Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

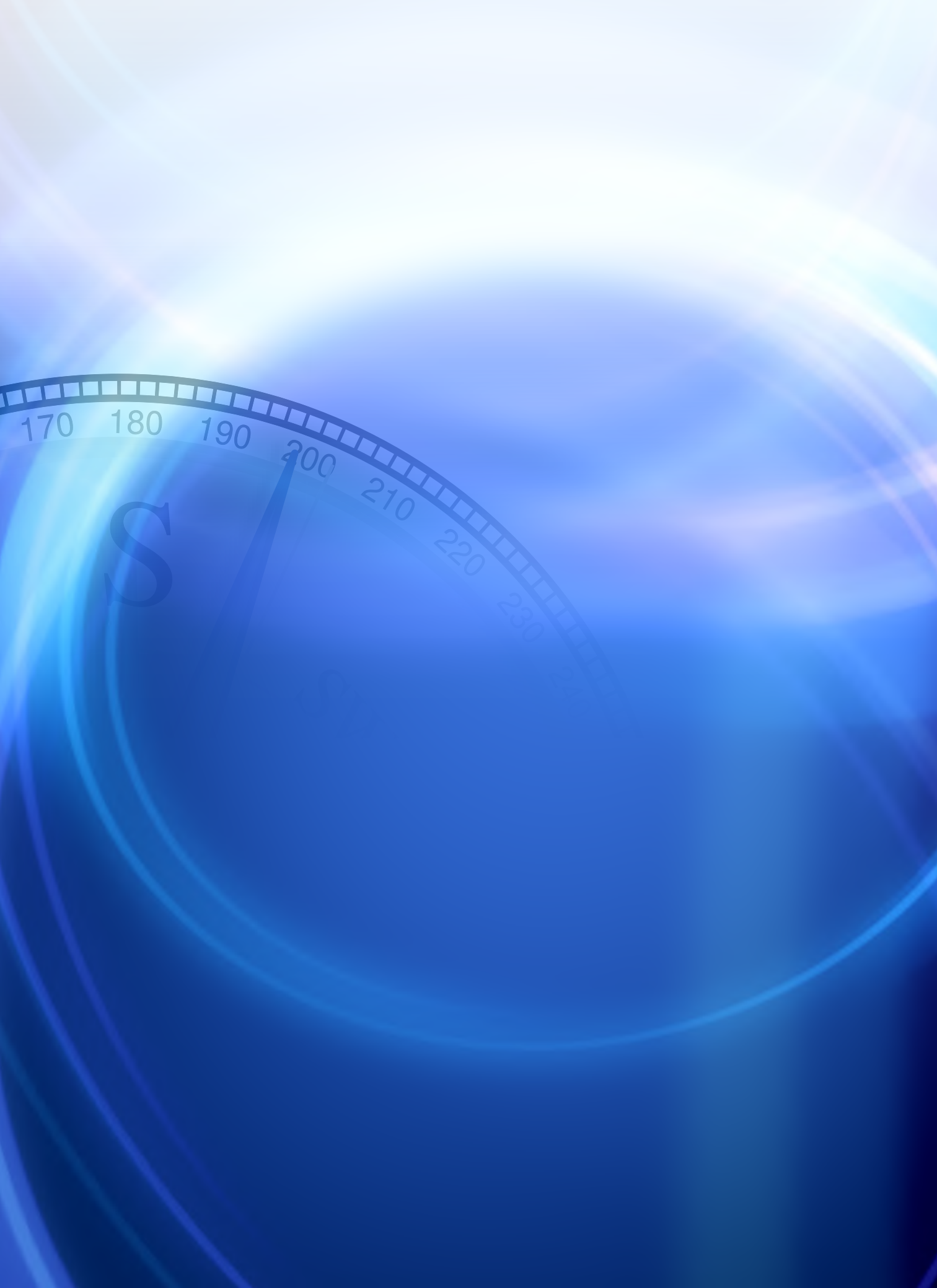
Journal Abbreviation: South Clin Ist Euras

Volume 36 • Issue 3 • September 2025

KARE

ISSN 2587-0998

www.scie.online


170
180
190
200
210
220
230
S

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

Contact: Yunus Emre Altuntaş

Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Denizer Cad., No: 1, 34865 Cevizli, İstanbul
Phone: +90-216-441 39 00 (23311) Phone 2: +90-216-458 30 00 (23311)
e-mail: info@scie.online, editor@scie.online

Owned by on behalf of the Director of University of Medical Sciences Kartal Dr. Lütfi Kırdar Health Practice and Research Center, İstanbul: Recep DEMİRHAN | Executive Editor: Recep DEMİRHAN | Publication Type: Periodical | Printed: Yıldırım Matbaacılık +90 212 629 80 37 | Printing Date: September 2025 | Circulation: 50

ISSN 2587-0998

www.scie.online

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

INTERNATIONAL ADVISORY BOARD

NATIONAL ADVISORY BOARD

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

NATIONAL ADVISORY BOARD

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

AIMS AND SCOPE

Southern Clinics of Istanbul Eurasia - SCIE (formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi / Medical Journal of Kartal Training and Research Hospital) is the scientific open access publication of University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital (the content may be accessed free of charge through the web site www.scie.online). Four issues are released every year in March, June, September, and December. The language of publication is English.

The aim of the journal is to publish high level clinical and experimental studies conducted in all medical branches, reviews comprising the latest research findings, reports on rare and educational cases, and letters to the editor.

