Dysbiosis in the oral and intestinal microbiomes has been demonstrated in patients with rheumatoid arthritis and other systemic inflammatory diseases through metagenome-wide association studies (MGWAS). Such microbial imbalance may contribute to systemic inflammation and disease activity. Therefore, incorporating dental evaluations into routine rheumatologic care and referring patients to dentists after diagnosis may improve both oral and systemic health outcomes. The condition of the mouth and gums can affect the body, and conversely, systemic well-being can impact oral health as well. Inflammation of the oral cavity is related to the spread of pathogenic microbes to remote body regions, which can cause systemic infection. Maintaining good oral hygiene is critical, as it can help prevent various dental issues such as cavities and gum disease, which may be a source of infection.[3]

The relationship between rheumatologic conditions and oral hygiene lies in the potential impact of these diseases on oral health. Some rheumatologic conditions, such as Sjögren's syndrome, can affect the salivary glands, leading to dry mouth and an increased risk of dental problems. Juvenile idiopathic arthritis has been linked to the development and progression of gingival inflammation, which may make periodontal diseases a significant problem for these patients.[4]

Additionally, medications used may have side effects that affect oral health, such as causing gum inflammation or increased susceptibility to infections. For example, methotrexate is known to often cause ulceration in the mouth, and the use of biologic disease-modifying antirheumatic drugs (bDMARDs) can lead to adverse oral effects manifested as mucosal changes. Therefore, individuals with rheumatologic diseases should pay extra attention to their oral hygiene routine, including regular dental check-ups, proper brushing and flossing, and maintaining good overall oral health practices.[5]

The aim of this study was to investigate the oral health status and hygiene habits of children with rheumatologic diseases followed up in the pediatric rheumatology outpatient clinic and to compare them with healthy controls.

MATERIALS and METHODS

Study Design and Survey Content

Patients under 18 years of age diagnosed with a rheumatic disease were recruited from a tertiary pediatric rheumatology clinic. The healthy control group was carefully matched to the patient group in terms of age and gender to ensure comparability. Healthy volunteers were recruited from the same community as the patient group, primarily among children attending the general pediatric outpatient clinics of our institution, with no known chronic or autoimmune disease. Demographic data, diagnosis, and treatment modalities were recorded from the patient files. The survey was administered through the Google Forms platform. The survey began with a brief description of the study's aims, and participants were asked to answer as accurately as possible. Each patient was asked to provide informed online consent explaining the purpose of the study and was given authorization to use the collected data.

Informed consent was obtained electronically from all participants and/or their legal guardians before the Google Form was sent, in accordance with institutional and ethical guidelines.

The survey was divided into three sections: general information, oral hygiene, and oral hygiene education. The questionnaire comprised two open-ended questions and 17 multiple-choice questions. Some questions were connected, so answering one question affected the ability to answer the next one. A comparative analysis was conducted between patients and healthy controls.

The complete questionnaire used in this study has been provided as Supplementary Material.

Statistical Analysis

IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis to evaluate the results of the study. Descriptive analyses were presented using appropriate measures such as proportions, medians, and interquartile range (IQR). Variables were compared between cases and controls using the chi-squared test or the Fisher exact test (two-tailed) for categorical variables. The Shapiro-Wilk test was used to test the normality of distribution for continuous variables. The Mann-Whitney U test was used to compare non-normally distributed continuous data between groups. $P<0.05$ was considered statistically significant.

Ethics

Written consent was obtained from each patient and control, or from their parent or guardian. Ethical approval for the study protocol was obtained from the Clinical Research Ethics Committee of Istanbul University, Istanbul Faculty of Medicine (Approval No: 2834454/23.08.2024). The study was conducted in compliance with the Declaration of Helsinki.

Table 1. Demographic characteristics in the cohort

Category	Patients (n=150)		Healthy controls (n=153)		p
	n	%	n	%	
Age (years), median (IQR)	13.0 (9.75–16)		12.0 (9.0–14.75)		0.06[ac]
Gender (female)	83	55.3	89	58.2	0.62[b]
Diagnosis of patients					
Familial mediterranean fever	64	42.7			
Juvenile idiopathic arthritis	25	16.7			
IgA vasculitis	14	9.3			
Behcet's disease	8	5.3			
Systemic lupus erythematosus	6	4.0			
Others	33	22.0			
Users of biologic disease-modifying antirheumatic drugs	37	24.7			

[a]: Mann Whitney U test; [b]: Chi-square test; [c]: p<0.05, statistically different. IQR: Interquartile range

RESULTS

A survey evaluating the oral hygiene habits of a total of 303 individuals was conducted. Among the respondents, 153 were healthy controls, and 150 were patients with rheumatic diseases. The median age of the patients was 13 (IQR: 9.75–16) years, while the median age of the healthy group was 12 (IQR: 9–14.75) years (p=0.06). Demographic characteristics and diagnoses of the patients are presented in Table 1.

The disease subgroups included Familial Mediterranean Fever (n=64, 42.7%), juvenile idiopathic arthritis (n=25, 16.7%), IgA vasculitis (n=14, 9.3%), Behçet's disease (n=8, 5.3%), systemic lupus erythematosus (n=6, 4.0%), and other connective tissue or vasculitic diseases (n=33, 22.0%). No statistically significant differences were observed between disease subgroups (FMF, JIA, IgA vasculitis, and others) and the type of toothbrush used (p=0.403), tooth-brushing frequency (p=0.752), or tooth-brushing duration (p=0.976).

When asked whether they had previously visited a dentist, 122 patients (81.3%) and 123 healthy controls (80.4%) answered affirmatively (p=0.83). The frequency of dental visits was higher between the ages of 5–9 in both groups, with 62 individuals (40.5%) in the healthy group and 55 individuals (36.7%) among the patients. There was no significant difference between the patient and healthy control groups in terms of tooth brushing habits, brushing times, flossing rate, and toothpaste content. The type of toothbrush used was predominantly manual, while the rate of electric toothbrush use was significantly higher in the healthy group (p<0.001) (Table 2).

Thirty-seven patients were taking biological disease-modifying antirheumatic drugs. Among these patients, 32 (86.5%) had previously visited a dentist, with the most common age group being 5–9 years (37.8%). The typical brushing time for these patients was 1–2 minutes (37.8%), and the preferred toothbrush choice was predominantly manual (89.2%). Within this group, 25 (67.6%) were unaware of the ingredients of toothpastes, with the most common type used being fluoride-free (64.9%). Approximately 56.8% of the patients in this group had not participated in any oral hygiene workshops, and an equal percentage expressed no interest in acquiring further information on oral hygiene practices.

Oral hygiene education from families was the most common source (74% in the patient group and 63.4% in the healthy group), with no significant difference compared to other parameters (p=0.22). Ninety-two patients (61.3%) and 102 controls (66.7%) reported not attending informative meetings about dental hygiene, with no significant difference compared to those who attended (p=0.33). Seventy-four patients (49.3%) and 104 controls (68%) said they would like to learn more about oral health (p<0.001) (Table 3).

DISCUSSION

Our study revealed that although the frequency of dental visits was similar between groups, children with rheumatic diseases were more likely to use manual toothbrushes and non-fluoride toothpaste. This finding underscores the need for improved oral hygiene awareness among this population.

Table 2. Oral hygiene habits

Category	Patients (n=150)		Healthy controls (n=153)		p
	n	%	n	%	
Have visited a dentist at least once	122	81.3	123	80.4	0.84[a]
Age at first dental visit?					0.638[a]
0–4 years	23	15.3	28	18.3	
5–9 years	55	36.7	62	40.5	
10–12 years	26	17.3	19	12.4	
>13 years	18	12	14	9.2	
How many times a day do you brush your teeth?					0.099[a]
Once a day (morning)	39	26	29	18.9	
Once a day (evening)	30	20	39	25.5	
Twice a day	76	50.7	72	47.1	
Three times	5	3.3	13	8.5	
How long do you brush your teeth?					0.636[a]
0–1 minute	39	26	36	23.5	
1–2 minutes	72	48	73	47.7	
2–3 minutes	31	20.7	39	25.5	
More than 3 minutes	8	5.3	5	3.3	
Children who brush their teeth before bed	113	75.3	124	81	0.23[a]
What type of toothbrush do you use?					0.001[ac]
Manual	140	93.3	115	75.2	
Electric	10	6.7	38	24.8	
Have you ever used dental floss?					0.088[a]
Never used	123	82	113	73.9	
Dental floss users	27	18	40	26.1	
Using other oral hygiene products at home	20	13.3	31	20.3	0.1[a]
If any, other products for oral hygiene					
Mouthwash	17	11.3	30	19.6	
Tongue cleaner	3	2.0	1	0.7	
Knowledge of toothpaste ingredients	60	40	78	8.4	0.14[a]
Children who use fluoride toothpaste	68	45.3	74	48.4	0.59[a]
Those who know the fluoride content of toothpaste	2	2.9	7	9.5	0.169[b]
Do you use braces?	6	4.0	4	2.6	0.54[b]
Have you ever had braces?	7	4.7	9	5.9	0.64[a]

[a]: Chi-square test; [b]:Fisher's exact test; [c]: p<0.05, statistically different

Aphthous stomatitis is a common manifestation in rheumatologic diseases. Recent studies have shown that the use of Sodium Lauryl Sulfate (SLS)-free toothpaste can reduce the frequency of recurrent aphthous ulcers compared with SLS-containing dentifrices. This finding highlights the potential relevance of toothpaste composition in maintaining oral health among pediatric rheumatology patients.[6]

According to the 2020 data from the Turkish Statistical Institute (TÜİK), the demographic group of children aged 5 to 14 years represents 15% of Turkey's total population. Given their significant representation, there is a pressing need to emphasize preventive and therapeutic services tailored to school-aged children for the betterment of public health. Furthermore, based on 2019 data from TÜİK, oral and den-

Table 3. Oral hygiene education

Category	Patients (n=150)		Healthy controls (n=153)		p
	n	%	n	%	
Who has educated you about oral hygiene?					0.22[a]
Family	111	74	97	63.4	
Dentist	25	16.7	36	23.5	
Internet	5	3.3	5	3.3	
No one	9	6.0	15	9.8	
Previous participation in oral health seminars	51	33.3	58	38.7	0.33[a]
Children who want to learn more about oral hygiene	104	68	74	49.3	0.001[ab]

[a]: Chi-square test; [b]: p<0.05, statistically different

tal health issues rank among the top five diseases affecting children aged 0–6 years (6.4%) and are the third most prevalent in the 7–14 age group (14.2%) in Türkiye.[7,8] This is a very important point for patients with chronic diseases such as JIA. Studies indicate that inadequate oral hygiene among JIA patients correlates with functional limitations in upper extremities and involvement of the temporomandibular joint. It's not surprising that proper brushing technique can be compromised by pain and restricted movement caused by hand and wrist involvement.[9]

Additionally, Yıldızer Keriş et al.[10] reported an elevated prevalence of temporomandibular joint disorders and oral health issues in rheumatic diseases such as rheumatoid arthritis (RA), primary Sjögren's syndrome (pSS), and ankylosing spondylitis, compared to healthy individuals. These findings underscore the intricate relationship between systemic rheumatic diseases and oral health outcomes. However, to the best of our knowledge, our study is the first to show this condition in patients with JIA. According to our results, patients had higher rates of tooth brushing than controls, but the difference was not statistically significant. As oral mucosal involvement is common in rheumatic diseases and may affect the quality of life of patients, and in some conditions, the outcome of the disease, considerable attention should be paid to this issue.

It is widely emphasized across various sources that children should be introduced to tooth brushing habits by the age of three, with brushing sessions lasting at least two to three minutes.[11] During the school years, it is advised that children engage in a daily oral hygiene routine by brushing their teeth a minimum of twice per day and participate in periodic dental examinations to ensure optimal oral health.[12] Establishing the habit of brushing teeth twice a day—in the morning before breakfast and at night after the last drink—is crucial for maintaining good oral hygiene by removing plaque and preventing dental caries and gum disease.[13]

When we examine the studies performed in healthy children, we find various reports. Çan et al.[14] reported that 25% of students brushed their teeth after every meal, whereas 75% brushed at least once a day. Meanwhile, Öztürk et al.[15] observed that 47.3% of students brushed their teeth 2–3 times daily. In our study, data indicates that a significant proportion of both patients and individuals in the control group adhere to these recommendations, with 50.7% of patients and 47.1% of controls reporting brushing their teeth twice daily. The slightly higher rate may suggest that individuals with rheumatic diseases may be more attentive to their oral health needs. This could be due to increased awareness prompted by their medical condition or advice from healthcare providers regarding the importance of oral hygiene in managing overall health.

Esmeray et al.[2] evaluated the oral health of children with Familial Mediterranean Fever through clinical dental examinations and reported poorer oral health compared with healthy controls. Both studies emphasize that oral health remains an underrecognized aspect of pediatric rheumatology and highlight the importance of preventive care and close collaboration between rheumatologists and dentists.

While the overall rates are similar between the groups, factors such as education level, socioeconomic status, and access to dental care may influence brushing habits. A limitation of this preliminary study is the lack of evaluation of these aspects in the cohort. As addressing factors that may influence tooth brushing habits may help im-

prove oral health outcomes, the researchers are planning future studies to better understand disparities in oral hygiene practices and develop targeted interventions to promote consistent tooth brushing habits by exploring these variables.

Despite a slightly higher prevalence of bedtime brushing in the healthy control group, no statistically significant difference was found between the two groups. This indicates that both groups generally adhere to the recommended practice of brushing before bedtime, which is crucial for removing plaque accumulated throughout the day and preventing dental issues such as cavities and gum disease.

In both groups of the research, the most frequently reported duration for tooth brushing was 1–2 minutes. Similarly, Öztürk et al.[15] found that 86.6% of students spent over one minute brushing their teeth. This duration is generally considered sufficient for effectively removing plaque and maintaining oral hygiene.

There was a significant difference between the groups in terms of the type of toothbrush used, favoring manual toothbrushes in patients (p=0.001). This disparity may reflect varying preferences or recommendations influenced by factors such as healthcare provider advice, accessibility, or cost considerations. Electric toothbrushes appear to be a beneficial alternative for patients with rheumatoid arthritis (RA), who may find manual brushing movements challenging and painful. However, only 10 patients (6.7%) used electric toothbrushes in our cohort. Children can be educated about these alternatives, which may have an impact on their compliance with tooth brushing recommendations.

The American Academy of Pediatric Dentistry and the European Federation of Periodontology advocate for the use of fluoride toothpaste as a measure to protect against dental caries.[16,17] Fluoride is an important ingredient in toothpaste, known for its ability to remineralize tooth enamel and protect teeth from decay.[18,19] The addition of dental floss and interdental brushing to tooth brushing effectively removes plaque from interdental spaces. According to our study, a significant proportion of the patient and control groups were unaware of the contents of toothpastes, and about half of the patients used toothpastes that did not contain fluoride.

Effective oral hygiene practices, such as flossing and mouthwash, are essential. Interestingly, only 7.3% of the patients and 13.7% of the control group used dental floss, and it was statistically more common among girls in both groups. The study by Walsh et al.[20] highlighted a stark contrast, where 75% of participants flossed Daily. These findings underscore cultural and regional variations in oral hygiene practices and highlight the importance of promoting consistent oral care routines globally.

Regular dental visits play a critical role in preserving oral health and preventing dental conditions. Despite the average number of individuals per dentist being higher in Türkiye (approximately 2300) compared to European Union countries (1500),[21] a significant majority of both patients and individuals in the control group reported having visited a dentist previously when queried about their dental history. The World Health Organization (WHO) emphasizes the importance of specific age groups and criteria for assessing community oral health and recommends assessments at 5, 12, and 15 years of age.[22] A notable finding of this study was the difference in dental visit patterns between different age groups. Both patients and control subjects had more frequent dental visits between the ages of 5 and 9. This period coincides with early childhood, a crucial time for establishing basic oral health habits and receiving preventive dental care.

The establishment of oral hygiene practices in childhood begins with parental guidance at home and continues throughout life.[23] Similarly, family members were identified as the primary oral hygiene educators in both the patient and healthy control groups. These findings highlight the central role of the family in shaping oral hygiene habits and knowledge in both patients and healthy individuals. Emphasizing oral health during these formative years is critical to improving and sustaining dental health outcomes in diverse patient populations. Unfortunately, a significant percentage of individuals in both cohorts reported not attending oral health education sessions.

A notable disparity was observed between patients and controls in their interest in advancing their knowledge of oral health. Patients with rheumatic diseases may have unique challenges related to oral hygiene due to their underlying condition or medications. It's essential for healthcare providers to educate these patients about the importance of maintaining good oral hygiene practices despite any challenges posed by their condition.[24] Tailored educational initiatives that underscore the crucial link between oral health and overall systemic well-being could prove beneficial. Such interventions might involve integrating comprehensive oral health education into rheumatic disease management protocols or employing patient-centered strategies to enhance engagement.

The study has several limitations that should be acknowledged. Although the sample size was considerable, it was not very large, which may limit the generalizability of the findings to larger populations with rheumatic diseases. In addition, this study was based solely on self-report measures rather than standardized clinical examinations. Studies incorporating comprehensive dental examinations to evaluate clinical factors, the effects of oral hygiene and dietary behaviors, and the social determinants of health identified in prior research seem to be beneficial.

CONCLUSION

This survey offers valuable insights into the oral hygiene practices of patients with rheumatic diseases in comparison to healthy controls. Understanding these habits is crucial as they directly impact oral health outcomes. A closer collaboration between rheumatologists and dentists is essential to promote proper hygiene measures and to address and prevent potential oral complications effectively. We anticipate that this paper will serve as a valuable resource for evaluating public health policies and encourage colleagues to develop and implement strategies aimed at enhancing patient care.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul University, Istanbul Faculty of Medicine Ethics Committee (No: 2834454, Date: 23/08/2024).

Informed Consent: Written informed consent was obtained from the parents.

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RESEARCH ARTICLE

The Importance of Coagulation Parameters in Patients with Early and Late PPROM: A Case-Control Study Conducted in a Tertiary Center

Tolga Çiftpınar[1], Merve Aldıkaçtıoğlu Talmaç[1], Sultan Mayuncur[2], Semra Yüksel[2], İsmail Özdemir[3]

[1]Department of Gynecologic Oncology, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
[2]Department of Obstetrics and Gynecology, University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, İstanbul, Türkiye
[3]Department of Maternal-Fetal Medicine, University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: Preterm premature rupture of membranes (PPROM) is associated with an increased risk of pregnancy complications. This study evaluated the changes in coagulation parameters in pregnant women with this condition. The aim of the study is to investigate how coagulation parameters, particularly clotting time tests such as PT and aPTT, vary in pregnant patients with PPROM, which is among the causes of premature birth.

Materials and Methods: This case-control study was retrospectively planned and conducted using data from a tertiary center where maternal-fetal treatment and monitoring were provided. The study participants were divided into three groups: the early PPROM group with complaints of water leakage at 12-24 weeks of gestation, the late PPROM group with complaints of water leakage at 24-37 weeks of gestation, and the control group who did not have any complaints at 12-37 weeks of gestation. The coagulation parameters examined were the activated partial thromboplastin time, prothrombin time, INR, and fibrinogen values.

Results: The study comprised 2086 pregnant women, among whom 606 were diagnosed with early PPROM, 609 were diagnosed with late PPROM, and 871 were included in the control group. Notably, significant prolongation was observed in the PT and aPTT values of the early PPROM and late PPROM patients compared to healthy pregnant women.

Conclusion: This study highlighted that the PT and aPTT might be prolonged in pregnant women with PPROM. The potential role of coagulation parameters in the pathophysiology of early and late PPROM may be helpful for effective management of these conditions.

Keywords: Partial thromboplastin time, preterm premature rupture of the membranes, prothrombin time

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INTRODUCTION

Premature birth is a well-known complication of pregnancy that affects both the newborn and mother.[1] The instruments fundamental to the prediction of this challenging condition have not been thoroughly explored. Premature birth mainly occurs for the following reasons: maternal or fetal stress, infection, excessive myometrial distension (such as multiple pregnancies), and fetomaternal hemorrhage.[2] Prior studies have suggested that hypercoagulation may be related to preterm birth.[3] Due to the physiological changes of pregnancy, the coagulation state increases. This occurs even in uncomplicated pregnancies.[4] In most cases, the trigger that initiates preterm labor remains unidentified. Previous studies suggest that thrombin is a uterotonic agent and that high tissue factor (TF) concentrations and the thrombin-antithrombin (TAT) complex play an etiological role in the occurrence of preterm birth.[2,5] However, the issue of coagulation status in patients with preterm birth is controversial. There is still a need for studies in the literature involving many patients for this discussion.

Address for Correspondence: Tolga Çiftpınar, Department of Gynecologic Oncology, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
E-mail: tolgaciftpinar@yahoo.com **ORCID ID:** 0000-0001-7406-0629

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Preterm premature rupture of membranes (PPROM) is a condition in pregnancy where the amniotic sac breaks before the onset of labor.[6] This condition is associated with an increased risk of pregnancy complications, including infection, preterm birth, and fetal distress.[7] During pregnancy, specific changes occur in the body, which can affect the blood clotting process. The coagulation process involves the binding of several proteins and is called the coagulation cascade. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) tests are blood tests used to measure certain stages of the coagulation cascade.[8] PT is used to evaluate the extrinsic and common pathways of coagulation. The international normalised ratio (INR) value is obtained by standardizing the PT to eliminate interlaboratory differences. The aPTT is used to assess the intrinsic and common mechanisms of coagulation. Increased blood volume and changes in hormone levels can affect the clotting process during pregnancy.[9] Therefore, PT and aPTT tests can be performed during pregnancy. These tests are used to detect pregnancy-related clotting problems. While there is some evidence to suggest that pregnancy itself is a procoagulant state, there is no direct evidence to suggest that early and late PPROM specifically causes hypercoagulation in pregnancy. This study aimed to estimate the hemostatic parameters of pregnant women with premature uterine contractions and water leakage in a large patient population and to establish possible coagulation markers that can be used as an investigative tool to identify women at risk of preterm delivery.

MATERIALS and METHODS

This study was an observational case-control study and was planned retrospectively. The coagulation test results (activated partial thromboplastin time (aPTT), prothrombin time (PT), INR, and fibrinogen tests) of healthy pregnant women without complaints of water leakage and pregnant patients diagnosed with PPROM, who were hospitalized during a period of 5 years (between 01.01.2015 and 01.01.2020), were examined. The clinic where the study was conducted is a tertiary center with approximately 1500 deliveries per month and special services for the treatment of PPROM patients. Healthy pregnant women who presented to the hospital for routine ultrasonography examination were evaluated as the control group. The groups were matched similarly regarding demographic criteria such as gestational age, the number of births, and maternal age. This study was conducted in accordance with the ethical standards of the Helsinki Declaration and Ethics Committee approval, which was received from University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee with decision number KAEK/2020.07.99/03.07.2020. Among the pregnant women with water leakage complaints before the 37th gestational week, those with a positive Amnisure test were classified as having PPROM and included in the study. Pregnant women with evidence of vascular disease (hypertension, preeclampsia, pregnancy-induced hypertension, IUGR), a diagnosis of placental abruption or diabetes mellitus, a history of past thromboembolic events, thrombophilia, and multiple pregnancies were not included. Routine blood tests were requested at regular intervals from patients with no other disease, and patients presented to the pregnancy outpatient clinic for routine examination. A control group was formed by selecting the appropriate number of patients from this patient population, with similar demographic data as the study groups. The study participants were divided into three groups: the early PPROM group with complaints of water leakage at 12–24 weeks of gestation, the late PPROM group with complaints of water leakage at 24–37 weeks of gestation, and the control group who did not have any complaints at 12–37 weeks of gestation. In the power analysis, a 5% margin of error, 80% power, and a standard effect size of 0.29 were determined. It was sufficient to include n = 190 patients in each group. However, with the advantage of being a tertiary center, many patients could be screened. Accordingly, 606 patients were included in the early PPROM group, 609 patients were included in the late PPROM group, and 871 patients were included in the control group.

Data analysis was performed using SPSS (version 21.0; SPSS Inc., Chicago, IL, USA). All data were prepared as the mean ± standard deviation or the median ± min-max. One-way ANOVA was used to compare parametric variables. Tukey's HSD was used as a post hoc test to compare subgroups. Pearson correlation analysis was used to estimate the relationships between variables. A p value less than 0.05 was considered statistically significant for all calculations.

RESULTS

A total of 2086 pregnant women were included in the study. Among these, 606 patients were classified as having early PPROM, 609 were classified as having late PPROM, and 871 were included in the control group. Demographic data, including maternal age, gestational age, gravidity, parity, and educational status, were compared between the three groups (Table 1).

Table 1. Demographic data of the study and control groups

	Early PPROM group (n=606)		Late PPROM group (n=609)		Control group (n=871)		p
	n	%	n	%	n	%	
Maternal age (years)	28 (18–43)		28 (18–44)		28 (18–42)		0.067
Education							<0.001
None	1	0.2	15	2.5	0	0	
Elementary School	30	5	14	2.3	37	4.2	
Middle School	194	32.0	181	29.6	253	29.0	
High School	328	54.1	352	57.6	514	59.0	
University	49	8.1	43	7.0	61	7.0	
Master's Degree	4	0.7	6	1.0	6	0.7	
Gravidity	2 (1–12)		2 (1–10)		2 (1–11)		0.57
Parity	1 (1–11)		1 (0–6)		1 (0–9)		0.53
Gestational age	18.51±2.95		28.94±3.51		29.26±3.70		<0.001

PPROM: Preterm premature rupture of membranes

Table 2. Comparison of coagulation test results

	Early PPROM group (n=606)	Late PPROM group (n=609)	Control Group (n=871)	p
PT (sec)	12.06±1.04	11.88±0.99	11.86±0.93	<0.001
aPTT	25.48±3.53	25.96±5.26	24.92±3.27	<0.001
INR	0.98±0.09	0.96±0.08	0.97±0.08	<0.001
Fibrinogen value	432±126	403±114	423±120	<0.001
Platelet value	260±66	252±120	250±69	0.076

PPROM: Preterm premature rupture of membranes; PT: Prothrombin time; aPTT: Activated partial thromboplastin time; INR: International normalised ratio

Table 3. The correlations among the groups

	PT p value	APTT p value	INR p value	Fibrinogen value p value	Platelet value p value
Early PPROM-late PPROM	0.004	0.100	<0.001	<0.001	0.193
Early PPROM-control	<0.001	0.023	0.100	0.357	0.076
Late PPROM-control	0.908	<0.001	0.121	0.006	0.953

PT: Prothrombin time; aPTT: Activated partial thromboplastin time; INR: International normalised ratio; PPROM: Preterm premature rupture of membranes

There was a significant difference among the groups in the PT, APTT, INR, and fibrinogen values (p<0.001). The comparison of coagulation test results among the groups is shown in Table 2.

When the PPROM groups were compared with the control group, the PT and APTT values differed significantly (p<0.001). The correlation between the groups is shown in Table 3.

DISCUSSION

Early and late PPROM are well-known complications of pregnancy that can affect both the newborn and mother.[10] The mechanisms essential to these challenging conditions have yet to be fully explored. Earlier studies have suggested that hypercoagulability may be related to amniotic fluid in the early weeks of pregnancy.[11] The incidence of preterm premature rupture of membranes (PPROM) is estimated to

be approximately 0.5% before 27 weeks gestation and approximately 1% between 27 and 34 weeks gestation, based on various studies.[12] Similarly, the incidence of early PPROM in the study population was 0.2%. This study aimed to investigate the changes in coagulation parameters in a large patient series of pregnant women with amniotic fluid leakage in the early weeks of pregnancy. This study revealed a significantly longer PT and aPTT in PPROM patients than in healthy pregnant women. Based on the literature, it is understood that there are few studies investigating coagulation parameters such as PT, aPTT, and fibrinogen values in patients with PPROM.[13,14] Our study showed that these values varied significantly compared to those of the control group. This study was a retrospective study, and the results of the patients' situations were considered. Our opinion is that this change in the coagulation tests is due to the state of coagulopathy that PPROM can cause in the body, rather than PPROM occurring because of the coagulopathy.

The PT test is a blood test that measures the time it takes for blood to clot.[15] In pregnant women, the PT can indicate the body's ability to form blood clots, as blood coagulability is increased during pregnancy. However, the PT can be affected by various factors, including changes in hormone levels, blood volume, and liver function.[16] In PPROM patients, some evidence suggests that the PT may be prolonged compared to that in women with normal pregnancies. However, there is also evidence that the PT is shortened, although the number of patients in these studies was limited.[11] This may be due to the release of factors from the amniotic fluid, which can activate the coagulation system and lead to increased consumption of clotting factors. Additionally, PPROM is often associated with inflammation and infection, which can further affect the coagulation system and lead to a more prolonged PT.[17] In our study, it was shown that PT was prolonged in a high number of pregnant women with PPROM.

PPROM in pregnancy can lead to increased levels of certain clotting factors in the blood, which can prolong the aPTT.[18] The aPTT test is a laboratory test that measures the time it takes for blood to clot. It is used to monitor the effectiveness of blood-thinning medications and diagnose bleeding disorders. A longer aPTT can indicate a potential clotting disease in a pregnant woman, increasing the risk of complications such as deep vein thrombosis or placental abruption.[19] During pregnancy, the body undergoes several changes that can affect blood clotting.[20] Hormonal changes can increase the levels of clotting factors in the blood while simultaneously reducing the levels of anticoagulants, which can lead to a hypercoagulable state. In cases of PPROM, there is an increased risk of infection, which can further increase clotting factors in the blood.[21] Similarly, our study found that the aPTT values were longer in pregnant women in the PPROM groups than in the control group.

Thrombin can bind to many cell surface receptors that regulate the cellular response through protease activity. In addition to the coagulation system, these include proteinase-activated receptor-1 (PAR-1). After thrombin binding, PAR-1 receptors activate several signaling pathways in cells, resulting in the production of matrix metalloproteinases and cytokines.[22] In cases such as premature rupture of the membranes of the placenta during pregnancy, tissue destruction and inflammation may develop due to the effects of thrombin on PAR-1 receptors.[23] Thrombin, via PAR-1 receptors, increases the inflammatory response by increasing the production of cytokines released as a result of infection or inflammation. As a result, destruction of the membranes of the placenta, edema, bleeding, and other signs of inflammation may occur. In addition, due to the effects of thrombin on PAR-1 receptors, the risk of delivery may be increased during PPROM. During pregnancy, thrombin production increases, and blood clot tendency increases. Excessive thrombin formation is associated with complications such as preeclampsia and HELLP syndrome.[24] These conditions harm the coagulation system by increasing thrombin production and platelet activation. In such cases, the prolongation of the PT and aPTT can be observed. The prolongation of the PT and aPTT in our study may be a precursor to this path. Studies including obstetric results should be planned to elucidate this issue.

In a previous study, it was observed that women who experienced preterm labor had shortened PT and aPTT values, indicating the activation of both intrinsic and extrinsic pathways in preterm birth. The observed shortening of the aPTT in women with preterm labor could potentially be explained by the slightly elevated VWF antigen levels and factor VIII activity found in the preterm birth group. However, it is important to note that this study had limitations in terms of its relatively small sample size.[11] In contrast, our study benefited from a significantly large sample size, which strengthens and supports the findings of the previous study. The study's limitations include its retrospective nature and the limited number of included coagulation parameters. However, when we look at the literature, we see that this study has the most extensive series evaluating the values of coagulation parameters in these two disease groups.

CONCLUSION

In conclusion, PPROM is a complex and significant complication of pregnancy that can have serious consequences for both the mother and newborn. The mechanisms underlying this condition are not fully understood, but our study suggests that coagulation parameters, such as prothrombin time PT and activated partial thromboplastin time (aPTT), may be altered in pregnant women with PPROM. Our findings indicate that both PT and aPTT are prolonged in women with PPROM, which could reflect a hypercoagulable state that contributes to the pathophysiology of this condition. The results also highlight the potential role of coagulation markers in the management and monitoring of PPROM patients. Further studies are needed to investigate the exact mechanisms behind these changes and their clinical implications for the treatment and outcomes of PPROM. Monitoring coagulation parameters may provide valuable insights into the risk factors associated with PPROM and help in the development of more targeted therapeutic strategies to manage this condition effectively.

Disclosures

Ethics Committee Approval: The study was approved by the University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (No: 2020.07.99, Date: 03/07/2020).

Informed Consent: Informed consent was obtained from all participants or their caregivers, where applicable.

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RESEARCH ARTICLE

Atherogenic Index of Plasma and Its Relationship with Acute Pancreatitis Severity: A Retrospective Cohort Study

Özgür Yılmaz[1], Sami Çifçi[2]

[1]Department of Internal Medicine, Kanuni Sultan Suleyman Training and Research Hospital, İstanbul, Türkiye
[2]Department of Gastroenterology, Başaksehir Çam and Sakura City Hospital, İstanbul, Türkiye

ABSTRACT

Objective: Acute pancreatitis (AP) varies in severity, making early identification of severe acute pancreatitis (SAP) essential. As lipid imbalance has been increasingly linked to inflammatory activation, the Atherogenic Index of Plasma (AIP) has been proposed as a potential prognostic marker. This study evaluated the association between AIP and AP severity and assessed whether AIP independently predicts SAP.

Materials and Methods: This retrospective cohort included 203 adult patients with acute pancreatitis. Classification of acute pancreatitis followed the Revised Atlanta Criteria. Demographic, laboratory, and lipid data were extracted from electronic records, and AIP was calculated using triglyceride and HDL-cholesterol values. Analyses included group comparisons, correlation testing, comprehensive ROC analyses, multivariable logistic regression, and a covariate-adjusted ROC.

Results: Among 203 patients, 128 had MAP and 75 had SAP. SAP patients showed significantly higher WBC, glucose, creatinine, AST, ALT, and CRP levels (all p<0.001) and lower HDL-C (p=0.024). Mean AIP was higher in SAP (0.59±0.15 vs. 0.53±0.20; p=0.016) but demonstrated limited discrimination (AUC 0.575; cut-off 0.390; sensitivity 96.0%, specificity 22.7%). AIP was significant in unadjusted and WBC-adjusted models (p=0.023 and p=0.043, respectively), but not in the fully adjusted model including WBC and glucose (p=0.196). The covariate-adjusted ROC showed excellent accuracy (AUC 0.892; sensitivity 84.0%, specificity 79.7%).

Conclusion: Although higher in severe cases, AIP did not independently predict severity. While insufficient alone, AIP may contribute supportive value when combined with inflammatory and metabolic markers.

Keywords: Acute pancreatitis, AIP, atherogenic index of plasma, HDL-cholesterol, severe acute pancreatitis, triglycerides

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INTRODUCTION

Acute pancreatitis (AP) is an inflammatory disorder of the pancreas with a broad clinical spectrum, ranging from mild, self-limiting disease to severe necrotizing pancreatitis complicated by organ failure and high mortality. Its global incidence has risen steadily over the past two decades, reaching 20–40 cases per 100,000 population annually.[1,2] Despite advances in diagnosis and management, mortality in severe cases may still reach 15–30%.[3,4] Early identification of patients at risk of severe disease is therefore essential to guide intensive monitoring and timely intervention.