The journal observes a double-blinded, peer-review process with external and independent reviewers in the evaluation and approval of manuscripts for publication.

The target population of the journal includes specialists in all medical branches, academicians, and relevant health care professionals.

Publication policy and editorial processes follow the guidelines of the International Committee of Medical Journal Editors, the World Association of Medical Editors, the Council of Science Editors, the European Association of Science Editors, and the Committee on Publication Ethics.

SCIE is indexed in the TUBITAK ULAKBIM TR Index, EBSCO, GALE, ProQuest, DOAJ, CABI, Scope Database, MIAR, Türk Medline, WorldCat and Türkiye Citation Index. The journal is financially supported by University of Health Sciences Kartal Dr. Lütfi Kırdar City Hospital.

Editor: Recep DEMİRHAN
Address: Kartal Dr. Lütfi Kırdar Şehir Hastanesi, Denizer Cad., No: 1, 34865 Cevizli, İstanbul
Phone: +90-216-441 39 00 (23311)
E-mail: editor@scie.online

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

INSTRUCTIONS FOR AUTHORS

About the Journal

Southern Clinics of Istanbul Eurasia - SCIE (formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi - The Medical Journal of Kartal Training and Research Hospital) is published four issue in English by the Kartal Dr. Lütfi Kırdar City Hospital, and is a peer reviewed general medical journal for all physicians, doctors, medical researchers, and health workers. The journal reports the advances and progress in current medical sciences and technology. The journal covers basic and clinical studies in medicine. Articles of clinical interest and implications will be given preference.

Contributions may be in the form of clinical and basic research articles, case reports, personal clinical and technical notes, and letters to the Editor. The Journal also publishes brief reports on original studies or evaluations, book reviews, and proceedings of scientific meetings. The Editor-in-Chief may request from the authors additional data, information, or complementary material concerning the manuscripts, and the authors must comply with such requests.

Manuscripts should be prepared in accordance with the Uniform Requirements for Manuscripts Submitted to Biomedical Journals regularly updated by the International Committee of Medical Journal Editors, available at http:// www.icmje.org.

Ethics

The editorial and publication processes of the journal are shaped in accordance with the guidelines of the International Council of Medical Journal Editors (ICMJE), the World Association of Medical Editors (WAME), the Council of Science Editors (CSE), the Committee on Publication Ethics (COPE), the European Association of Science Editors (EASE), and National Information Standards Organization (NISO).

All manuscripts presenting data obtained from research involving human subjects must include a statement that the written informed consent of the participants was obtained and that the study was approved by an institutional review board or an equivalent body. This institutional approval should be submitted with the manuscript. Authors of case reports must submit the written informed consent of the subject(s) of the report or of the patient's legal representatives for the publication of the manuscript.

All studies should be carried out in accordance with the World Medical Association Declaration of Helsinki, covering the latest revision date. Patient confidentiality must be protected according to the universally accepted guidelines and rules. Manuscripts reporting the results of experimental studies on animals must include a statement that the study protocol was approved by the animal ethics committee of the institution and that the study was conducted in accordance with the internationally accepted guidelines, including the Universal Declaration of Animal Rights, European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Principles of Laboratory Animal Science, and the Handbook for the Care and Utilization of Laboratory Animals. The authors are strongly requested to send the approval of the ethics committee together with the manuscript. In addition, manuscripts on human and animal studies should describe procedures indicating the steps taken to eliminate pain and suffering.

Submission and peer reviewing

The official language of the Journal is English. Following an initial evaluation and elimination for sufficient priority, manuscripts are subject to blind peer review by at least two reviewers. The Editor, who judges and analyzes the entire review process, reaches a final decision to accept or reject a manuscript, or to recommend a revision. The Editor has the right to reject a revised manuscript.

Copyright - Authors' approval - Conflict of interest

The authors should disclose all issues concerning financial relationship, conflict of interest, and competing interest that may potentially influence the results of the research or scientific judgement. All financial contributions or sponsorship, financial relations, and areas of conflict of interest should be clearly explained in a separate letter to the editor at the time of submission, with full assurance that any related document will be submitted to the Journal when requested.

Manuscripts should be sent with the Copyright-Authors' Approval-Conflict of Interest Letter signed by the author(s). A copy of this letter can be found at web site. Manuscripts will not be accepted for evaluation until the receipt of this document by the Journal.

The Editorial Office inspects all submitted manuscripts concerning plagiarism and duplication. If an ethical problem is detected, the editorial office will act according to the COPE guidelines.

Submitting a manuscript

SCIE accepts only on-line submission via the official web site (please click, http://www.scie.online/en/?s=online_submission) and refuses printed manuscript submissions by mail. All submissions are made by the on-line submission system called Journal Agent, by clicking the icon "Online manuscript submission" at the above mentioned web site homepage. The system includes directions at each step but for further information you may visit the web site.

Important notice

Before the corresponding author submits the manuscript, all authors must obtain ORCİD ID number and provide it to the corresponding author.

Manuscript preparation

The author(s) must declare that they were involved in at least 3 of the 5 stages of the study stated in the "acknowledgement of authorship and transfer of copyright agreement" as "designing the study", "collecting the data", "analyzing the data", "writing the manuscript" and "confirming the accuracy of the data and the analyses". Those who do not fulfill this prerequisite should not be stated as an author.

The number of authors should not exceed 6 for clinical, basic and experimental studies, 4 for case reports and technical notes, and 3 for letters to the editor and reviews. In multi-center or multi-discipline studies, each author's contribution regarding the 5 stages mentioned above should be stated clearly. For this kind of multi-center or multi-discipline studies with excessive number of authors, the editor has the right to request that the number of authors be reduced.