According to the 2012 Revised Atlanta Classification (RAC), acute pancreatitis is categorized into mild, moderately severe, and severe forms based on the presence, duration, and consequences of organ failure, as well as local complications.[5] Although this system improves diagnostic consistency, it does not provide real-time prognostic information. Several scoring systems, such as the Bedside Index for Severity in Acute Pancreatitis (BISAP), Ranson's criteria, and the Modified CT Severity Index (MCTSI), are commonly used for early risk assessment; however, their diagnostic performance is variable, and some require imaging or parameters that may not be immediately available in the acute setting.[6–9]

Address for Correspondence: Özgür Yılmaz, Department of Internal Medicine, Kanuni Sultan Suleyman Training and Research Hospital, İstanbul, Türkiye
E-mail: dr_ozguryilmaz@hotmail.com **ORCID ID:** 0009-0000-4976-4771

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Disturbances in lipid metabolism are increasingly recognized in the pathophysiology of AP. Hypertriglyceridemia accounts for 5–10% of cases and is the third most common etiology after gallstones and alcohol.[10] Experimental and clinical studies have shown that triglyceride (TG) hydrolysis by pancreatic lipase generates cytotoxic free fatty acids (FFAs), which induce acinar injury, microvascular dysfunction, and systemic inflammation.[11,12] Conversely, high-density lipoprotein cholesterol (HDL-C) exerts antioxidant and anti-inflammatory effects, and low HDL-C levels have been associated with organ failure and increased disease severity in AP.[13,14] These opposing biological roles suggest that combined lipid indices may provide insights into inflammatory and metabolic stress during early disease.

The Atherogenic Index of Plasma (AIP) combines triglyceride and HDL-C levels into a single indicator of atherogenic dyslipidemia. Because it is derived from routinely measured lipid parameters, AIP reflects the balance between pro-inflammatory triglycerides and the anti-inflammatory, antioxidant functions of HDL-C.[15,16] Recent studies have shown that elevated AIP at admission is associated with a higher likelihood of severe acute pancreatitis. Cho et al.[17] reported that increased AIP independently predicted severe disease in a Korean cohort, while Wu et al.[18] demonstrated that AIP was linked to both severe pancreatitis and the development of acute kidney injury, a major contributor to morbidity. These observations, together with mechanistic evidence that systemic inflammation rapidly decreases HDL-C and increases triglyceride concentrations, support the concept that AIP may serve as an early surrogate marker of metabolic and inflammatory stress in acute pancreatitis.[17]

Although these findings are promising, several uncertainties remain. Reported AIP cut-off values vary across studies, the timing of lipid measurement is not standardized, and data on its additive value over established scoring systems are limited. Further research is therefore needed to clarify whether AIP provides independent and clinically meaningful prognostic information in acute pancreatitis.

The present study aims to evaluate the relationship between the AIP and disease severity in acute pancreatitis and to determine whether AIP serves as an independent predictor of severe acute pancreatitis in a retrospective patient cohort.

MATERIALS and METHODS

Study Design and Settings

This retrospective cohort study included adult patients diagnosed with acute pancreatitis who were hospitalized in the Internal Medicine ward of our tertiary care center between 1 January 2022 and 31 December 2024. Patient data, including demographic characteristics, comorbidities, laboratory values, and imaging findings, were obtained from the institutional electronic medical record system. The diagnosis of acute pancreatitis was established according to the 2012 Revised Atlanta Classification, requiring the presence of at least two of the following: typical abdominal pain, elevation of serum amylase or lipase to at least three times the upper limit of normal, or radiological evidence consistent with acute pancreatitis.[5] Disease severity was defined based on the same criteria; patients without organ failure and without local or systemic complications were categorized as having mild acute pancreatitis (MAP), whereas those with persistent organ failure lasting more than 48 hours, as defined by the Modified Marshall scoring system, were classified as having severe acute pancreatitis (SAP).[19] Patients who met the criteria for "moderately severe" disease, that is, those with transient organ failure or local complications, were included in the MAP group to maintain a binary classification suitable for the analytical design of the study.[20] Exclusion criteria included chronic pancreatitis, pancreatic malignancy, cirrhosis, chronic kidney disease stage ≥ 3, thyroid dysfunction, pregnancy, active systemic infection, chronic inflammatory disorders, use of lipid-lowering therapy within the previous three months, known primary hyperlipidemia, and incomplete laboratory data within 24 hours of admission. After application of these criteria, a total of 203 patients were included in the final analysis.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Local Ethics Committee of Kanuni Sultan Suleyman Training and Research Hospital (decision date: 21.04.2025, number: E-80929729-000-274110217). Because of the retrospective nature of the study, the requirement for written informed consent was waived. All data were anonymized before analysis to ensure patient confidentiality.

Calculation of Atherogenic Index of Plasma

Serum TG and HDL-C levels were obtained from admission laboratory records. Measurements were performed using enzymatic colorimetric assays on a Roche Cobas 8000 analyzer (Roche Diagnostics, Mannheim, Germany), according to the hospital's routine laboratory procedures. In this study, both triglycerides (TG) and HDL-cholesterol (HDL-C) were measured in mg/dL. The AIP was calculated using the formula $\log_{10}$(TG/HDL-C). Additional laboratory parameters, including amylase, lipase, glucose, calcium, creatinine, and C-reactive protein (CRP), were retrieved from electronic medical records. All lipid measurements (triglycerides and HDL-cholesterol) were obtained within the first 24 hours of hospital

admission as part of the routine initial laboratory evaluation. All biochemical analyses were conducted in the hospital's central laboratory following standard operating protocols.

Outcomes

The primary outcome of the study was to determine the association between the AIP and the severity of acute pancreatitis, classified as mild or severe based on the Revised Atlanta Criteria. Secondary outcomes included evaluating the relationship between AIP and key laboratory parameters, assessing its discriminative ability for predicting severe disease through ROC analysis, and determining whether AIP remained an independent predictor of severity in multivariable logistic regression models.

Statistical Analysis

Statistical analyses were performed using Python 13.3 (pandas, numpy, scikit-learn, matplotlib) and IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed with the Kolmogorov–Smirnov and Shapiro–Wilk tests. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were summarized as median (Q1–Q3). Group comparisons were conducted using the independent-samples t-test or Welch's t-test when variances were unequal, and the Mann–Whitney U test for non-normally distributed data. Categorical variables were compared with Pearson's chi-square test. Correlations between AIP and clinical or biochemical parameters were examined using Pearson or Spearman correlation coefficients based on variable distribution. To evaluate independent predictors of SAP, multivariable binary logistic regression analysis was performed by incorporating AIP together with white blood cell (WBC) count and serum glucose, which were selected due to their clinical relevance and statistical significance in univariate analyses. Odds ratios (ORs) with 95% confidence intervals (CIs) and Wald statistics were reported. Multicollinearity was assessed through variance inflation factor (VIF) and tolerance values, with VIF <5 considered acceptable. Discriminative performance was evaluated using two receiver operating characteristic (ROC) analyses. First, univariable ROC curves were generated for AIP, triglyceride, and HDL-C to quantify their individual ability to distinguish between mild and severe acute pancreatitis. Second, an adjusted ROC curve was constructed using the predicted probabilities obtained from the final multivariable logistic regression model, in which AIP, white blood cell count, and serum glucose were included as covariates. All ROC analyses were performed in Python, and the area under the curve (AUC), optimal cut-off values, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using the Youden index. Graphical outputs were generated in high resolution. A two-tailed p-value <0.05 was considered statistically significant.

Table 1. Baseline demographic and clinical characteristics of patients with mild and severe acute pancreatitis

Parameters	MAP (n=128)		SAP (n=75)		p
	n	%	n	%	
Age, years	54.5 (34–75)		52 (36–68)		0.725[U]
Sex					
Female	61	47.7	35	46.7	0.892[†]
Male	67	52.3	40	53.3	
BMI, kg/m²	27.2±3.6		26.8±4		0.406[t]
Length of hospital stay (day)	5 (4–6)		9 (7–20)		<0.001[U]
DM	67	52.3	30	40	0.089[†]
HT	63	49.2	39	52	0.702[†]
Smoking (Yes)	66	51.6	39	52	0.952[†]
Etiology					0.209[†]
Idiopathic	43	33.6	31	41.3	
Gallstones	29	22.7	8	10.7	
Alcohol-related	25	19.5	20	26.7	
Drug-induced	26	20.3	14	18.7	
Autoimmune	5	3.9	2	2.7	
Pancreatitis type					
Interstitial edematous pancreatitis	116	90.6	30	40	<0.001[†]
Necrotizing pancreatitis	12	9.4	45	60	

Values are presented as mean±standard deviation (SD), median (interquartile range: Q1–Q3), or number (percentage). [U]: Mann–Whitney U test; [t]: Independent Samples t-test; [†]: Pearson chi-square test. MAP: Mild acute pancreatitis; SAP: Severe acute pancreatitis; DM: Diabetes mellitus; HT: Hypertension; BMI: Body mass index

RESULTS

A total of 203 patients were included, comprising 128 with MAP and 75 with SAP. Baseline demographic variables, including age, sex, body mass index, diabetes mellitus, hypertension, smoking status, and etiological factors, did not differ significantly between the two groups (all p>0.05). The median length of hospital stay was markedly longer in the SAP group (9 vs. 5 days; p<0.001). Edematous pancreatitis predominated in MAP, whereas necrotizing pancreatitis was substantially more frequent in SAP (p<0.001). Detailed characteristics are presented in Table 1.

Table 2. Comparison of laboratory and biochemical parameters between mild and severe acute pancreatitis

Parameters	MAP (n=128)	SAP (n=75)	p
WBC, $\times 10^9$/L	8.14±1.02	9.07±1.03	<0.001[t]
Glucose, mg/dL	118.4±25.5	164.8±35.6	<0.001[t]
Creatinine, mg/dL	0.91±0.22	1.38±0.34	<0.001[t]
Total Cholesterol, mg/dL	186.6±31.2	182.3±29.4	0.333[t]
LDL-C, mg/dL	108.8±27.8	110.5±29	0.678[t]
AST, U/L	27 (18–33)	36 (30–45)	<0.001[U]
ALT, U/L	24 (19–32)	34 (24–39)	<0.001[U]
Amylase, U/L	192 (177–204)	193 (179–210)	0.264[U]
Lipase, U/L	616.5 (490–723)	621 (506–739)	0.971[U]
Calcium, mg/dL	9.20 (8.75–9.70)	9.30 (9–9.6)	0.584[U]
CRP, mg/L	20 (17–22.5)	27 (24–33)	<0.001[U]
Triglyceride, mg/dL	162.5 (118.5–216)	165 (134–211)	0.399[U]
HDL-C, mg/dL	46 (40–54)	42 (36–49)	0.024[U]

Values are presented as mean±standard deviation (SD) or median (interquartile range: Q1–Q3). [U]: Mann–Whitney U test; [t]: Independent Samples t-test. MAP: Mild acute pancreatitis; SAP: Severe acute pancreatitis; WBC: White blood cell; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein

Biochemical analyses revealed significantly higher white blood cell counts, serum glucose, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and CRP levels in SAP patients compared with MAP (all p<0.001). HDL levels were modestly but significantly lower in SAP (p=0.024). No significant differences were observed in total cholesterol, LDL-C, TG, amylase, lipase, or calcium values (Table 2).

AIP values were compared between the MAP and SAP groups. Levene's test indicated that the assumption of equal variances was violated, F(1, 201) =6.84, p=0.010. Accordingly, an independent-samples t-test with unequal variances was performed. The mean AIP value was significantly higher in the SAP group (M=0.59, SD=0.15) compared with the MAP group (M=0.53, SD=0.20), t(188.25)=-2.43, p=0.016, with a mean difference of -0.061 (95% CI: -0.1106 to -0.0114). The distribution of AIP values across severity groups is illustrated in Figure 1.

In correlation analysis, AIP demonstrated a negative association with age in the MAP group (ρ=-0.232, p=0.008)

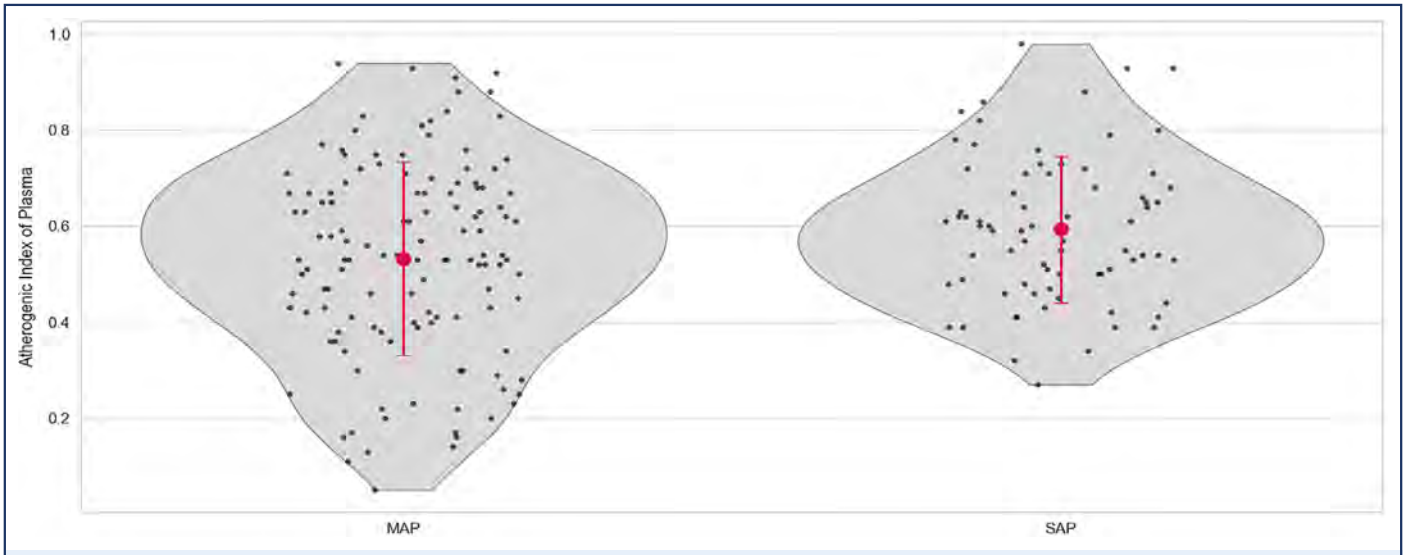

Figure 1. Distribution of AIP values in mild (MAP) and severe (SAP) acute pancreatitis

AIP: Atherogenic index of plasma; MAP: Mild acute pancreatitis; SAP: Severe acute pancreatitis

Table 3. Correlation of AIP with demographic and biochemical variables

	MAP (n=128)		SAP (n=75)	
	r/ρ	p	r/ρ	p
Age[ρ]	**-0.232**	**0.008**	-0.027	0.816
BMI[r]	-0.025	0.783	0.063	0.590
Length of hospital stay[ρ]	-0.020	0.819	-0.134	0.252
WBC[r]	0.069	0.442	-0.009	0.939
Glucose[r]	0.064	0.471	-0.037	0.749
Creatinine[r]	0.113	0.204	0.077	0.513
Total cholesterol[r]	0.041	0.646	-0.036	0.760
LDL-C[r]	-0.020	0.821	-0.199	0.087
AST[ρ]	0.075	0.400	-0.139	0.234
ALT[ρ]	0.057	0.521	**0.258**	**0.025**
Amylase[ρ]	0.115	0.198	-0.166	0.156
Lipase[ρ]	-0.137	0.123	-0.121	0.300
Calcium[ρ]	0.160	0.072	0.075	0.524
CRP[ρ]	0.046	0.604	0.104	0.376

Values are presented as correlation coefficients. [r]: Pearson correlation coefficient; [ρ]: Spearman correlation coefficient. AIP: Atherogenic index of plasma; MAP: Mild acute pancreatitis; SAP: Severe acute pancreatitis; BMI: Body mass index; WBC: White blood cell; LDL-C: Low density lipoprotein cholesterol; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein

and a weak positive correlation with ALT in the SAP group (ρ=0.258, p=0.025). No other significant correlations were identified (Table 3).

ROC analysis demonstrated that AIP alone had limited discriminative ability for identifying severe pancreatitis, with an AUC of 0.575. Using a cut-off value of 0.390, AIP yielded 96.0% sensitivity, 22.7% specificity, 42.1% positive predictive value, and 90.6% negative predictive value. TG (AUC 0.536) and HDL-C (AUC 0.405) showed similarly poor performance (Fig. 2).

Binary logistic regression analyses evaluating the contribution of AIP to SAP are presented in Table 4. In Model 1, AIP was significant (OR 6.817, 95% CI 1.307–35.563; p=0.023), although the overall model fit was not significant. In Model 2, AIP remained significant (OR 6.397; p=0.043), and WBC emerged as an independent predictor (OR 2.587; p<0.001). In the fully adjusted Model 3, AIP was no longer significant (p=0.196), whereas both WBC and glucose remained strong independent predictors (both p<0.001). Model performance improved progressively across models (NR^2: 0.06 → 0.27 → 0.61), with no evidence of multicollinearity (VIF<5.0; tolerance >0.20).

To evaluate AIP's discriminative capacity after adjustment for confounders, a model-based ROC curve was generated using predicted probabilities from the fully adjusted logistic regression model (Model 3). This adjusted ROC demonstrated excellent discriminative performance (AUC 0.892), with 84.0% sensitivity, 79.7% specificity, 70.8% PPV, and 89.5% NPV (Fig. 3).

DISCUSSION

This study evaluated the predictive performance of the AIP in acute pancreatitis and demonstrated that AIP values were significantly higher in patients with SAP compared with those with mild disease. The group difference was also

Table 4. Evaluation of AIP's contribution to severe acute pancreatitis using different binary logistic regression models

	B	SE	Wald	df	p	OR	95% CI	
							LL	UL
Model 1								
AIP	1.919	0.843	5.187	1	0.023	6.817	1.307	35.563
Model 2								
AIP	1.856	0.915	4.112	1	0.043	6.397	1.064	38.458
WBC	0.951	0.184	26.814	1	<001	2.587	1.805	3.708
Model 3								
AIP	1.519	1.175	1.670	1	0.196	4.566	0.456	45.699
WBC	0.917	0.230	15.861	1	<001	2.501	1.593	3.926
Glucose	0.054	0.009	38.011	1	<001	1.055	1.037	1.073

All models were adjusted for age, BMI, sex (female), smoking status (non-smoker), diabetes mellitus (yes), and hypertension (yes). Model 1: NR^2=0.06, χ^2=9.12, p=0.238; Model 2: NR^2=0.27, χ^2=44.99, p<0.001; Model 3: NR^2=0.61, χ^2=119.28, p<0.001. B: Regression coefficient; SE: Standard error; OR: Odds ratio; 95% CI: 95% confidence interval; LL: Lower limit; UL: Upper limit; Wald: Wald test value; df: Degrees of freedom; p: significance level; NR^2: Nagelkerke R-squared; χ^2: Chi-square test; VIF: Variance inflation factor; AIP: Atherogenic index of plasma; WBC: White blood cell

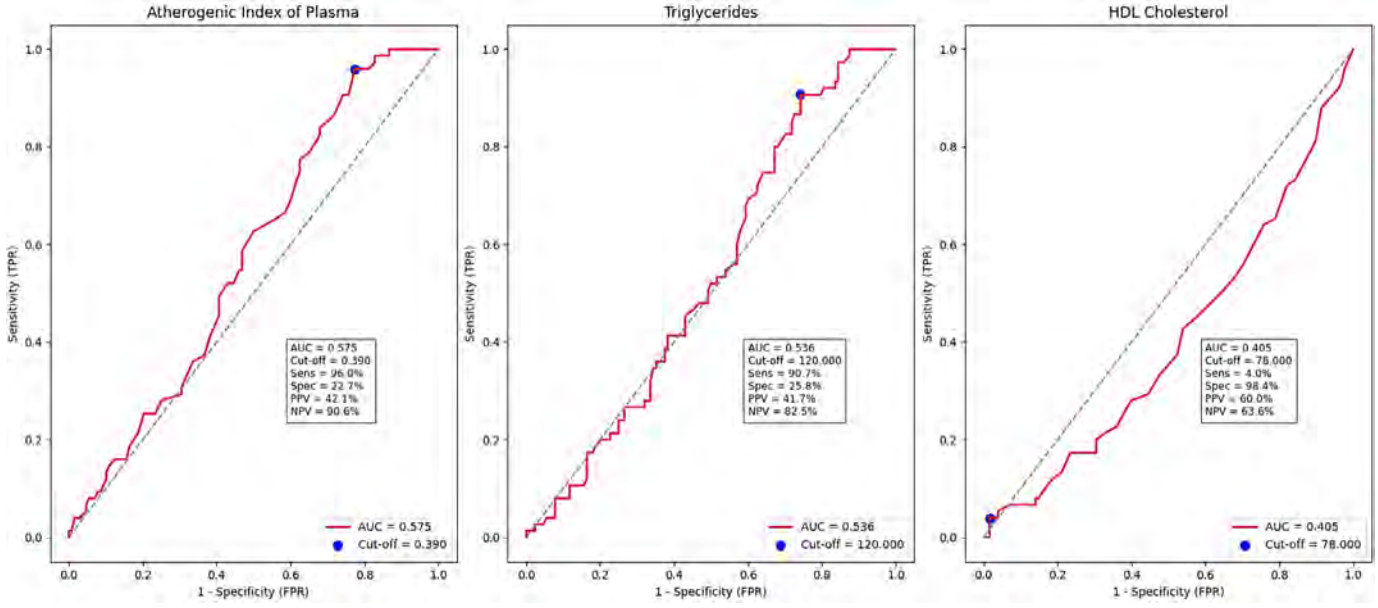

Figure 2. ROC curves showing the discriminative performance of AIP, triglyceride, and HDL-C for identifying severe acute pancreatitis

ROC: Receiver operating characteristic; AIP: Atherogenic index of plasma; HDL-C: High-density lipoprotein cholesterol

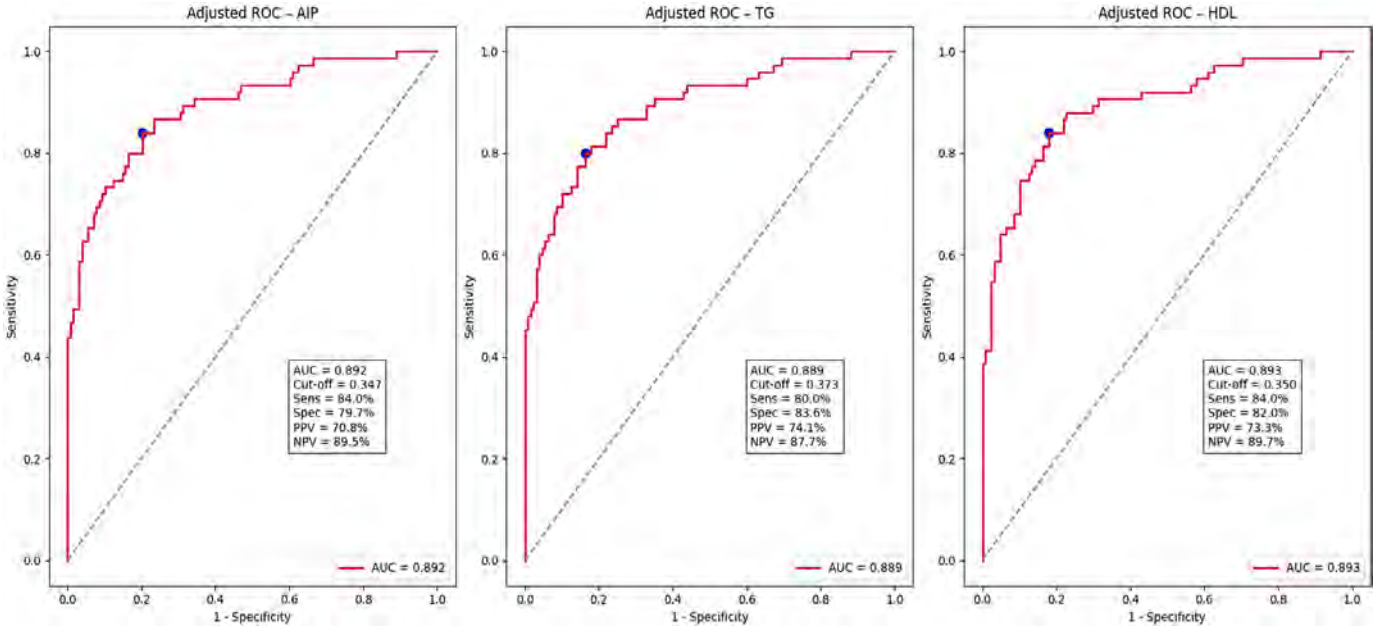

Figure 3. ROC curve of AIP adjusted for WBC and glucose using the final multivariable logistic regression model (Model 3)

ROC: Receiver operating characteristic; AIP: Atherogenic index of plasma; WBC: White blood cell

clearly depicted in the AIP distribution (Fig. 1), highlighting the shift toward higher metabolic–inflammatory burden in SAP. Furthermore, AIP showed modest correlations with age in MAP and with ALT in SAP, suggesting partial overlap between lipid dysregulation, hepatocellular stress, and systemic inflammation. However, despite these associations,

AIP exhibited only limited discriminatory capacity and, critically, did not remain an independent predictor once white blood cell (WBC) count and serum glucose were included in the multivariable logistic regression model. These findings indicate that AIP alone cannot serve as a reliable standalone biomarker for early severity assessment.

Our results partially align with earlier studies reporting elevated AIP levels in SAP. In a prospective cohort, Cho et al.[17] demonstrated that AIP was significantly higher in SAP compared with mild AP and remained an independent predictor after multivariable adjustment. Similarly, Wu et al.[18] found AIP to be significantly associated with AKI and SAP, although the reported AUC values, approximately 0.65, indicated only moderate discriminative performance. In both studies, AIP demonstrated predictive value for severe acute pancreatitis; however, neither achieved high diagnostic accuracy. Consistent with these observations, the AIP ROC performance in our cohort was similarly modest (AUC 0.575), reinforcing the conclusion that AIP alone has limited discriminative strength. These findings, supported by prior clinical evidence showing that triglyceride elevation and HDL reduction parallel inflammatory severity in acute pancreatitis—particularly in hypertriglyceridemia-associated cases—suggest that AIP largely reflects the metabolic response to systemic inflammation rather than functioning as a robust independent prognostic marker.[17,21,22]

Our multivariable findings diverge from earlier reports largely because prior studies did not adjust for essential inflammatory and metabolic predictors, particularly WBC and glucose. They often relied on smaller or more homogeneous cohorts and seldom evaluated AIP alongside a broader panel of laboratory parameters. By incorporating these critical covariates within a structured multivariable binary logistic regression framework, our study is among the first to demonstrate that AIP loses its apparent predictive significance once key upstream physiological determinants are accounted for. This methodological distinction likely explains the discrepancy between our results and previously published associations.

A distinguishing strength of our work is the comprehensive multivariable modeling approach that incorporated major inflammatory and metabolic predictors. In contrast with earlier studies, our analysis showed that WBC and glucose were strong and independent determinants of SAP (both $p<0.001$), and their inclusion in the binary logistic regression models eliminated the statistical significance of AIP. This finding is biologically plausible: AIP is derived from triglyceride and HDL concentrations, which undergo rapid cytokine-driven alterations during acute inflammatory states. Feingold and Grunfeld demonstrated that TNF-α and IL-6 markedly suppress HDL synthesis and accelerate HDL clearance during the acute-phase response, while Pirillo and Catapano reported proportional HDL reductions with increasing inflammatory severity.[23,24] Additionally, prior clinical and experimental data have shown that stress hyperglycemia and hypertriglyceridemia contribute to metabolic instability and correlate with AP severity.[25] Taken together, these observations suggest that AIP reflects the broader metabolic-inflammatory milieu rather than functioning as an independent prognostic marker, supporting its use as a potential adjunctive but not standalone indicator.

The strong performance of our fully adjusted model with an AUC of 0.892 further underscores the superiority of composite approaches integrating inflammatory and metabolic indicators. This finding is consistent with the broader AP literature. Venkatesh et al.[26] showed that composite models incorporating inflammatory and biochemical parameters outperform single biomarkers. Mofidi et al.[27] reported that inflammatory markers, particularly WBC, were strongly associated with organ failure and mortality. Our findings extend this evidence by demonstrating a substantial improvement in predictive performance when WBC and glucose are included alongside AIP in a multivariable framework.

Nevertheless, some limitations merit consideration. The retrospective design may introduce residual confounding despite adjustment. The sample size, while larger than many prior AIP–AP studies, may still not be sufficient to detect smaller effect sizes in subgroup analyses. In addition, lipid measurements were taken at a single time point; future work should evaluate dynamic lipid changes across different disease stages. Moreover, because this was a single-center study, the results may reflect local laboratory standards, patient demographics, and institutional management practices, which may limit broader applicability. Variations in early resuscitation intensity, analgesic strategies, nutritional timing, and imaging schedules could also have influenced lipid profiles and clinical parameters. Additionally, although standardized severity criteria were applied, subtle differences in clinical documentation or timing of assessment may have introduced classification variability.

CONCLUSION

AIP levels were higher in severe acute pancreatitis, but its independent significance diminished after adjusting for inflammatory and metabolic markers. While AIP alone is insufficient for early severity assessment, it may still provide supportive value when incorporated into multivariable models alongside WBC and glucose. Future prospective studies should clarify its additive role within integrated prediction frameworks.

Disclosures

Ethics Committee Approval: The study was approved by the Kanuni Sultan Suleyman Training and Research Hospital Ethics Committee (No: E-80929729-000-274110217, Date: 21/04/2025).

Informed Consent: Because of the retrospective nature of the study, the requirement for written informed consent was waived. All data were anonymized before analysis to ensure patient confidentiality.

Conflict of Interest Statement: No conflict of interest was declared by the authors.

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RESEARCH ARTICLE

Effect of Water Temperature on Bowel Cleansing Quality: A Prospective Observational Study

Nurettin Şahin[1], Ufuk Mete Yıldız[2]

[1]Department of General Surgery, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Türkiye
[2]Department of General Surgery, Bahçelievler State Hospital, İstanbul, Türkiye

ABSTRACT

Objective: The effectiveness of bowel preparation in colonoscopy is influenced by several factors, including the type of preparation used, timing, and level of hydration. However, the impact of water temperature consumed during bowel preparation on cleansing quality has not been adequately described in the literature. This prospective observational study aimed to compare the effects of cold and lukewarm water consumption during bowel preparation on bowel cleansing quality, patient tolerance, and procedure-related outcomes.

Materials and Methods: A total of 260 patients were included in the study. Participants were divided into two groups according to the temperature of the water consumed during bowel preparation: cold water (2–6°C) and lukewarm water (24–28°C). All patients followed the same bowel preparation protocol, consisting of a sodium phosphate solution and an enema. Bowel cleansing quality was assessed using the Boston Bowel Preparation Scale.

Results: Nausea was more frequently observed in the lukewarm water group (p=0.030), while no significant differences were found in other adverse effects. The withdrawal time was shorter in the lukewarm water group (2.7±1.5 min vs. 3.2±1.8 min; p=0.003). The mean total BBPS score was significantly higher in the lukewarm water group (7.37±1.67 vs. 6.43±2.17; p<0.001).

Conclusion: Consumption of lukewarm water during bowel preparation significantly improved bowel cleansing quality, enhanced patient tolerance, and reduced procedure time. These findings suggest that water temperature is an overlooked yet important variable that should be considered in routine colonoscopy preparation protocols.

Keywords: Boston Bowel Preparation Scale (BBPS), bowel preparation, colonoscopy, water temperature

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INTRODUCTION

Colorectal cancer (CRC) ranks as the third leading cause of cancer-related mortality worldwide, with approximately one million new cases reported annually. Colonoscopy remains the gold standard method for the early diagnosis and prevention of CRC, as it allows for the direct detection and removal of precancerous lesions. High-quality colonoscopy has been shown to significantly reduce mortality associated with colorectal cancer.[1,2]

The diagnostic and therapeutic efficacy of colonoscopy largely depends on the endoscopist's experience and, to a great extent, on the quality of bowel preparation. Inadequate bowel cleansing (IBC) may result in failure to reach the cecum, reduced mucosal visibility, and decreased adenoma detection rates (ADR).[3] Despite the availability of different bowel preparation regimens, inadequate preparation rates have been reported to reach up to 30%.[4] This situation adversely affects not only procedural success but also patient comfort, overall cost, and the need for repeat colonoscopy.[5]

Numerous studies have extensively investigated the factors leading to IBC. Age, sex, constipation, history of abdominal surgery, diabetes, compliance with preparation instructions, and the interval between bowel preparation and colonoscopy have been identified as major determinants.[4]

Address for Correspondence: Nurettin Şahin, Department of General Surgery, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Türkiye
E-mail: dr.nurettinsahin@gmail.com **ORCID ID:** 0000-0001-7440-0574

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Therefore, establishing an effective and safe bowel preparation protocol is of great clinical importance.

Bowel preparation solutions are generally classified into two main categories: high-volume (HV) and low-volume (LV) formulations. HV polyethylene glycol (PEG, 4 L) solutions have long been considered the standard; however, poor palatability and gastrointestinal discomfort often lead to reduced patient compliance. In contrast, LV preparations (1–2 L PEG, sodium phosphate [NaP], or sodium picosulfate with magnesium citrate [SPMC]) provide comparable cleansing quality with better tolerability and fewer adverse effects.[6,7]

In addition to the type of bowel preparation agent, the method of administration, dosage, timing, and dietary protocol also influence the effectiveness of cleansing. However, to date, no study has evaluated the impact of the temperature of water consumed during colonoscopy preparation on bowel cleansing quality. This study aimed to assess the effect of this simple yet potentially clinically significant factor on the effectiveness of bowel preparation.

MATERIALS and METHODS

Study Design and Ethical Approval

This prospective observational study was conducted in the Department of General Surgery at Bahçelievler State Hospital between February and July 2025. The study protocol was approved by the local ethics committee (Approval No: 2024-15-17, Date: December 25, 2024). Written informed consent was obtained from all participants before inclusion, and the study was performed in accordance with the principles of the Declaration of Helsinki.

Study Population

Patients scheduled for elective colonoscopy at the Endoscopy Unit of the General Surgery Department were divided into two groups according to the temperature of the water consumed during bowel preparation: the cold-water (CW) group and the lukewarm-water (LW) group. Patients in the CW group were instructed to drink water at 2–6°C (kept in the refrigerator door for 6 hours), while those in the LW group were instructed to drink water at 24–28°C (kept at room temperature for 6 hours). The allocation sequence was known only to the endoscopy secretary who provided the instructions, and patients were assigned sequentially to the CW or LW groups. Individuals under 18 years of age, pregnant or breastfeeding women, and those with renal failure, ileus, toxic megacolon, gastrointestinal obstruction, inflammatory bowel disease, or previous colorectal surgery were excluded. Patients unable to provide consent or with contraindications to bowel preparation were also excluded.