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

Manuscripts should be designed in the following order: title page, abstract, main text, references, and tables, with each typeset on a separate page.

Title page: This page should only include the title of the manuscript, which should be carefully chosen to better reflect the contents of the study. Author names should not appear in the title and subsequent pages.

Abstract: It should not exceed 300 words. Abstracts should be structured in four paragraphs using the following subtitles: Objectives, Methods, Results, and Conclusion. Abstracts of case reports should be unstructured.

Main text: The body consists of Introduction, Patients/Materials and methods, Results, and Discussion. Use "Patients and methods" for clinical studies, and "Materials and methods" for animal and laboratory studies.

The Introduction section clearly states the purpose of the manuscript and includes a brief summary of the most relevant literature.

The Patients/Materials and Methods section describes the study population and the study design, with adequate information on the techniques, materials, and methods used. A clear description of the statistical methods should also be given.

The Results section should provide a detailed report on the findings of the study. Data should be concisely presented, preferably in tables or illustrations, which should not exceed the page layout of the Journal.

The Discussion section should mainly rely on the conclusions derived from the results of the study, with relevant citations from the most recent research.

Letter to the Editor: Letters to the editor should not exceed 350 words.

References: References should be numbered in the order in which they are mentioned in the text. Only published articles or articles in press can be used in references. Unpublished data or personal communications should not be used. The style should conform to the standards described in detail in "Citing Medicine-The NLM Style Guide for Authors, Editors, and Publishers" (http://www.nlm.nih.gov/citingmedicine), which is recommended in the most recent update of "Uniform Requirements for Manuscripts Submitted to Biomedical Journals". A brief presentation of these standards can also be found at http://www.nlm.nih.gov/bsd/uniform_requirements.html. Journal titles should be abbreviated according to the Index Medicus. The Journal's title is abbreviated as "South Clin Ist Euras".

The style and punctuation should follow the formats outlined below:

Standard journal article:

Napolitano LM, Corwin HL. Efficacy of red blood cell transfusion in the critically ill. Crit Care Clin 2004;20:255-68.

All authors if six or fewer should be listed; otherwise, the first six and "et al." should be written.

Epub ahead of print Articles:

Rupprecht H, Heppner HJ, Wohlfart K, Türkoglu A. The geriatric polytrauma: Risk profile and prognostic factors. Ulus Travma Acil Cerrahi Derg 2017 Jan 05. doi: 10.5505/tjtes.2016.77177. [Epub ahead of print].

Personal author(s):

Enzingerz FM, Weiss SW. Soft tissue tumors. St. Louis: Mosby; 1995. p. 27-50.

Editor(s), compiler(s) as author:

Günal İ, Barton NJ, Çallı İ, editors. Current management of scaphoid fractures. Twenty questions answered. London: The Royal Society of Medicine Press; 2002.

Chapter in a book:

Henick DK, Kennedy DW. Fungal sinusitis. In: Stankiewicz JA, editor. Advanced endoscopic sinus surgery. St Louis: Mosby; 1995. p. 69-80.

Conference paper:

Kouzelis A, Matzaroglou C, Kravvas A, Mylonas S, Megas P, Gliatis J. Anterior cruciate ligament reconstruction: patellar tendon autogaft versus four strand hamstring tendon. In: Proceedings of the 9th Turkish Sports Traumatology, Arthroscopy and Knee Surgery Congress; 2008 Oct 14-18; İstanbul, Türkiye. p. 223. Unpublished conference papers should not be used in the reference list.

Direct use of references is strongly recommended and the authors may be asked to provide the first and last pages of certain references. Publication of the manuscript will be suspended until this request is fulfilled by the author(s).

Figures and tables

All illustrations (photographs, graphics, and drawings) accompanying the manuscript should be referred to as "figure". All figures should be numbered consecutively and mentioned in the text. Figure legends should be added at the end of the text as a separate section. Each figure should be prepared as a separate digital file in "jpeg" format, with a minimum of 9×13 cm and at 300 dpi or better resolution.

All illustrations should be original. Illustrations published elsewhere should be submitted with the written permission of the original copyright holder.

For recognizable photographs of human subjects, written permission signed by the patient or his/her legal representative should be submitted; otherwise, patient names or eyes must be blocked out to prevent identification. Microscopic photographs should include information on staining and magnification.

Upon the author's request, color prints will be considered for publication; however, the authors are responsible for the extra cost of printing color illustrations. Each table should be prepared on a separate page, either at the end of the text file or as a separate supplementary file, with table heading on top of the table. Table heading should be added to the main text file on a separate page when a table is submitted as a supplementary file.

Checklist

Covering letter

- Signed by all contributors
- Previous publication / presentations mentioned

Southern Clinics of Istanbul Eurasia

Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

Source of funding mentioned

Conflicts of interest disclosed

ORCİD ID number of all contributors

Authors

Last name and given name provided along with Middle name initials (where applicable)

Author for correspondence, with e-mail address provided

Number of contributors restricted as per the instructions

Identity not revealed in paper except title page (e.g. name of the institute in Methods, citing previous study as 'our study', names on figure labels, name of institute in photographs, etc.)