Bowel Preparation Protocol

All patients were instructed to follow a clear liquid diet one day prior to colonoscopy. The clear liquid diet included water, strained broth without solid particles, pulp-free fruit juices (excluding purple-colored fruits such as grapes and blackberries), black tea or coffee without milk, and clear carbonated or non-carbonated soft drinks. Bowel cleansing was achieved using two 45 mL oral doses of sodium phosphate (NaP) solution and two 210 mL Fleet enemas. The bowel preparation was administered the day before the procedure, and a split-dose regimen was not used. Preparation began at 16:00 with the administration of the first Fleet enema, followed by one dose of NaP solution at 18:00 and another at 22:00. After each NaP dose, patients were advised to drink 2 liters of water. A final Fleet enema was administered two hours before the procedure to complete the preparation.

Colonoscopy Procedure

All colonoscopies were performed by the same surgical endoscopy team using Fujifilm series colonoscopes. Cecal intubation was confirmed by visualization of the appendiceal orifice and the ileocecal valve. Procedures were performed under sedation with intravenous midazolam (2–5 mg) and fentanyl (50 µg), or under general anesthesia when necessary. Therapeutic interventions such as biopsy, polypectomy, clip application, and argon plasma coagulation were performed when indicated.

Assessment of Bowel Cleanliness

The quality of bowel cleanliness was assessed using the Boston Bowel Preparation Scale (BBPS). The right, transverse, and left colon segments were each scored from 0 to 3. The right colon included the cecum and ascending colon; the transverse colon included the hepatic flexure, transverse colon, and splenic flexure; and the left colon included the descending colon, sigmoid colon, and rectum. The total BBPS score was the sum of the three segment scores, ranging from 0 to 9. A total BBPS score ≥ 6 was considered adequate bowel preparation. All evaluations were performed by endoscopists blinded to group allocation.

Statistical Analysis

When planning the study, it was assumed that a difference of at least 0.8–1.0 points in BBPS between the two groups would be clinically significant. With a significance level of

α=0.05 and a target power of at least 80%, it was calculated that approximately 120 patients per group would be sufficient. Considering potential dropouts, 130 patients were included in each group.

Descriptive statistics were expressed as mean, standard deviation, median, minimum–maximum, frequency, and percentage values. The distribution of quantitative variables was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Non-normally distributed continuous variables were analyzed using the Mann–Whitney U test, while categorical variables were analyzed using the Chi-square test or Fisher's exact test when appropriate. Statistical analyses were performed using SPSS version 28.0 (IBM Corp., Armonk, NY, USA), and p<0.05 was considered statistically significant.

Clinical Trial Registration: This study was registered at ClinicalTrials.gov (Identifier: NCT07295405).

RESULTS

A total of 260 patients who underwent elective colonoscopy between February and July 2025 were included in the study. Among them, 130 patients were randomized to the CW group and 130 to the LW group. The mean age of all participants was 51.6±12.1 years (range, 19–77 years), and 50.4% were male. The mean body mass index (BMI) was 28.1±5.3 kg/m². At least one comorbidity was present in 43.5% of the patients, with hypertension (23.1%) and diabetes mellitus (15.4%) being the most common. Active smoking was reported by 32.3% and alcohol consumption by 5% of participants.

Regarding bowel preparation, 97.7% of patients reported adequate fluid intake, and 97.3% demonstrated full adherence to medication instructions. Adverse effects related to the preparation process occurred in 40.4% of patients. The most common adverse effects were nausea (24.2%) and vomiting (8.5%), followed by headache (5.4%), abdominal pain (4.2%), and dizziness (2.3%). The demographic and clinical characteristics of the patients are summarized in Table 1.

The most frequent indications for colonoscopy were constipation (20.8%), screening (18.8%), and abdominal pain (18.8%). General anesthesia was used in 32.7% of procedures, and the cecal intubation success rate was 91.9%. The mean total procedure time was 8.3±3.6 minutes, and the mean withdrawal time (cecum-to-anus withdrawal time) was 3.0±1.7 minutes.

On endoscopic evaluation, 68.1% of patients had normal colonoscopy findings, while polyps were detected in 19.2%. Other findings included inadequate preparation (4.6%), diverticulosis (4.2%), tumor (2.3%), and colitis (1.5%). The mean total Boston Bowel Preparation Scale (BBPS) score was 6.9±1.99, indicating overall adequate bowel cleansing. The colonoscopy indications, procedural characteristics, and bowel preparation quality are summarized in Table 2.

No significant differences were observed between the CW and LW groups regarding age, sex distribution, or BMI (p>0.05). Lifestyle factors such as comorbidity, smoking, and alcohol use were also similar between groups. However, a family history of colorectal cancer (21.5% vs. 11.5%; p=0.030) and allergic diseases (11.5% vs. 1.5%; p=0.001) were significantly more frequent in the LW group.

Compliance with the bowel preparation protocol, including medication intake and adequate hydration, did not differ significantly between groups (p>0.05). Although the overall incidence of adverse effects was higher in the LW group (46.2% vs. 34.6%), the difference was not statistically significant (p=0.058). When specific adverse events were analyzed, nausea was significantly more frequent in the LW group (30.0% vs. 18.5%; p=0.030). No significant differences were found in other adverse effects (vomiting, abdominal pain, headache, etc.). The comparison of demographic and clinical characteristics between the cold and lukewarm water groups is presented in Table 3.

Regarding colonoscopy indications, constipation (24.6%) and abdominal pain (19.2%) were most common in the LW group, while constipation (16.9%) and rectal bleeding (13.1%) predominated in the CW group. Weight loss as an indication was observed only in the CW group, showing a statistically significant difference (p=0.013).

When procedural characteristics were evaluated, the cecal intubation rate was similar between the two groups (90.0% vs. 93.8%; p=0.255). There was no significant difference in the total procedure time (8.2±3.8 minutes vs. 8.4±3.3 minutes; p=0.881), whereas the withdrawal time was significantly shorter in the lukewarm water group (2.7±1.5 minutes vs. 3.2±1.8 minutes; p=0.003).

In terms of colonoscopic findings, the rate of normal colonoscopy was significantly higher in the LW group (73.8% vs. 62.3%; p=0.047), while inadequate bowel preparation was significantly more frequent in the CW group (7.7% vs. 1.5%; p=0.034). There were no significant differences between groups regarding the rates of polyps, diverticula, colitis, or tumors (Fig. 1).

According to the BBPS assessment, the LW group achieved significantly higher scores across all colonic segments. The mean BBPS scores for the right, transverse, and left co-

Table 1. Demographic and clinical characteristics of the patients

	Min-max	Median	Mean±SD	n	%
Age (years)	19.0–77.0	53.0	51.6±12.1		
Gender					
Female				129	49.6
Male				131	50.4
BMI (kg/m²)	8.0–48.9	27.7	28.1±5.3		
Comorbidity					
(–)				147	56.5
(+)				113	43.5
Hypertension				60	23.1
Diabetes mellitus				40	15.4
Asthma / COPD				13	5.0
Coronary artery disease				11	4.2
Other comorbidities				6	2.3
Smoking				84	32.3
Alcohol consumption				13	5.0
Allergy				17	6.5
Previous abdominal surgery				51	19.6
Family history of colorectal cancer				43	16.5
Anticoagulant use				35	13.5
Compliance with medication					
No				7	2.7
Yes				253	97.3
Adequate water intake					
No				6	2.3
Yes				254	97.7
Adverse effect					
(–)				155	59.6
(+)				105	40.4
Nausea				63	24.2
Vomiting				22	8.5
Headache				14	5.4
Abdominal pain				11	4.2
Dizziness				6	2.3
Fatigue				3	1.2
Syncope				1	0.4

SD: Standard deviation; BMI: Body mass index; COPD: Chronic obstructive pulmonary disease

lon were 2.35±0.79 vs. 2.05±0.99 (p=0.018), 2.48±0.70 vs. 2.15±0.88 (p=0.001), and 2.57±0.58 vs. 2.23±0.84 (p=0.001), respectively. The total BBPS score was also significantly higher in the LW group (7.37±1.67 vs. 6.43±2.17; p<0.001). These findings indicate that LW water consumption significantly improves the quality of bowel preparation (Fig. 2). The comparative data on colonoscopy indications, procedural characteristics, and bowel preparation quality between the cold and lukewarm water groups are presented in Table 4.

DISCUSSION

The quality of colonoscopy largely depends on adequate bowel preparation, which directly influences diagnostic accuracy and the adenoma detection rate (ADR). In contrast,

Table 2. Colonoscopy indications, procedural characteristics and bowel preparation quality

	Min-Max	Median	Mean±SD	n	%
Indication					
Constipation				54	20.8
Screening				49	18.8
Abdominal pain				49	18.8
Bleeding				37	14.2
Anemia				17	6.5
Dyspepsia				16	6.2
Positive fecal occult blood				15	5.8
Diarrhea				7	2.7
Weight loss				6	2.3
Perianal disease				5	1.9
History of polyps				5	1.9
Cecal intubation achieved				239	91.9
Procedure time (min)	1.0–27.0	8.0	8.3±3.6		
Withdrawal time (min)	0.0–13.0	3.0	3.0±1.7		
Findings					
Normal				177	68.1
Polyp				50	19.2
Poor preparation				12	4.6
Diverticulum				11	4.2
Tumor				6	2.3
Colitis				4	1.5
Bowel preparation quality (BBPS)					
Right colon	0.00–3.00	2.00	2.20±0.91		
Transverse colon	0.00–3.00	2.00	2.32±0.81		
Left colon	0.00–3.00	3.00	2.40±0.74		
Total BBPS score	0.00–9.00	7.00	6.90±1.99		

inadequate bowel preparation reduces the sensitivity of colonoscopy, prolongs the procedure time, increases the risk of adverse events, and raises the likelihood and cost of repeat examinations.[8] Several scales have been developed to assess the quality of bowel preparation, including the BBPS, the Ottawa Scale, and the Aronchick Scale. Among these, the BBPS is recognized as the most valid and widely used scoring system for evaluating bowel cleanliness.[1] In the present study, bowel cleanliness was assessed using the BBPS.

In this prospective observational study, we investigated the effects of water temperature consumed during bowel preparation on bowel cleansing quality, procedure duration, and patient tolerance before elective colonoscopy. Our findings demonstrated that patients who consumed LW had significantly higher BBPS scores, shorter withdrawal times, and greater overall satisfaction. These results suggest that water temperature, a variable not sufficiently explored in the literature, may represent a clinically meaningful factor influencing bowel preparation quality.

Physiologically, the temperature of ingested fluids can affect gastric and intestinal motility. Sun et al.[9] reported that both cold (4°C) and hot (50°C) water delayed gastric emptying, whereas fluids at 37°C accelerated it. Similarly, Fujihira et al.[10] demonstrated that cold water (2°C) suppressed gastric contractions compared to warm (37°C) and hot (60°C) water. These physiological mechanisms suggest that warm water may facilitate intestinal transit and enhance the efficacy of bowel preparation. In our study, the higher BBPS scores observed in the LW group may represent the clinical reflection of this physiological effect.

Table 3. Comparison of demographic and clinical characteristics between cold and Lukewarm Water Groups

	Cold (n=130)				Lukewarm (n=130)				p	
	Mean±SD	n	%	Median	Mean±SD	n	%	Median		
Age (years)	50.5±12.2			53.0	52.7±11.9			53.5	0.188	m
Gender										
Female		62	47.7			67	51.5		0.535	X^2
Male		68	52.3			63	48.5			
BMI (kg/m²)	27.7±5.0			27.6	28.4±5.5			28.0	0.177	m
Comorbidity										
(-)		80	61.5			67	51.5		0.104	X^2
(+)		50	38.5			63	48.5			
Smoking		36	27.7			48	36.9		0.112	X^2
Alcohol consumption		5	3.8			8	6.2		0.393	X^2
Allergy		2	1.5			15	11.5		0.001	X^2
Previous abdominal surgery		21	16.2			30	23.1		0.160	X^2
Family history of colorectal cancer		15	11.5			28	21.5		0.030	X^2
Anticoagulant use		15	11.5			20	15.4		0.364	X^2
Medication compliance										
No		4	3.1			3	2.3		0.702	X^2
Yes		126	96.9			127	97.7			
Adequate water intake										
No		3	2.3			3	2.3		1.000	X^2
Yes		127	97.7			127	97.7			
Adverse effects										
(-)		85	65.4			70	53.8		0.058	X^2
(+)		45	34.6			60	46.2			
Nausea		24	18.5			39	30.0		0.030	X^2
Vomiting		14	10.8			8	6.2		0.181	X^2
Fatigue		2	1.5			1	0.8		1.000	X^2
Abdominal pain		8	6.2			3	2.3		0.123	X^2
Headache		4	3.1			10	7.7		0.099	X^2
Dizziness		2	1.5			4	3.1		0.409	X^2
Syncope		0	0.0			1	0.8		1.000	X^2

m: Mann-whitney u test; X^2: Chi-square test (Fischer test). SD: Standard deviation; BMI: Body mass index

Zessner-Spitzenberg et al.,[1] using the Aronchick Scale, reported that patients with excellent or good bowel preparation had higher ADR and greater success in completing colonoscopy. Interestingly, they also observed that the mean number of detected polyps increased as the quality of bowel preparation decreased. Pantaleón Sánchez et al.[11] found that patients with IBC who underwent repeat colonoscopy within a short interval had a higher incidence of adenomas, serrated polyps, and colorectal cancer. Similarly, Wong et al.[12] reported that poorer bowel preparation was associated with a lower neoplasia detection rate. In the present study, although the detection rate of polyps was proportionally higher in the CW group, this difference was not statistically significant.

Previous studies have demonstrated that patient education prior to colonoscopy can improve bowel preparation quality and shorten procedure duration.[13,14] In our study, all patients received face-to-face instruction, which may have contributed to the high rate of adequate preparation. The mean total BBPS score was 6.9±1.99, indicating an overall satisfactory level of bowel cleanliness.

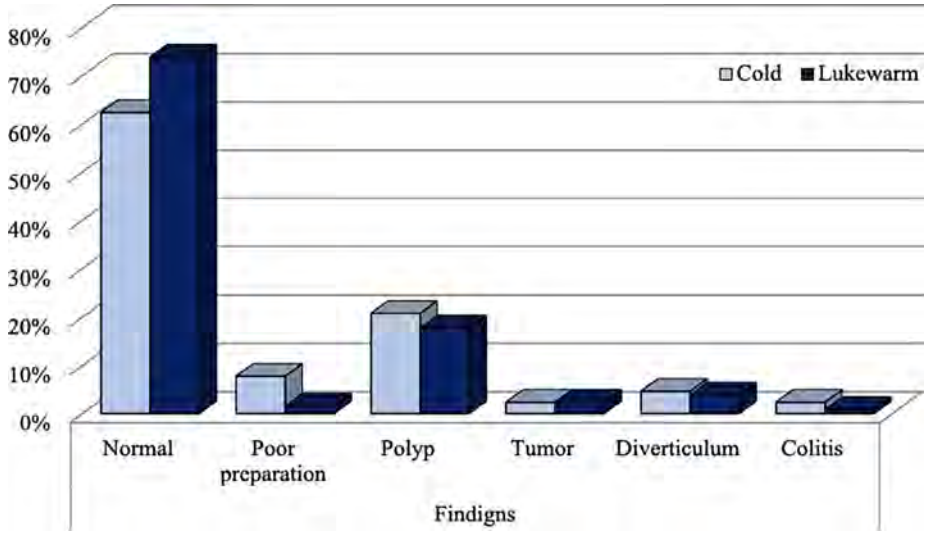

Figure 1. Distribution of colonoscopic findings in the cold-water (CW) and lukewarm-water (LW) groups

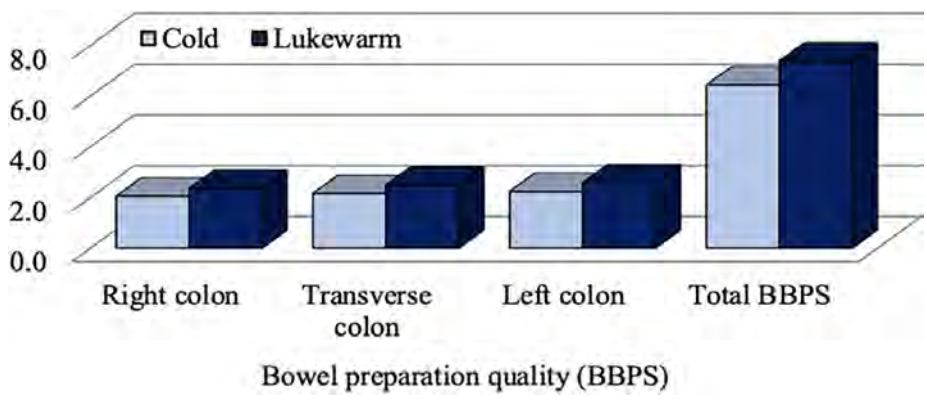

Figure 2. Comparison of Boston bowel preparation

Before colonoscopy, a low-residue diet (LRD) or clear liquid diet (CLD) is commonly recommended.[8] Song et al.[15] reported that an LRD did not affect the quality of bowel preparation compared with a CLD but improved patient tolerance. Patients following an LRD demonstrated better compliance with the bowel preparation regimen, fewer side effects, and a greater willingness to repeat the same regimen in the future. Similarly, Alvarez-Gonzalez et al.[16] found that an LRD provided superior tolerability as well as more adequate bowel cleansing. For these reasons, the European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend an LRD prior to colonoscopy.[17] In the present study, all patients followed a CLD, which resulted in adequate bowel cleansing.