Presentation and format

Double spacing

Margins 2 cm from all four sides

Page numbers included at bottom

Title page contains all the desired information

Abstract page contains the full title of the manuscript

Abstract provided (structured abstract of 300 words for original articles, meta analysis (Backgroud, Methods, Results, Conclusions) and review articles (Objective, Data sources, Study selection, Results, Conclusions)

Key words provided (three or no more than 6 words) Introduction should be short and arresting. State the purpose of the article and summarize the rationale for the study or observation. Give only strictly pertinent references

The references cited in the text should be after punctuation marks

References according to the journal's instructions, punctuation marks checked

Language and grammar

Uniformly American English

Write the full term for each abbreviation at its first use in the title, abstract, keywords and text separately unless it is a standard unit of measure. Numerals from 1 to 10 spelt out

Numerals at the beginning of the sentence spelt out

Check the manuscript for spelling, grammar and punctuation errors

If a brand name is cited, supply the manufacturer's name and address (city and state/country).

Species names should be in italics

Tables and figures

No repetition of data in tables and graphs and in text

Actual numbers from which graphs drawn, provided

Figures necessary and of high quality (colour)

Table and figure numbers in Arabic letters (not Roman)

Labels pasted on back of the photographs (no names written)

Patients' privacy maintained (if not permission taken)

Credit note for borrowed figures/tables provided

Write the full term for each abbreviation used in the table as a footnote

Editor: Recep DEMİRHAN

Address: Kartal Dr. Lütfi Kırdar Şehir Hastanesi,
Denizer Cad., No: 1, 34865 Cevizli, İstanbul

Phone: +90-216-441 39 00 (23311)

E-mail: info@scie.online, editor@scie.online

Publisher: KARE Publishing - KARE Medya

Address: Göztepe Mah., Fahrettin Kerim Gökay Cad., No: 200,
Da: 2, Göztepe, Kadıköy, İstanbul

Phone: +90-216-550 61 11

Fax: +90-216-550 61 12

E-mail: kare@kareyayincilik.com

Southern Clinics of Istanbul Eurasia
Formerly Kartal Eğitim ve Araştırma Hastanesi Tıp Dergisi

CONTENTS

Volume 36 Issue 3 Year 2025

SCIE DOI: 10.14744/scie.2025.70431
South. Clin. Ist. Euras. 2025;36(3):205-212

Original Article

Is Restrictive Transfusion in the Burn Intensive Care Unit a Dream?

Bülent Kaya,[1] Sezer Yakupoğlu,[2] Elif Bombacı,[2] Nur Benzonana,[1] Gaye Filinte,[3] Recep Demirhan[4]

[1]Department of Infectious Diseases And Clinical Microbiology, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye
[2]Department of Anesthesia And Reanimation, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye
[3]Department of Plastic And Reconstructive Surgery, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye
[4]Department of Thoracic Surgery, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye

Submitted: 08.08.2025
Revised: 08.08.2025
Accepted: 13.08.2025

Correspondence: Bülent Kaya, Department of Infectious Diseases And Clinical Microbiology, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye

E-mail: badeatakaya@hotmail.com

Keywords: Bloodstream infections; burns; intensive care unit; restrictive transfusion.

ABSTRACT

Objective: In patients admitted to burn intensive care units (ICUs), increase the need for blood transfusions. In parallel with prolonged ICU stays, the risk of bloodstream infections (BSIs) also increases. This study aims to examine the relationship between transfusion and BSIs and to promote the practice of restrictive transfusion.

Methods: 158 patients with severe burns (≥20% total body surface area) were treated in the burn ICU of our hospital over five years. The hemoglobin (Hb) threshold for restrictive transfusion was defined as 7 g/dL, while for liberal transfusion it was set at 10 g/dL.

Results: Of the 158 patients included in the study, 17.7% (n=28) were female. The mean age of the patients was 41±15 years. The average total body surface area (TBSA) burned was 42.7±17% (range: 20–92%). The causes of burns were flame in 79.2% (n=125), electricity in 10.1% (n=16), boiling water in 7% (n=11), hot oil and steam in one patient each (0.6%), and chemicals in 2.5% (n=4). A statistically significant relationship was found between the total number of transfusions and burn percentage, length of stay in the burn ICU, number of escharotomy procedures performed, final hemoglobin (Hb), white blood cell (WBC) count, and number of fresh frozen plasma (FFP) units ($p<0.05$). Restrictive transfusion was adopted in 72.5–86.8% of erythrocyte suspension (ES) transfusions. Among the BSIs, the most commonly isolated pathogens were coagulase-negative staphylococci (CNS) in 28.5% (n=45), A. baumannii in 19.6% (n=31), and P. aeruginosa in 12.7% (n=20). A statistically significant association was found between the number of transfusions and the presence of CNS and P. aeruginosa isolates ($p<0.05$), whereas no such association was found with A. baumannii ($p>0.05$). The rate of BSIs caused by Candida species was 4.5% (n=7).

Conclusion: Were commend a restrictive transfusion strategy in burn ICU patientsto minimize transfusion-related reactions and BSI risk while ensuring optimal patient support.