According to the ESGE guidelines, both HV and LV PEG-based regimens, as well as non-PEG-based regimens, can be used for bowel preparation.[17] Hernandez et al.,[18] in a study comparing low-, medium-, and high-volume bowel preparation agents in hospitalized patients, reported that LV regimens could be preferred due to their comparable cleansing efficacy and better tolerability. Scalvini et al.[19] compared 1 L-PEG, 2 L-PEG, and MCSP regimens and demonstrated that the 1 L-PEG regimen provided superior bowel cleansing. Similarly, Waldmann et al.[20] found no significant difference between high- and low-volume preparations in terms of bowel cleansing quality.

In the present study, an oral NaP preparation was used and supported with an enema. Overall bowel cleansing was

Table 4. Comparison of colonoscopy ındications, procedural characteristics, and bowel preparation quality between cold and Lukewarm Water Groups

	Cold (n=130)				Lukewarm (n=130)				p	
	Mean±SD	n	%	Median	Mean±SD	n	%	Median		
Indication										
Screening		23	17.7			26	20.0		0.634	X^2
Weight loss		6	4.6			0	0.0		0.013	X^2
Anemia		10	7.7			7	5.4		0.452	X^2
Fecal occult blood (FOB)		9	6.9			6	4.6		0.425	X^2
Bleeding		17	13.1			20	15.4		0.594	X^2
Dyspepsia		10	7.7			6	4.6		0.302	X^2
Abdominal pain		24	18.5			25	19.2		0.874	X^2
Diarrhea		3	2.3			4	3.1		0.702	X^2
Constipation		22	16.9			32	24.6		0.125	X^2
Perianal disease		4	3.1			1	0.8		0.176	X^2
History of polyps		2	1.5			3	2.3		0.652	X^2
Cecal intubation achieved		117	90.0			122	93.8		0.255	X^2
Procedure time (min)	8.2±3.8			8.0	8.4±3.3			8.0	0.881	m
Withdrawal time (min)	3.2±1.8			3.0	2.7±1.5			2.0	0.003	m
Findings										
Normal		81	62.3			96	73.8		0.047	X^2
Poor preparation		10	7.7			2	1.5		0.034	X^2
Polyp		27	20.8			23	17.7		0.580	X^2
Tumor		3	2.3			3	2.3		1.000	X^2
Diverticulum		6	4.6			5	3.8		1.000	X^2
Colitis		3	2.3			1	0.8		0.620	X^2
Bowel preparation quality (BBPS)										
Right colon	2.05±0.99			2.00	2.35±0.79			3.00	0.018	m
Transverse colon	2.15±0.88			2.00	2.48±0.70			3.00	0.001	m
Left colon	2.23±0.84			2.00	2.57±0.58			3.00	0.001	m
Total BBPS	6.43±2.17			7.00	7.37±1.67			8.00	0.000	m

m: Mann-whitney u test; X^2: Chi-square test (Fischer test). SD: Standard deviation

adequate, and 97.3% of patients reported full compliance with the medication regimen.

Split-dose administration is widely recommended to enhance bowel cleansing quality and improve patient compliance. Numerous studies in the literature have shown that split-dose regimens improve both cleansing efficacy and patient tolerance. Menees et al.[21] reported that split-dose bowel preparation significantly increased the quality of bowel cleansing. Likewise, Tian et al.,[22] in a randomized controlled trial comparing two low-volume split-dose PEG electrolyte regimens before morning colonoscopy, found that the 1.5 L (evening) + 0.75 L (morning) regimen achieved higher cleansing efficacy than the 0.75 L (evening) + 1.5 L (morning) regimen, with both achieving adequate bowel preparation rates exceeding 80%.

Additionally, Yadlapati et al.[23] demonstrated that split-dose administration in hospitalized patients improved the adequacy of preparation and reduced the need for repeat colonoscopy.

In our study, although a split-dose protocol was not applied, bowel cleansing was still found to be satisfactory, suggesting that other variables—such as water temperature—may have contributed to preparation quality.

The timing of bowel preparation administration is another critical factor influencing colonoscopy success. Several studies have shown that taking the final dose of the preparation closer to the procedure time significantly improves cleansing quality. Seo et al.[24] reported that when the interval between the last dose and the start of colonoscopy was 3–5 hours, bowel cleansing quality was superior. Similarly, Gao et al.,[25] in a meta-analysis, showed that shortening the interval between bowel preparation and colonoscopy resulted in better cleansing and higher polyp detection rates.

In line with these findings, the ESGE guideline recommends that the final dose of the preparation should be taken no more than 5 hours and completed at least 2 hours before colonoscopy.[17]

In the present study, despite the interval between the last dose and colonoscopy exceeding 5 hours, bowel cleansing was still found to be adequate.

In addition to efficacy, the safety profile of bowel preparation agents is of paramount importance. Tadano et al.[26] reported that bowel cleansing agents were associated with 78 serious adverse events, including intestinal obstruction, ischemic colitis, electrolyte disturbances, spontaneous esophageal rupture, Mallory–Weiss syndrome, and anaphylaxis. Hernandez et al.[18] also noted that low-volume preparations were associated with fewer complaints of unpleasant taste and nausea.

Reumkens et al.[6] compared NaP and high-volume PEG solutions and found that the incidence of hypokalemia was significantly higher in the NaP group (17.2%) compared with the PEG group (4.8%). The rates of hyponatremia were 0.9% vs. 3.3%, hyperphosphatemia 37.3% vs. 0.65%, and hypocalcemia 15.6% vs. 8.1%, respectively. Kamran et al.[27] reported that the use of adjunct agents during bowel preparation reduced adverse effects such as bloating and vomiting. In our study, adverse events related to the preparation process were observed in 40.4% of patients, most commonly nausea (24.2%) and vomiting (8.5%), while headache (5.4%), abdominal pain (4.2%), and dizziness (2.3%) were less frequent. No serious adverse events were observed.

Identifying risk factors associated with inadequate bowel preparation is crucial to improving colonoscopy quality. Scalvini et al.[19] identified male sex, history of constipation, smoking, previous pelvic surgery, and the presence of psychiatric, neurological, or renal disorders as predictors of poor bowel cleansing. Wong et al.[12] associated advanced age and smoking with inadequate preparation. Sadeghi et al.[28] found that older age, BMI > 25 kg/m², abdominal circumference >95 cm, smoking, low fruit-and-vegetable intake, low literacy, and low physical activity were correlated with insufficient preparation. Similarly, Shi et al.[29] identified male sex, inpatient status, and the spring season as independent risk factors for poor bowel cleansing. Therefore, in patients at high risk for inadequate bowel preparation, enhanced education and optimized preparation protocols may help improve cleansing quality.

Overall, our study is consistent with previous literature and highlights that "water temperature," a factor not previously emphasized, may also play a significant role in bowel preparation quality. This parameter represents a cost-free and easily applicable improvement strategy that could be incorporated into clinical practice.

This study has several limitations. Being conducted at a single center with a relatively limited sample size and the inability to fully monitor at-home preparation conditions may have influenced the results to some extent. Nevertheless, the prospective design, balanced group allocation, and use of a standardized bowel preparation protocol strengthen the reliability and overall validity of the findings.

CONCLUSION

This study demonstrates that the temperature of the water consumed during bowel preparation before colonoscopy has a clinically significant impact on the quality of bowel cleansing and procedural efficiency. The use of lukewarm water was found to significantly improve bowel preparation scores, shorten withdrawal time, and enhance patient comfort. These findings indicate that not only the volume but also the temperature of hydration is a determining parameter in bowel preparation.

From a clinical standpoint, the use of lukewarm water represents a simple, safe, cost-free, and easily applicable method that may be integrated into routine bowel preparation protocols. This approach has the potential to improve both endoscopic image quality and patient satisfaction, thereby enhancing the diagnostic efficacy of colonoscopy.

Future multicenter randomized studies investigating the potential effects of water temperature on adenoma detection rate, intestinal microbiota composition, and electrolyte balance will help further clarify the clinical relevance of this parameter. Moreover, its impact on patient comfort and cost-effectiveness, particularly in repeated colonoscopies, should be further supported by subsequent research.

Disclosures

Ethics Committee Approval: The study was approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Non-interventional Ethics Committee (No: 2024-15-17, Date: 25/12/2024).

Informed Consent: Written informed consent was obtained from all participants before inclusion, and the study was performed in accordance with the principles of the Declaration of Helsinki.

Conflict of Interest Statement: All authors declare that there is no conflict of interest.

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SYSTEMATIC REVIEW

Toxic Tides of Electronic Waste: A Comprehensive Assessment of Health and Environmental Impacts

Shiuli Rathore, Rakhi Rajput, Rohit Kumar Singh, Geetika Bajpai, Hari Sharan Singh, Sachin Kumar Tripathi

Department of Forensic Medicine and Toxicology, King George's Medical University, Lucknow, India

ABSTRACT

E-waste has emerged as a crucial environmental concern for many governments globally as a result of the quick development in the usage of electronic and electrical equipment worldwide. According to several studies, dangerous compounds in electronic waste may result in environmental tragedies and health issues for people if proper recycling practices are not adopted. This justifies a reconsideration of the current e-waste management procedures. This report summarizes the advancements made, identifies areas for improvement, and critically evaluates earlier studies on the production of e-waste and management strategies of the key Asia Pacific countries that produce digital garbage. This is done in light of the nation's growing e-waste generation and the significance of e-waste management. The digital era has ushered in unprecedented convenience and innovation, but it has also given rise to a significant challenge: e-waste. The serious effects of inappropriate e-waste disposal on the environment and human health are highlighted by this in-depth investigation. It emphasizes the urgent need for responsible practices, global collaboration, and innovative, sustainable solutions to address this complex issue and ensure a healthier, more sustainable future.

Keywords: Asia Pacific, challenges, environmental management, e-waste, health impacts

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INTRODUCTION

The Asia Pacific region is characterized by its high population density and quick pace of development, making it one of the most prominent and dynamic areas on a worldwide scale. Furthermore, the rapid industrialization observed in numerous nations within this region may be attributed to the availability of a relatively low-cost labour force, which has been further facilitated by the inflow of foreign direct investments. The electrical and electronics industry has experienced a notable transformation due to advancements in technology and commercial developments, resulting in major benefits for this sector. The presence of dangerous compounds in electrical and electronic equipment poses a significant threat to both the environment and human health, hence exacerbating the ongoing climate crisis. Despite its role in improving living conditions, the necessity of such equipment cannot be overlooked. The increase in the quantity of electronic garbage (e-waste) can be attributed to the escalating demand for electronic products and the pursuit of greater financial gains.[1]

The escalating quantity of electronic garbage (e-waste) is a significant concern for both the environment and local populations worldwide due to the incorrect disposal practices associated with e-waste. The electronic waste in question leads to the emission of perilous compounds that have detrimental effects on both human health and the environment. The yearly production of electronic garbage (e-waste) is seeing a significant increase. In the year 2019, the global production of electronic garbage exceeded 50 million cubic meters. The Asia Pacific area alone accounted for the production of 24.9 million tonnes of e-waste, constituting a significant portion of the total global amount. The creation of e-waste increased at a rate three times faster than the growth of the world population. By the year 2030, it is projected that the global production of electronic garbage (e-waste) will exceed 74 million tonnes.[2] The rate of recycling, however, is not commensurate with the quantity. Furthermore, a significant portion of the generated electronic trash is now being directed towards landfilling, a prevalent approach to e-waste disposal on a global scale. The

Address for Correspondence: Rakhi Rajput, Department of Forensic Medicine and Toxicology, King George's Medical University, Lucknow, India
E-mail: rakhirajpoot1@gmail.com **ORCID ID:** 0009-0003-3376-3047

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primary challenges associated with current e-waste management practices include insufficiently efficient trash collection and recycling systems, as well as a lack of mechanisms to hold electrical and electronic equipment (EEE) manufacturers accountable for the disposal of end-of-life products. The inappropriate implementation of e-waste recycling practices might potentially result in significant adverse consequences for both the environment and human health.[3] Although many studies discuss electronic waste generation, recycling, treatment, and environmental oversight, only a few have specifically looked at how electronic waste in selected Asia Pacific countries affects both human health and the environment.

Second, accordingly, more work is required to ensure wiser and more sustainable worldwide production, consumption, supervision, and disposal of e-waste since many nations, especially those in the Asia Pacific area, are not managing e-waste created effectively.[4] More corporate efforts are required to address the growing e-waste problem through adequate research and training. It is also noted that more e-waste is created than is securely recycled in many nations throughout the world. The problems with managing e-waste in today's digitally linked world are mostly caused by the unsustainable ways we now make, use, and discard electronic gadgets. By creating the essential, needed, and required e-waste legislation, implementing proper e-waste management techniques would help to attain sustainable development goals and lessen the global climate catastrophe.

Thirdly, there have been studies and conversations about the production and handling of e-waste for a long time. However, the issues and difficulties associated with the creation and treatment of e-waste continue.[5] This review seeks to evaluate the current electronic waste (e-waste) management practices in the major e-waste-producing nations of the Asia Pacific region, aiming to mitigate the adverse impacts on the environment and human health caused by improper recycling and disposal. Through a careful examination of existing research on e-waste generation and environmental management in different countries, the review identifies challenges, assesses progress, and suggests management approaches and policy frameworks to address e-waste issues. This significantly decreases the health and environmental problems associated with e-waste.[6]

MATERIALS and METHODS

A comprehensive literature search was conducted across Google Scholar, PubMed, and Web of Science databases for studies published between January 2010 and June 2024. The following search terms and Boolean operators were used, and the first assessed date was 29th of January. The terms used are: "e-waste" OR "electronic waste" OR "waste electrical and electronic equipment") AND ("Asia Pacific" OR "India" OR "China" OR "developing countries") AND ("environmental impact" OR "health hazard" OR "management strategies"). Only peer-reviewed, English-language articles were included. Conference papers, editorials, and grey literature were excluded. Manual screening of reference lists of included studies was also performed to identify additional relevant articles. Two independent reviewers screened all titles and abstracts for relevance. Full-text screening was performed for potentially eligible studies. Any disagreement between reviewers was resolved through discussion and consensus.

Additionally, manual searches of the cited papers were done as additional article research. In order to screen all referenced publications in accordance with PRISMA rules, the citation manager application was used to enter all cited articles. To prevent biased research, several keywords and tactics were chosen. The investigation methodology specified during the literature review was used to filter the publications. Several publications were chosen for a more thorough investigation after the titles and abstracts of the papers were examined. Some of them were excluded following a thorough investigation, while the remainder were chosen for inclusion in this systematic review. We excluded 55 (Fig. 1) redundant and unrelated papers that did not primarily focus on e-waste after thoroughly inspecting the research and conducting the literature review. The objective of this approach is to gain an understanding of domestic e-waste output, connect it with regional and international production, and demonstrate the effectiveness of e-waste treatment in contributing to environmental sustainability. Additionally, we described the chosen model for estimating and forecasting. This study primarily emphasizes the economic, environmental, and social aspects of sustainable management, with a particular focus on the consumer market and the supply chain network. However, more documentation about the manufacturing, collection, and handling of e-waste is needed.

PRISMA Flow Chart

The PRISMA 2020 flow diagram (Fig. 1) summarizes the selection process. A total of 2,990 records were initially identified through the database search. After removing duplicates, 2,450 records were taken forward for screening. Out of these, 420 articles were screened by title and abstract, and 232 were excluded at this stage. The remaining 188 articles were assessed in full, but 154 did not meet the required quality standards and were therefore excluded. In the end, 34 studies were included in the qualitative analysis.