INTRODUCTION

Blood component transfusion is an indispensable part of the treatment of patients admitted to intensive care units (ICUs). Advanced age, chronic diseases, surgical interventions, gastrointestinal bleeding, prolonged ICU stays resulting in malnutrition, frequent blood draws for routine laboratory testing, and major tissue trauma—as in the case of burns—and the associated numerous surgical procedures are among the leading causes of blood transfusions.[1-3]

Although the primary objective is to replace erythrocytes and platelets and to correct coagulopathy, transfusions can lead to a wide range of complications, including acute hemolytic transfusion reactions, allergic and anaphylactic reactions, febrile non-hemolytic transfusion reactions, transfusion-associated circulatory overload, transfusion-related acute lung injury, graft-versus-host disease, and transfusion-transmitted infections.[3,4] As the surface area and depth of burns increase, patients' ICU stays are prolonged, resulting in additional transfusion requirements and increased BSI incidence. The World Health Organization (WHO) recommends safe and rational use of blood to reduce unnecessary and unsafe transfusions, improve patient outcomes and safety, and thereby minimize the risk of adverse events such as errors, transfusion reactions, and transmission of infections.[5]

Numerous studies have compared restrictive (maintaining Hb above 7 g/dL) and liberal (maintaining Hb above 10 g/dL) transfusion strategies in ICUs, and they generally support restrictive transfusion.[6,7] However, specific standards must be established for the implementation of these approaches in burn ICUs.

In ICU patients, the risk of anemia—alongside the increase in surgical interventions and radical dressing procedures proportional to burn area—heightens the need for erythrocyte suspension (ES) transfusions.[3] An experienced surgeon and intensive care specialist can predict, in advance of a specific surgical procedure, how many units of blood a patient may lose and the transfusion requirement. Given the lack of a well-established blood donation culture in society, difficulties in blood supply, material costs, and transfusion-related complications, there is a need to establish standards for restrictive transfusion practices.

In our study, we aimed to promote restrictive transfusion in burn ICUs, not only to reduce various transfusion-related complications and improve cost-effectiveness, but also to decrease or prevent bloodstream infections (BSIs).

MATERIALS AND METHODS

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 24/01/2025, No: 2025/010.99/12/23) and was conducted in accordance with the principles of the Declaration of Helsinki.

Between January 1, 2020, and December 31, 2024, a total of 482 patients admitted and followed in the burn ICU of our hospital were identified via the hospital automation system. Seventy-four pediatric patients under 18 years of age were excluded from the study, and the remaining 408 adult patients were screened. Of these, 158 patients with a burn surface area of ≥20% were included in the study.

Demographic data, comorbidities, Glasgow Coma Scale (GCS) and APACHE II scores calculated on the day of admission, causes and percentages of burns, burn depths, length of stay in the burn ICU, number of escharotomies, blood types, initial and final hemoglobin (Hb) levels measured after ICU admission, number of transfused erythrocyte suspensions (ES), fresh frozen plasma (FFP), apheresis platelet suspensions (PS), pooled PS, and cryoprecipitate units were recorded in an Excel spreadsheet. Patients were divided into three groups based on their Hb levels: <7 g/dL, 7–10 g/dL, and>10 g/dL to evaluate the efficacy of restrictive (Hb<7 g/dL) and liberal (Hb>10 g/dL) ES transfusion strategies in the burn ICU, pre- and post-transfusion Hb levels were recorded for each group.

Microorganisms isolated from patients who received ES transfusions and were diagnosed with BSI were also recorded in the Excel spreadsheet. Only the first positive culture was included in the analysis of cases which the same microorganism was isolated multiple times from the same patient. The relationship between the number of ES transfusions and the incidence of BSI was examined.

Statistical Analysis

Patient data collected for the study were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) for macOS version 30.0 (IBM Corp., Armonk, NY). Frequencies and percentages were used for categorical variables, and mean, standard deviation, median, minimum, and maximum values were used for continuous variables. The Kolmogorov–Smirnov test was used to assess the normality of variable distribution. For comparisons between groups, the Mann–Whitney U test was used for two groups, the Kruskal–Wallis H test for more than two groups, and the chi-square test was used for categorical variables. Spearman's correlation analysis was used to examine relationships between continuous variables. A p-value <0.05 was considered statistically significant.

RESULTS

Of the 158 patients included in the study, 17.7% (n=28) were female and 82.3% (n=130) were male. The mean age of the patients was 41±15 years. The distribution of demographic and clinical characteristics is presented in Table 1. Upon admission to the burn ICU, the mean Glasgow Coma Scale score was 10.5±5, and the mean APACHE II score was 27.8±9.9. Comorbidities included hypertension (HT) in 21 patients (13.3%), diabetes mellitus (DM) in 10 patients (6.3%), and coronary artery disease (CAD) in 6 patients (3.8%) (Table 1).

The mean burn percentage was 42.7±17% (range: 20–92%). The most common cause was flame burns in 79.2% (n=125) of patients. Among these, 11 patients (8.8%) also had inhalation injury. Burn etiologies included electrical burns in 10.1% (n=16), scalds from boiling water in 7% (n=11), hot oil and steam burns in one patient each (0.6%), and chemical burns in 2.5% (n=4). The chemical burn agents were hydrogen peroxide, tar, soda-cyanide, and thinner. Partial-thickness burns were present in 11.4% (n=18), mixed-depth (partial/full-thickness) burns in 69% (n=109), and full-thickness burns in 19.6% (n=31). The average length of stay in the burn ICU was 26.7±19.8 days. On average, each patient underwent 4.2±3.2 escharotomy procedures (Table 1).

The relationship between the total number of ES transfusions administered to burn patients and their demographic and clinical findings is shown in Table 2. If a statistically significant relationship was found between the variables, the direction of the correlation was assessed using the correlation coefficient (r). A positive correlation coefficient indicated a direct relationship between the variables, whereas a negative coefficient indicated an inverse relationship. The interpretation of correlation strength was as follows:

- 0.00–0.29: weak correlation
- 0.30–0.49: low correlation
- 0.50–0.69: moderate correlation

Table 1. Distribution of demographic and clinical findings of patients

Variables (N=158)	n (%)	Average±SS	Median (Min-Max)
Age	41±15	40 (18-85)	
Gender			
Female	28 (17.7)		
Male	130 (82.3)		
Glascow comascale (hospitalization day)		10.5±5	14.5 (3-18)
APACHI II score (hospitalization day)		27.8±9.9	30 (1-55)
Diabetesmellitus	10 (6.3)		
Hypertension	21 (13.3)		
Hypothyroidism	3 (1.9)		
Mentalretardation	2 (1.3)		
Schizophrenia	6 (3.8)		
Substance addiction	3 (1.9)		
Alcohol addiction	2 (1.3)		
Coronary artery disease	6 (3.8)		
Congestive heart failure	1 (0.6)		
Chronic obstructive pulmonary disease	1 (0.6)		
Depression	1 (0.6)		
Cerebrovascular disease	3 (1.9)		
Atrial fibrillation	2 (1.3)		
Alzheimer's disease	1 (0.6)		
Bronchial asthma	1 (0.6)		
Obesity	2 (1.3)		
Prostate cancer	1 (0.6)		
Malignant melanoma	1 (0.6)		
Mood disorder	1 (0.6)		
Vertigo	2 (1.3)		
Cause of burn			
Flame	125 (79.1)		
Electric	16 (10.1)		
Scalds	11 (7)		
Hot oil	1 (0.6)		
Hot steam	1 (0.6)		
Chemical	4 (2.5)		
Inhalation injury	11 (8.8)		
Burn (%)		42.7±17	40 (20-92)
Burn depth			
Partial thickness	18 (11.4)		
Partial thickness/ Full thickness burn	109 (69)		
Full thickness burn	31 (19.6)		
Length of stay in ICU (days)		26.7±19.8	23.5 (1-156)
Escharotomy surgery		4.2±3.2	3 (1-21)
Hb on ICU admission(mg/dl)		15.3±3.1	15.6 (4.6-24.3)
HCT on ICU admission(%)		46.1±9.1	47.1 (15.2-72.6)
PLT on ICU admission(x103/µL)		279.7±116.4	270 (73-931)
WBC on ICU admission(µL)		22016.3±11257.7	19695 (2460-62960)
Hb at discharge from ICU (mg/dl)		9.1±1.4	9 (3.9-15)
HCT at discharge from ICU (%)		27.8±4.3	27.8 (11.8-45.4)
PLT at dischargefrom ICU (x103/µL)		283.5±207.4	272 (7-1080)
WBC at dischargefrom ICU (µL)		12493±10004.9	10180 (440-68410)
Blood groups			
A Rh (-)	8 (5.1)		

A Rh (+)	61 (38.6)		
AB Rh (-)	1 (0.6)		
AB Rh (+)	13 (8.2)		
B Rh (-)	3 (1.9)		
B Rh (+)	19 (12)		
O Rh (-)	3 (1.9)		
O Rh (+)	50 (31.6)		
ES transfusion		14.7±12.7	12 (1-68)
FFP transfusion		9.7±9.9	7 (1-55)
Apheresis TS transfusion		3.1±4.5	1 (1-16)
Pooled TS transfusion		3.4±3	2 (1-13)
Kryoprespitate transfusion		3.3±3	2.5 (1-9)
Bloodstreaminfectionisolates			
Acinetobacter baumannii	31 (19.6)		
Aeromonas punctata (caviae)	1 (0.6)		
Bacillus cereus group	2 (1.3)		
Candida albicans	2 (1.3)		
Candida parapsilosis	5 (3.2)		
Corynebacterium Species	4 (2.5)		
Difteroid basil	1 (0.6)		
Enterobacter aerogenes	2 (1.3)		
Enterobacter cloacae	2 (1.3)		
Enterococcus faecalis	7 (4.4)		
Enterococcus faecium	1 (0.6)		
Enterococcus gallinarum	1 (0.6)		
Escherichia coli	3 (1.9)		
Klebsiella oxytoca	1 (0.6)		
Klebsiella pneumoniae	5 (3.2)		
CNS	45 (28.5)		
Microbacterium flavescens/laevaniformans	1 (0.6)		
Pantoea dispersa	1 (0.6)		
Propionibacterium acnes	1 (0.6)		
Proteus mirabilis	2 (1.3)		
Providencia rettgeri	1 (0.6)		
Pseudomonas aeruginosa	20 (12.7)		
Pseudomonas putida	1 (0.6)		
Serratia marcescens	4 (2.5)		
Sphingomonas paucimobilis	2 (1.3)		
Staphylococcus aureus	2 (1.3)		
Stenotrophomonas maltophilia	3(1.9)		
Turicellaotitidis	1 (0.6)		

APACHE: Acute Physiology and Chronic Health Evaluation; Hb: Hemoglobin; HCT: Hematocrit; PLT: Platelet; WBC: White Blood Cell; ES: Erythrocyte suspension; FFP: Fresh frozen plasma; TS: Thrombocyte suspension; ICU: Intensive Care Unit; CNS: Coagulase negative Staphylococci.

- 0.70–0.89: strong correlation
- 0.90–1.00: very strong correlation

Upon examination of the table, statistically significant correlations ($p<0.05$) were identified between the total number of transfusions and the following variables: Burn percentage (weak, positive correlation), length of stay in the burn ICU (strong, positive correlation), number of escharotomy procedures (moderate, positive correlation), discharge hemoglobin (Hb) and white blood cell (WBC) counts (weak, negative correlations), and number of FFP units transfused (strong, positive correlation).