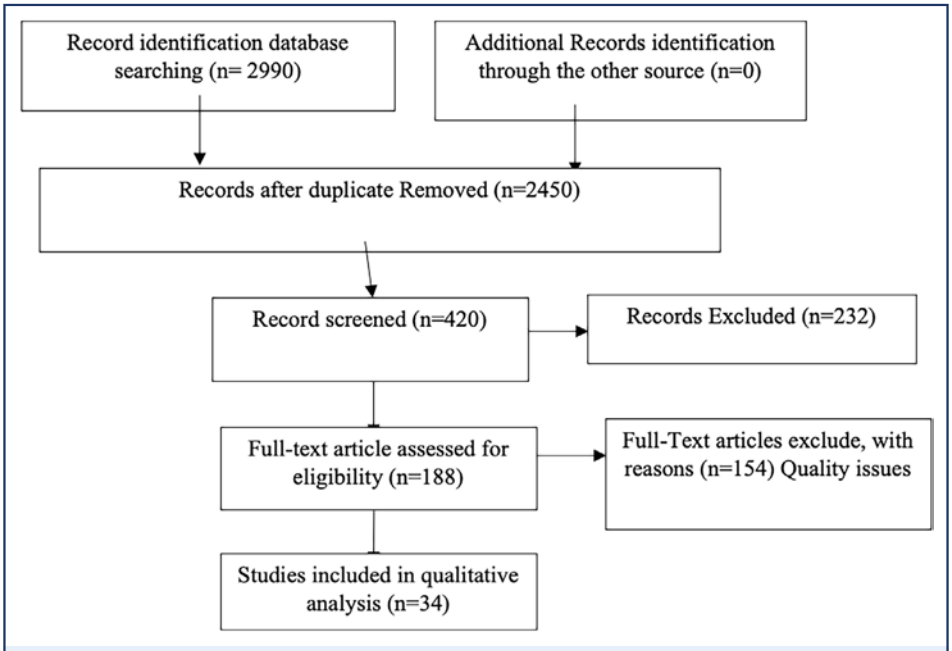

Figure 1. Prisma chart

Production of E-Waste Worldwide

In 2021, 53.6 million metric tonnes of electronic waste were generated worldwide, with an average annual growth rate of 2.5 Mt, according to the World E-Hide Monitor. In 2014, 44.4 Mt of electronic waste was produced—a more than 20% increase over the year before. It indicates hazardous conditions. The USA generates 13.1 Mt of electronic waste annually, or 13.3 kg per person—more than any other country in the survey. However, only two metric tonnes of all electronic waste are appropriately handled, meaning it is legally collected, recorded, and recycled, in accordance with US EPA laws.[7] According to a study in the USA, an American family uses more than 20 pieces of electronic equipment on average. With 42.3% of the 12 Mt of generated e-waste, Europe appears to operate the most structured and effective electronic waste handling processes. Asia produced the most e-waste, yet only 2.9 Mt of it was recycled. E-waste creation per capita worldwide is highest in Europe. India produces the most e-waste, followed by the United States and China, with China producing 10.1 Mt—one of the greatest amounts. It contributes 7.3 kg globally, whereas its per capita obligation is 2.4 kg. The amount of electronic waste released has increased by 58% in the last nine years. With 595 kt, or 21% of the region, Saudi Arabia is the leading producer of e-waste among Arab nations, according to the United Nations E-waste Monitoring. Currently, only 22% of the hazardous waste produced is handled; the remainder is untreated or left over.[6] Most of the e-waste is generated by developed countries and illegally exported to underdeveloped and developing countries, including India, China, Brazil, Ghana, Nigeria, and Pakistan.[8] The social, economic, and environmental factors are used to organize the technical parts of waste electrical and electronic equipment and the sustainability evaluation.[9] First-level e-waste treatment is shown in Figure 1.[10]

To address resource management, financial stability, policies, environment, and user inclusion, economic statistics, consumer behaviour, and national-level e-waste data are used to generate the parameters—whether certain metrics are both quantitative and qualitative. In the short term, models can also be useful for improving preparedness and precisely predicting the growth of e-waste in the region. Grey model e-waste forecasting, for example, allows for an accurate and imaginative prognosis.[11]

The current level of electronic waste manufacturing in Saudi Arabia is exceedingly hazardous. That necessitates a strong and concrete e-waste management and framework of regulations spanning from international trade to garbage collection at the municipal level, according to a comparative analysis of international e-waste management models. Social awareness and raising public perceptions of the problem's importance can both contribute to improved outcomes and boost the effectiveness of the aforementioned strategy. The most widely used and applied frameworks for behaviour analysis in the management of e-waste are the Extended

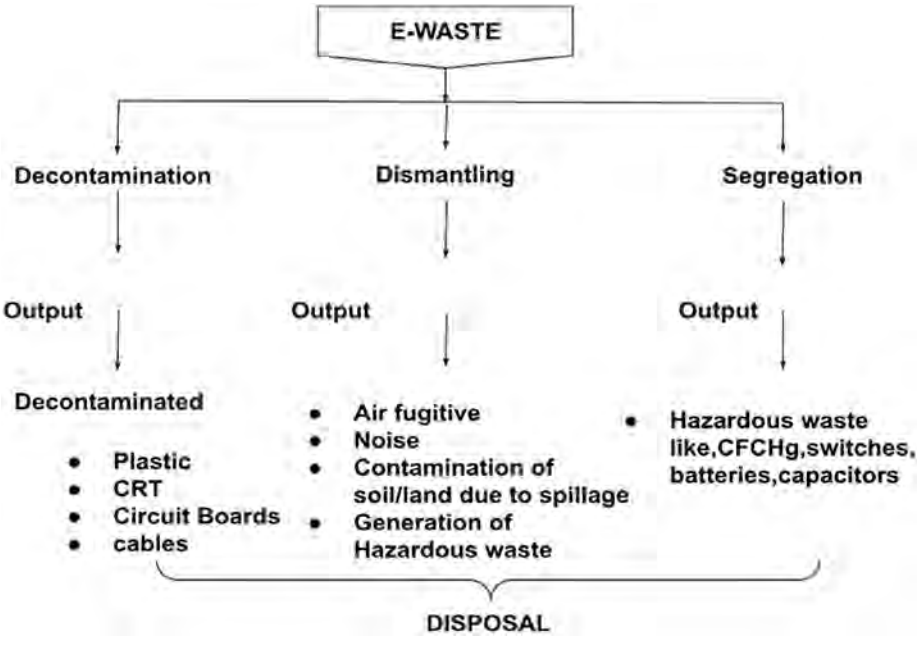

Figure 2. 1st level e-waste treatment

Producer Responsibility and Value-Belief-Norm Theory. By facilitating the efficient conversion of waste prior to landfilling, these frameworks will improve the handling of electronic waste operations and encourage ecological sustainability.[12]

Electronic Waste Supply Chain Network

Economic circulation and sustainable e-waste treatment both depend on supply chain consideration. Supply chain networks consist of two primary components: the governmental and unauthorised. It has been reported that the informal one is small. It needs to implement technology more efficiently in the conveyance of goods and services. This process is time-consuming, labour-intensive, and is mostly unregulated.[13] Sustainable management is challenging because of inappropriate management practices, including acid leaching, disassembly, and improper landfilling, whereas the adoption of formal recycling is hindered by their prevalence and presence. The management, segregation, and dismantling of e-waste are all made more challenging by the variety of its components (Fig. 2). Although EPR (Extended Producers' Responsibility) is thought to be the most practical strategy, its implementation framework is inadequate. The Analytical Hierarchy Process and Quality Function Deployment for decision-making, assessments, and system management may both be used to manage e-waste. Utilizing both structures will increase the supply chain network's effectiveness by helping to govern the predefined important elements. This model is used to handle the largest e-generator handling systems, demonstrating the importance of this procedure (Fig. 3). Additionally, research found that each rise of $1,000 in GDP would result in a 0.5-kilogram increase in the production of e-waste. This unequivocally calls for dynamic and sustainable management.[14–16] The reuse and recycling of electronic garbage, or "e-waste," have grown in significance in today's technologically advanced society. Even while recycling e-waste saves resources and lessens the amount of hazardous trash dumped in landfills, it additionally causes health effects that need to be addressed.

Management of Electronic Waste

We live in a time of rapid technological progress. Smartphones have largely replaced traditional mobile phones, LED and LCDs have largely replaced televisions, and desktop computers have largely been replaced by laptops and tablets. When a new product model is released, the previous model becomes obsolete and is discarded.[17] In affluent nations like the US, UK, Japan, and South Korea, among others, hundreds of thousands of tonnes of electronic waste are generated annually. The cost of processing electronic waste is unaffordable in developed nations. Because shipbuilding is relatively cheap, waste is shipped to countries that are developing. In developing nations, labourers, factory owners, and locals can all indiscriminately salvage valuable goods from this waste material. They collect what is valuable and trash the remaining items. For

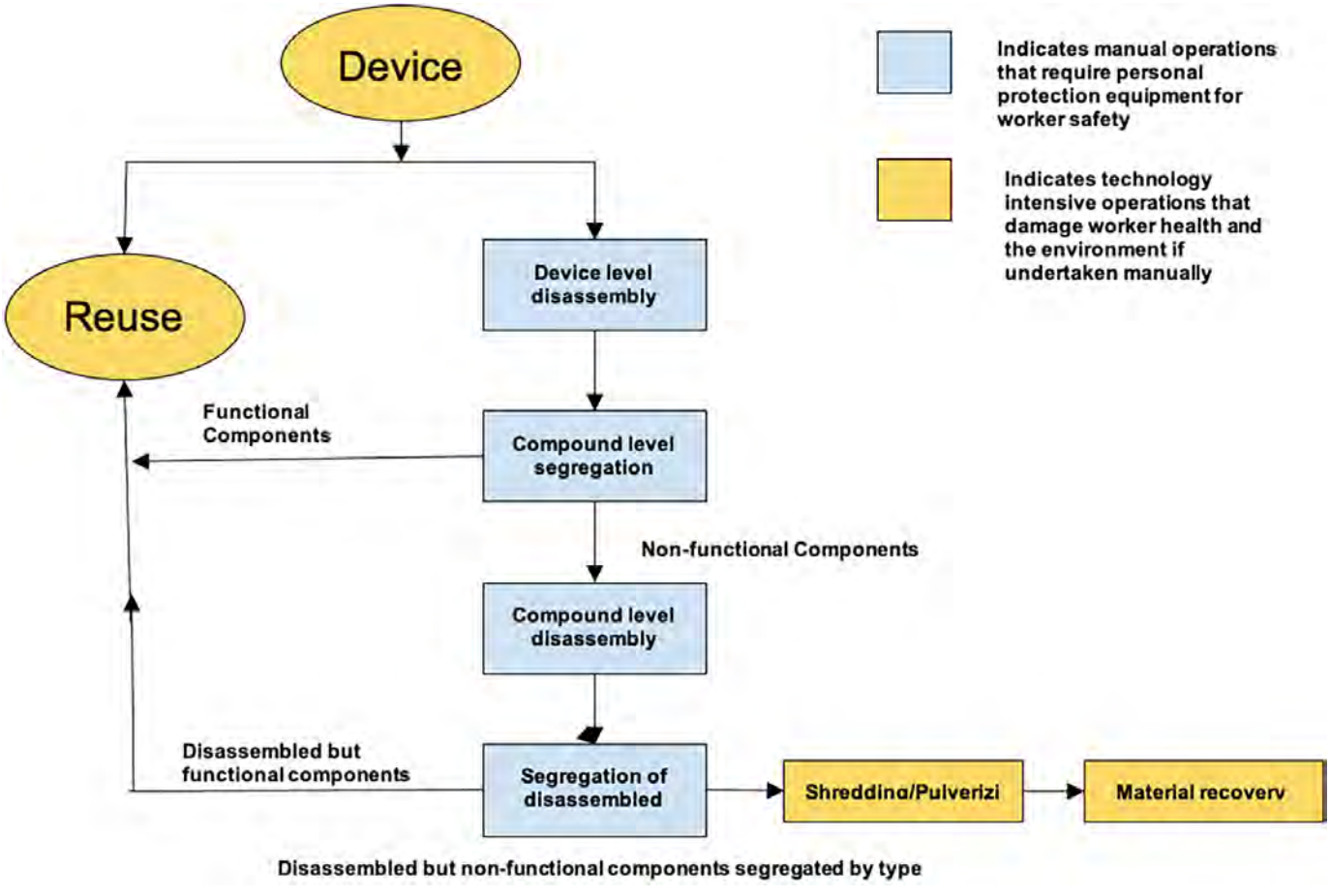

Figure 3. Various processes in e-waste recycling

the restoration of valuable chemical substances, acid baths and electronic burns are being used. Such approaches may be detrimental to people and have been associated with substantial health issues. India possesses urban e-waste processing centres that rapidly recycle raw electronic waste, particularly in cities like Chennai, Mumbai, and New Delhi. The capital city of India releases more than fifteen thousand tonnes of electronic garbage annually.[18] On the contrary, fourteen thousand tonnes of e-waste have been transported, primarily because of Chennai's immediate proximity to the port. Roughly 19,000 tonnes of electronic waste were generated in the city of Mumbai in the year 2007. Dioxin-like PCB compounds are widespread in the Indian atmosphere, which is an indication of the shipbreaking and e-waste shredding operations carried out in Mumbai's large industrial sector.[18]

Dangerous Recycling Operation

Several extremely harmful compounds, such as heavy metals like lead (Pb), mercury (Hg), arsenic (As), copper (Cu), cadmium (Cd), nickel (Ni), zinc (Zn), gold (Au), silver (Ag), and beryllium (Be); persistent organic pollutants (POP), such as polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs); polybrominated diphenyl ethers (PBDEs); and polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDDs/Fs), are reported to be emitted or formed during the recycling process of e-waste. The environment, humans, and animals are all harmed by the toxic chemicals released by these pollutants.[19] Combustion of electric wires and printed circuit boards and heat treatment of polymer products are suspected to be the sources for high PCBs in e-waste sites of India, especially the most toxic, PCB-126.[18] Open burning, disassembly, incineration, ash washing, acid baths, and other practices are activities that are part of informal e-waste recycling, which emits numerous toxic or dangerous substances, including brominated flame retardants (BFRs), chlorine, neurotoxins, heavy metals (Cd, Cu, Ni, Pb, and Zn), volatile nitrogen compounds, and persistent organic pollutants (POP).[20] People exposed to these dangerous

substances are impacted by recycling, including those who suffer acute lung damage from breathing in heavy metal fumes. Fine particulate matter from combustion results in cardiovascular and pulmonary illnesses.[21]

Impact of E-Waste Recycling

Workplace dangers

Electronic device disassembly and processing are required for e-waste recycling, which exposes employees to several occupational risks. Some of these dangers consist of:

Exposure to toxic chemicals

Hazardous compounds may be exposed as a consequence of improper handling and insufficient safety precautions, which can cause neurological illnesses, skin disorders, and respiratory difficulties.[22]

Exposure to particulate matter

The breaking down and burning of electronic parts may release particles into the air that, when breathed in, can aggravate respiratory conditions like coughing and wheezing and harm the lungs. Due to the laborious dismantling of electrical equipment, workers in e-waste recycling may potentially suffer bodily accidents, including cuts, burns, and injuries to their muscles.[23]

Pollution of the environment

Recycling e-waste has a negative influence on the environment and the neighbouring populations' health in addition to that of the employees. Inadequate recycling and disposal procedures may contaminate agricultural land and groundwater by leaching heavy metals and other hazardous compounds into the soil. These dangerous compounds may enter the body via the consumption of crops produced in polluted soil.[24]

Water pollution

Incorrect disposal or recycling may result in the discharge of poisons into water bodies, harming aquatic ecosystems and potentially compromising supplies of drinking water. This can lead to numerous health issues, including organ damage and gastrointestinal problems.[25]

Unofficial recycling methods

Reprocessing electronic waste is often done informally by marginalized groups in many poor nations, putting such people at serious health risk. These unregulated informal practices sometimes entail consuming e-waste to retrieve valuable components, which introduces dangerous toxins into the atmosphere. Due to extensive exposure to harmful chemicals, these populations are more likely to develop respiratory illnesses, skin ailments, and other health problems.[26]

Risks to Vulnerable Populations' Health

Children and pregnant women are two groups more susceptible to the negative effects of recycling e-waste on their health. Due to exposure to pollutants, children who live close to informal recycling facilities may have developmental delays and cognitive disabilities. Proximity to electronic waste contaminants during pregnancy could raise the likelihood of negative pregnancy outcomes.[27]

Reliable Recycling Methods

Concerns about the health effects of recycling e-waste are being addressed. Health risks may be considerably reduced by the use of responsible recycling techniques, such as the use of protective equipment for employees, suitable ventilation, and the application of safety laws.[28]

DISCUSSION

According to the study conducted by Chaturvedi et al.,[29] in India, the majority of electronic waste recycling is mainly done on an informal basis. Just 5% of all e-waste is appropriately collected and recycled, with the unorganized sector handling 95% of this. There have been 4.5 lakh child laborers between the ages of 10 and 14 who have been involved in the collection and processing of e-waste. Without safety precautions, extended exposure to these discarded e-wastes during recycling causes serious harm to brain development, heart function, lung cancer, the nervous system, respiratory syndromes, and skin conditions. In 2018, India's yearly e-waste processing capacity was 4.56 times smaller than its share of e-waste generation (Fig. 4). Lack of infrastructure for recycling and ignorance of the proper disposal process are the main causes of the rising value of e-waste, according to Rajesh et al.[30].

The health of recycling employees and the environment at large may be negatively impacted by the current management practices in India, according to observations. The recycling operations that are conducted present a complete risk. Urban poor individuals typically use methods like acid bathing to remove valuable and reusable components from electronic waste without considering any safeguards for their personal safety or health. Moreover, the challenge of recycling electronic waste in the entire country is made worse by the active engagement of children and women in these types of programs. Businesses that recycle e-waste in India pres-

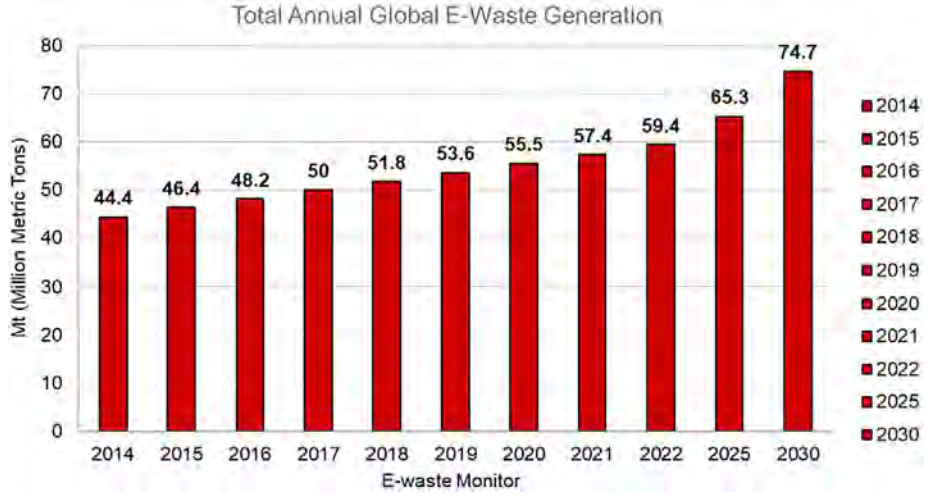

Figure 4. E-waste generation total annual global[30]

ent major risks to both the environment and the health of the people who work there. Numerous studies have demonstrated that the health of those who live close to the e-waste recycling plants is negatively impacted, in addition to the individuals who perform the recycling operation. One of the main issues in India is that the majority of those working in the recycling industry are poor and illiterate; thus, they are completely ignorant of the risks that recycling e-waste poses to both the environment and human health. Such recycling locations may result in uncontrolled pollution of the soil, air, and water, and this pollution, however, is neither tracked nor measured, according to Wath et al.[31].