Regarding blood types, 38.7% (n=61) of patients had A RhD (+), and 31.7% (n=50) had O RhD (+). A mean of 14.7±12.7 units of erythrocyte suspension (ES) was transfused per patient (Table 1). The distribution of pre- and post-transfusion Hb levels among burn patients is shown in Table 3. A total of 1242 ES transfusions were administered. There was a statistically significant difference

Table 2. Investigation of the relationship between patients' transfusion numbers and demographic and clinical characteristics

	Number of ES
Age	
r	-0.072
p	0.366
Glascow coma scale	
r	-0.014
p	0.861
APACHE II Score	
r	-0.019
p	0.810
Burn (%)	
r	0.160
p	0.045
Length of stay in burn ICU	
r	0.757
p	<0.001
Escharotomy surgery	
r	0.684
p	<0.001
Hb on ICU admission (mg/dl)	
r	0.100
p	0.212
HCT on ICU admission (mg/dl)	
r	0.127
p	0.112
PLT on ICU admission (mg/dl)	
r	0.059
p	0.461
WBC on ICU admission (mg/dl)	
r	0.038
p	0.639
Hb at discharge from ICU (mg/dl)	
r	-0.187
p	0.019
HCT at discharge from ICU (mg/dl)	
r	-0.177
p	0.027
PLT at discharge from ICU (mg/dl)	
r	-0.098
p	0.222
WBC at discharge from ICU (mg/dl)	
r	-0.214
p	0.007
FFP	
r	0.808
p	<0.001

APACHE: Acute Physiology and Chronic Health Evaluation; Hb: Hemoglobin; HCT: Hematocrit; PLT: Platelet; WBC: White Blood Cell; ES: Erythrocyte suspension; FFP: Fresh frozen plasma; ICU: Intensive Care Unit.

Table 3. Distribution of hemoglobin measurements of patients before and after transfusion

	Post-transfusion hemoglobin		
	<7	7-10	>10
Pre-transfusion hemoglobin			
<7	2 (2.9)	50 (72.5)	17 (24.6)
7-10	43 (4.3)	822 (82.3)	134 (13.4)
>10	6 (3.4)	151 (86.8)	17 (9.8)

* p=0.042

Table 4. Distribution of transfusion numbers according to demographic and clinical characteristics of patients

Variables	Number of ES	
	Median (Min-Max)	p-value
Gender		0.814
Female	11.5 (1-47)	
Male	12 (1-68)	
Hypertension		0.124
No	12 (1-47)	
Yes	14 (1-68)	
Burn depth		0.400
Partial thickness/ Full thickness burn	13 (1-56)	
Partial thickness	11.5 (1-30)	
Full thickness burn	8 (1-68)	
CNS		0.003
No	10 (1-68)	
Yes	15 (3-47)	
Pseudomonas aeruginosa		0.003
No	10 (1-68)	
Yes	17.5 (1-47)	
Acinetobacter baumannii		0.069
No	10 (1-68)	
Yes	15 (2-45)	

CNS: Coagulase negative Staphylococci.

between pre- and post-transfusion Hb values (p<0.05). Among patients with pre-transfusion Hb<7 mg/dL, 72.5% (n=50) had post-transfusion Hb levels of 7–10 mg/dL, and 24.6% (n=17) had levels >10 mg/dL. Of those with pre-transfusion Hb>10 mg/dL, 86.8% (n=151) had post-transfusion Hb between 7–10 mg/dL, while 3.4% (n=6) had levels <7 mg/dL. Among patients whose pre-transfusion Hb levels were between 7–10 mg/dL, 82.3% (n=822) remained within the same range post-transfusion (Table 3).

The most frequently isolated microorganism from the blood cultures of patients who received ES transfusions was coagulase-negative staphylococci (CNS), identified in

28.5% (n=45) of patients. This was followed by *Acinetobacter baumannii* in 19.6% (n=31) and *Pseudomonas aeruginosa* in 12.7% (n=20) (Table 1). The distribution of transfusion counts according to patients' demographic and clinical characteristics is presented in Table 4. A statistically significant difference was found between the number of transfusions and BSIs caused by CNS and *P. aeruginosa* ($p<0.05$). As the number of ES transfusions increased, the incidence of BSIs caused by these microorganisms also rose. However, there was no statistically significant relationship between the number of ES transfusions and BSIs due to *A. baumannii* ($p>0.05$). The isolation rate of *Candida species* was 4.5% (n=7), five of which were *C. parapsilosis*. Multiple microorganisms were isolated from the blood cultures of some patients.

DISCUSSION

Burn injuries predominantly result from occupational exposure, particularly in high-risk and hazardous work environments, which explains the male predominance (82.3%) observed in our study. Flame burns, electrical injuries, and chemical burns accounted for 91.8% of all burn cases (Table 1), with flame burns being the most frequent etiology (79.1%, n=125). Although workplace accidents were the primary source, some incidents also stemmed from residential fires. Similarly, Abda et al.[8] reported a male predominance (76.1%) among burn patients, with flame exposure as the most common cause (63%). In our cohort, 8.8% (n=11) of patients with flame burns also had inhalation injuries, and these patients exhibited larger total body surface area (TBSA) burns. Inhalation injury typically affects the upper airway and may lead to acute respiratory arrest due to edema, which can manifest early or evolve within hours and may take up to six days to resolve.[9] Electrical and chemical burns were exclusively occupational in origin. Although external injuries may appear minor in electrical burns, severe damage to deeper tissues often occurs, with the severity directly related to voltage level.[10]

The most common comorbidities were hypertension (HT), diabetes mellitus (DM), and coronary artery disease (CAD) (Table 1). In addition, 3.8% (n=6) of patients were diagnosed with schizophrenia and had sustained burns from fires they had initiated in their own homes.