India's whole electronic waste management framework is labour-intensive, and the majority of the recovering and recycling activities are performed using obsolete technologies and procedures, which might end up in the discharge of uncontrolled harmful substances. A comprehensive examination of the chemical risks related to the treatment of e-waste was carried out by Tsydenova and Bengtsson.[32] According to the report by Sthiannopkao et al.,[1] many different kinds of toxins are released into the workplace and environment as a consequence of unregulated recycling activities. The authors also note that in nations like China and India, the sheer quantity of e-waste generated, along with the crude recycling methods, is already having a negative impact on the environment and the general population. Metals from e-waste, for instance, are dissolved in strong acid solutions in these major countries and then extracted. In a similar way, a study conducted by Kaliyavaradhan et al.[3] found that electronic waste is hand-cleaned of plastic before being mechanically shredded. Besides that, it is widespread in developing nations to burn waste and unwanted scrap in the open. Such activities operate without exercising any necessary measures concerning the safety and well-being of the employees. Additionally, the workers and the residents are subjected to the toxins via their food intake, skin contact, dust consumption, and inhalation.

CONCLUSION

Unprecedented levels of ease, communication, and invention have been brought about by the digital era. E-waste, or electronic garbage, is a severe burden that mankind must now face as a result of this amazing transition. This in-depth analysis has looked at the many adverse consequences that e-waste has on the environment and public health, creating a narrative that emphasises the pressing necessity for responsible and sustainable e-waste disposal.

E-waste significantly contributes to soil, air, and water contamination. When electronic gadgets are inappropriately disposed of in landfills, their hazardous and precious metal-filled interiors contaminate the soil and groundwater. Brominated flame retardants, cadmium, lead, and mercury are simply a handful of the poisons that invade ecosystems and endanger animals and human populations by entering the food chain. Furthermore, energy-intensive e-waste disposal procedures like recycling and cremation emit greenhouse gases, accelerating climate change. The hazardous impact of e-waste on the environment is a serious issue that cannot be disregarded.

E-waste poses serious and well-documented risks to human health. Direct contact with the harmful materials

present in electronic gadgets may cause a variety of health concerns, including cancer, neurological diseases, respiratory troubles, and developmental abnormalities. Informal e-waste workers in underdeveloped nations are especially at risk because they often lack protective gear and knowledge of the dangers they confront. The interconnectedness of e-waste's health consequences emphasises how urgent it is to solve this hidden danger to the public. Healthful waste is a global issue that cuts across national boundaries and requires shared accountability.

International laws and programs like the Basel Convention and the Waste Electrical and Electronic Equipment Directive show that the issue of e-waste is understood to be a global one. However, strict enforcement and international collaboration are necessary for these restrictions to be successful. The ethical aspect of e-waste also emphasizes the need for a fundamental change in consumer behaviour and business practices. Sustainable e-waste disposal methods that take into account the complete lifespan of electronic equipment are the way ahead. Principles of the circular economy, extended producer responsibility, and eco-design provide potential ways to limit the production of electronic trash, encourage responsible disposal, and encourage recycling.

Innovation and technology are essential, with improvements in material recovery, safe dismantling methods, and e-waste monitoring systems having the potential to completely change the industry. In conclusion, the damage that electronic waste does to the environment and human health is a complex situation that has to be addressed right now. A comprehensive strategy for managing e-waste is necessary due to the interdependence of these effects. To enforce strict legislation, encourage conscientious usage, and improve enduring e-waste disposal practices, governments, industry, and consumers must work together. To promote a culture of ethical electronic use and disposal, education and awareness are equally important.

The e-waste problem is a symbol of modern consumer culture and technological advancement. Effective management requires coordinated efforts among government, industries, and consumers to take urgent action toward a more responsible and ethical approach to the use and disposal of electronic devices to preserve the environment, protect public health, and secure a sustainable future. A coordinated, multi-sectoral approach can reduce environmental and health risks caused by electronic waste and guarantee a more ecologically sound, healthy planet for generations to come.

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CASE REPORT

GnRH Agonist Therapy for Fertility Optimization in Women With Inaccessible Submucous Fibroids

Hale Göksever Çelik[1], Damla Sakar[2], Alara Ak[2], Faruk Buyru[3]

[1]Department of Obstetrics and Gynecology, Acıbadem Mehmet Ali Aydınlar University, Acıbadem Fulya Hospital, İstanbul, Türkiye
[2]Acıbadem Mehmet Ali Aydınlar University Faculty of Medicine, İstanbul, Türkiye
[3]Department of Obstetrics and Gynecology, Acıbadem Fulya Hospital, İstanbul, Türkiye

ABSTRACT

We present a 31-year-old patient who underwent hysteroscopic myomectomy following gonadotropin-releasing hormone agonist treatment due to inaccessible submucous myomas. At the first operation, 15 fibroids and one endometrioma in the right ovary were removed. Hysteroscopy was not performed to remove these submucous fibroids, as all of them covered the uterine cavity, and if they were removed, the walls of the uterine cavity would adhere, resulting in Asherman syndrome. Following laparoscopic myomectomy, the patient was started on leuprolide treatment, a gonadotropin-releasing hormone agonist, for two months. Then hysteroscopy was conducted, and it was observed that all submucous fibroids had undergone significant degeneration, with reduction in size, softening, and could be easily excised.

Keywords: Fibroid, hysteroscopy, myomectomy

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INTRODUCTION

Fibroids are benign tumors developing from the muscle tissue of the uterus. They are common, affecting approximately 80–90% of women by the age of 50, especially among those of reproductive age due to hormone-induced growth.[1] The exact cause of leiomyomas (fibroids) is not fully understood, but their development is believed to be influenced by a combination of genetic, hormonal, and environmental factors. A genetic mutation may trigger the onset of the condition, and different types of fibroids can arise through various molecular pathways. Hormones, particularly estrogen and progesterone, also play a crucial role in the growth and maintenance of these tumors, as fibroids tend to grow during the reproductive years when these hormones are active and shrink after menopause when hormone levels drop.[2]

Uterine leiomyomas, especially those that distort the endometrial cavity, are widely thought to negatively impact fertility and contribute to various reproductive issues such as miscarriage, preterm labor, and placental abruption. They are also linked to other pregnancy complications, including early bleeding, premature rupture of membranes (PROM), pelvic pain, and restricted fetal growth.[3] Other than their effect on fertility, they lead to symptoms such as irregular menstrual bleeding and dysmenorrhea.[4–6]

The primary treatment approaches include medical management, interventional radiology, and surgical procedures.[7] Medical management encompasses both nonhormonal medications, such as nonsteroidal anti-inflammatory drugs and tranexamic acid, as well as hormonal therapies, including combined oral contraceptives, levonorgestrel intrauterine

Address for Correspondence: Hale Göksever Çelik, Department of Obstetrics and Gynecology, Acıbadem Mehmet Ali Aydınlar University, Acıbadem Fulya Hospital, İstanbul, Türkiye
E-mail: hgoksever@yahoo.com **ORCID ID:** 0000-0002-5162-3262

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systems, gonadotropin-releasing hormone (GnRH) agonists or oral antagonists, progesterone receptor modulators, and aromatase inhibitors. GnRH agonists are commonly used to reduce the size of fibroids by downregulating pituitary GnRH receptors, thereby inducing a hypoestrogenic state. These agents also represent a valuable option in the preoperative phase to decrease fibroid volume prior to myomectomy.[8]

Surgical intervention is the most commonly chosen approach for the treatment of uterine fibroids. The decision between conservative and nonconservative methods depends on the specific characteristics of the fibroids as well as the patient's preferences. Myomectomy is considered a conservative treatment option for managing symptoms of uterine fibroids, while hysterectomy is generally recommended as a definitive surgical solution for patients who do not wish to preserve their fertility.

CASE REPORT

A 31-year-old nulliparous woman presented to the infertility clinic with menstrual irregularity and a fertility wish for 2 years. Hysterosalpingography was performed to assess the patency of the Fallopian tubes, and no abnormalities were detected regarding the tubes. Multiple intramural and submucous fibroids indenting the uterine cavity were revealed by ultrasonography and hysterosalpingography. She underwent laparoscopic myomectomy, during which 15 fibroids and one endometrioma, located on the right ovary, were excised.

However, hysteroscopy was not performed to remove submucous fibroids, as all of them covered the uterine cavity, and if they were removed, the walls of the uterine cavity would adhere, resulting in Asherman syndrome. In the postoperative period, the patient was started on leuprolide treatment, a gonadotropin-releasing hormone (GnRH) agonist, for two months. Following this treatment, hysteroscopy was conducted, and it was observed that all submucous fibroids had undergone significant degeneration, with reduction in size, softening, and could be easily excised (Fig. 1). The patient was monitored for six months, and then frozen embryo transfer was planned.

Written informed consent for publication of her clinical details and images was obtained from the patient.

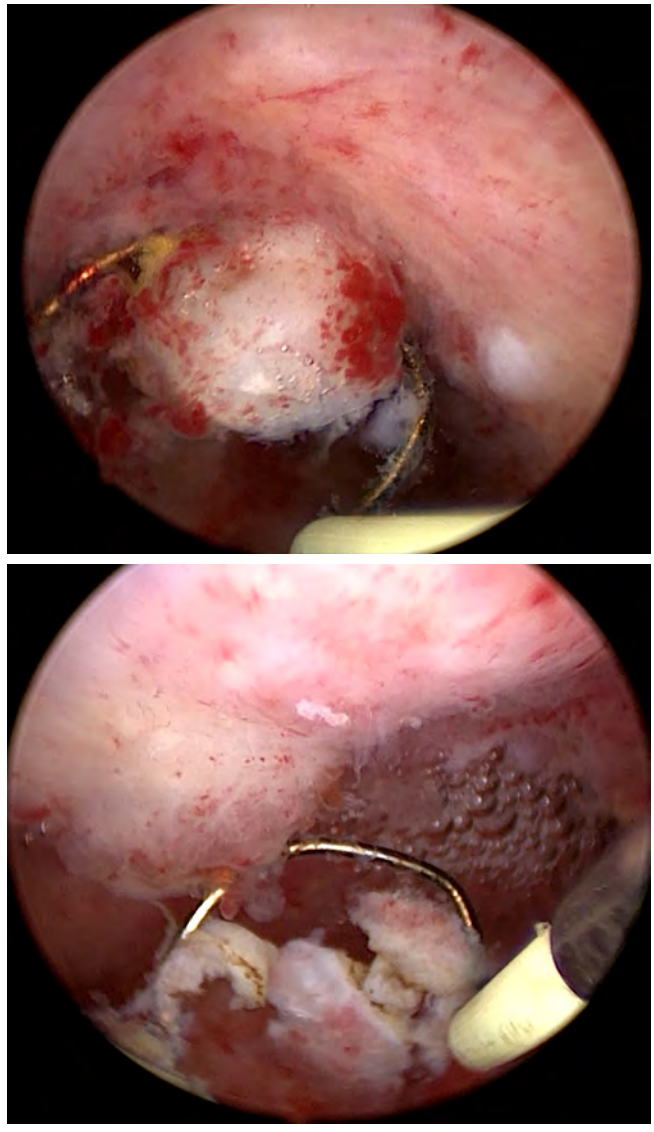

Figure 1. Hysteroscopic view of the fibroids that can be easily excised after GnRH agonist treatment

GnRH: Gonadotropin-releasing hormone

DISCUSSION

Fibroids are a significant cause of infertility in women. These benign tumors arise from the muscle tissue of the uterus and can be located in various layers of the uterine wall. The localization of fibroids influences their impact on fertility. While subserosal fibroids, located on the outer layer of the uterus, generally do not affect fertility, intramural and submucosal fibroids have been associated with infertility. Therefore, it is crucial to treat fibroids in women who want to become pregnant.[9]

In certain cases, fibroids cannot be surgically removed due to their size or location. In such situations, hormone therapy is utilized to reduce their size. GnRH agonists are commonly employed either postoperatively or as a primary treatment to shrink the size of fibroids. GnRH agonists, in particular, can reduce fibroid size by lowering estrogen levels in the blood.[10] Although these medications are preferred for perimenopausal women or as part of postoperative treatment,

GnRH agonists play an important role preoperatively in facilitating surgery and minimizing adverse outcomes associated with the operation, as demonstrated in this case.[11] The use of GnRH agonists prior to surgery can reduce the size of fibroids, which in turn minimizes blood loss and shortens the duration of the operation. Furthermore, in cases where a hysterectomy is required, GnRH agonists can facilitate a vaginal hysterectomy rather than an abdominal hysterectomy by reducing the size of the uterus.[12]

CONCLUSION

In our case, GnRH agonists were administered prior to hysteroscopy to remove submucosal fibroids. This approach was chosen because performing hysteroscopy on these fibroids without prior treatment may increase the risk of developing Asherman syndrome, a condition that can itself lead to infertility.[13]

By utilizing GnRH agonists, the size of the submucosal fibroids was reduced, thereby making the subsequent hysteroscopy safer and more effective. The use of GnRH agonists prior to hysteroscopy may be valuable in reducing potential complications and achieving better medical outcomes, as demonstrated in our case.

Disclosures

Informed Consent: Written informed consent for publication of her clinical details and images was obtained from the patient.

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LETTER TO THE EDITOR

Comment on "A Retrospective Evaluation of Acute Poisoning Cases in Emergency Departments: Focus on Suicide Attempts by Poisoning"

Efe Kanter

Department of Emergency Medicine, Izmir Katip Çelebi University, Faculty of Medicine, İzmir, Türkiye

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Dear Editor,

I read with great interest the article by Gün entitled "A Retrospective Evaluation of Acute Poisoning Cases in Emergency Departments: Focus on Suicide Attempts by Poisoning", which provides valuable data from a mixed rural and urban population and underlines the burden of self-poisoning in daily emergency practice.[1] This single-center study from Tokat-Turhal State Hospital analyzes 138 poisoning cases (July 2021 to June 2023) in a mixed rural-urban setting. The clear comparison between suicidal and non-suicidal cases and the detailed description of toxic agents are important strengths of this work.

There are several points that I believe could help readers interpret the results more clearly and may guide future studies in this field. First, the reported incidence of poisoning among all emergency visits (0.048%) appears considerably lower than the rates of 0.8-5 percent that have been described in other series from Türkiye and abroad.[2,3] As the author notes, this likely reflects the small-town mixed rural-urban catchment and the hospital's role, rather than simple underreporting.[1] This difference is likely to reflect local characteristics, but it might also be influenced by case definition, coding practices, or the exclusion of patients discharged directly from triage. Clarifying whether only patients with a final diagnosis of poisoning or those requiring observation or admission were counted could help readers interpret the incidence more accurately.

Another aspect that drew my attention was the high proportion of mushroom and corrosive ingestions among non-suicidal patients, which seems to be a noticeable regional pattern. A more detailed breakdown according to age groups and intentional versus unintentional exposure could highlight preventable patterns, particularly in children and young adults. Linking these data with poison severity or the need for specific interventions, as underlined in other reports from the region, might also support local public health strategies.[3,4]

I also wondered whether the comparison between suicidal and non-suicidal cases is based on univariate analysis. Because variables such as age, psychiatric history, agent type, time to the emergency department, and initial status are interrelated, a multivariable model could identify independent predictors of suicide attempts or intensive care needs. Using structured assessment tools and documenting long-term outcomes, as shown in other clinical reports, might further standardize outcome evaluation and facilitate comparison with other cohorts.[4,5]

Finally, the authors rightly emphasize the role of psychiatric disease. In this cohort, suicide attempts were linked to much higher intensive care admissions, with no deaths in that group, while two delayed methanol deaths occurred in non-suicidal patients.[1] Prospective studies, including structured psychiatric assessment and longer follow-up, would help determine the risk of recurrent self-poisoning and the effectiveness of preventive interventions.

Despite these methodological considerations, the article makes a meaningful contribution by highlighting local poisoning patterns and the heavy clinical impact of suicide attempts by drug overdose. I would like to thank the author for drawing attention to this topic and hope that these remarks will be useful when planning future work.

Sincerely,

Address for Correspondence: Efe Kanter, Department of Emergency Medicine, Izmir Katip Çelebi University, Faculty of Medicine, İzmir, Türkiye
E-mail: efekanter@hotmail.com **ORCID ID:** 0000-0002-0208-950X

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REPLY TO THE LETTER TO THE EDITOR

Reply to the Letter to the Editor: Comment on "A Retrospective Evaluation of Acute Poisoning Cases in Emergency Departments: Focus on Suicide Attempts by Poisoning"

Mehmet Gün

Department of Emergency Medicine, Şile State Hospital, İstanbul, Türkiye

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We would like to thank the author of the letter for their interest in our study entitled "A Retrospective Evaluation of Acute Poisoning Cases in Emergency Departments: Focus on Suicide Attempts by Poisoning" and for the constructive and thoughtful comments. These remarks provide an opportunity to further clarify our findings and the context of our study center.

As discussed in our manuscript, the observed incidence of poisoning should be interpreted in light of local and institutional characteristics. Our hospital serves a mixed rural–urban population in a relatively small district, and this structure likely influenced the overall case distribution. The analysis included patients who were formally registered and diagnosed with acute poisoning in the emergency department database. Differences in case definitions and coding practices across healthcare settings may also contribute to variations between studies.

Regarding clinical outcomes, suicide attempts in our cohort were predominantly related to drug ingestion and were associated with a greater need for intensive monitoring and care. In contrast, adverse outcomes in non-suicidal cases were mainly related to delayed presentation after toxic exposure.

We appreciate the author's suggestions regarding prospective study designs and structured psychiatric assessments. These constructive comments offer valuable direction for future research, and we believe that such academic exchanges contribute meaningfully to the interpretation of current findings and to the development of the field.

Sincerely,

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Address for Correspondence: Mehmet Gün, Department of Emergency Medicine, Şile State Hospital, İstanbul, Türkiye
E-mail: drmgun1@gmail.com **ORCID ID:** 0000-0003-3466-6014

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