Burns involving more than 20% of TBSA are classified as severe, as they trigger a cytokine storm that leads to pathophysiological changes not only at the burn site but also in remote tissues.[10-12] Therefore, our study included only patients with ≥20% TBSA burns. The mean TBSA burned was 42.7±17%, with mixed partial-thickness/full-thickness burns being the most prevalent type (69%). Patients were hospitalized in the burn ICU for an average of 26.7±19.8 days. As TBSA percentage and burn depth increased, so did the risk of mortality.

At ICU admission, patients had a mean Hb level of 15.3±3.1 mg/dL, which declined to 9.1±1.4 mg/dL at discharge. Unlike other types of trauma, early-stage burn trauma is characterized by intravascular fluid loss, which leads to hemoconcentration rather than anemia, thus explaining the initially elevated Hb levels observed upon ICU admission.[3,12] Early leukocytosis is also a common response to burn trauma. Patients' mean white blood cell (WBC) count at ICU admission was 22,016.3±11,257.7, decreasing to 12,493±10,004.9 by discharge.

Restrictive transfusion strategies are generally recommended for critically ill patients, those with gastrointestinal bleeding, post-cardiac surgery patients, and those with isolated troponin elevation due to cardiac ischemia, but not for acute coronary syndrome.[13,14] Due to extensive tissue loss and frequent surgical interventions, erythrocyte suspension (ES) transfusions are commonly employed in the treatment of severely burned patients.[3] In our study, the average number of ES transfusions per patient was 14.7±12.7. Although the commonly accepted practice has been to use a 1:1 ratio of ES to fresh frozen plasma (FFP), our findings revealed a ratio of 1.5:1. While the 1:1 ratio is not a strict guideline, patient-specific factors and a restrictive transfusion approach should guide transfusion practices. Vlaar APJ et al.[15] proposed a 2:1 ratio, although with a conditional recommendation and low certainty of evidence.

There was a weak and statistically insignificant inverse correlation between ES transfusion and patients' age, Glasgow Coma Scale scores, and APACHE II scores upon ICU admission ($p>0.05$). Greater burn depth and TBSA involvement were associated with longer ICU stays, which in turn necessitated more transfusions. We found a strong correlation between ICU length of stay and the number of ES transfusions ($p<0.001$, Table 2). There was also a weak association between ES transfusions and TBSA percentage ($p=0.045$), and an almost strong correlation with the number of escharotomy surgeries ($p<0.001$, Table 2). These findings suggest that the primary determinants of ES transfusion are the frequency of surgical interventions and prolonged ICU stays. Du et al.[3] also concluded that ES transfusion offers limited benefit for patient outcomes.

Consistent with the classification described by Lotterman et al.[14] we stratified patients into three groups based on their pre-transfusion Hb levels. Due to the retrospective nature of our study, the groups were not evenly distributed. Over five years, a total of 1242 ES transfusions were administered to 158 patients. In all three groups, Hb levels significantly increased post-transfusion, with most post-transfusion values remaining within the 7-10 mg/dL range ($p<0.042$, Table 3). Although restrictive transfusion was the goal, radical and hemorrhagic wound dressings and escharotomy procedures (mean 4.2±3.2 surgeries per patient, Table 1) necessitated anticipation of blood loss and the maintenance of existing Hb levels (Table 3). ES transfusions did not demonstrate a statistically significant impact on mortality ($p>0.05$, Table 4). As in the study by Heard et al.,[16] mortality increased in parallel with TBSA burned, a finding corroborated by our results.[16] No significant correlations were observed between ES transfusions and sex,

HT, or burn depth (p>0.05, Table 4).

Severe burns compromise skin integrity, suppress immune responses, increase invasive procedures, and prolong hospitalization, all of which render patients susceptible to bloodstream infections (BSIs).[17] Tang et al.[17] identified the five most common BSI pathogens in burn patients as *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Candida species*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia*, with only five isolates of *Staphylococcus aureus*. Similar to the findings by Nitsani et al.,[18] numerous studies—including ours and that of Tang CQ—highlight the predominance of Gram-negative organisms in BSIs among burn patients.[17-19]

Among ES-transfused patients, coagulase-negative staphylococci (CNS) were the most frequently isolated pathogens in blood cultures (28.5%, n=45) (p=0.03, Tables 1 and 4). For accurate identification, at least two aerobic and anaerobic blood culture sets should be obtained from each patient, and CNS should be present in at least one bottle per set. Given that CNS are part of the skin flora, clinicians should exercise caution in distinguishing true bacteremia from contamination; if considered pathogenic, appropriate treatment should be initiated. Such isolations are common in burn patients due to disrupted skin integrity. The second most frequent isolate was *A. baumannii* (19.6%), followed by *P. aeruginosa*, *Enterococcus faecalis*, and *Candida species* (*C. parapsilosis* and *C. albicans*) (Table 1). When comparing the three most frequently isolated BSI pathogens in transfused patients, infections caused by CNS (p=0.03) and *P. aeruginosa* (p=0.03) were significantly more frequent (Table 4). No significant association was found between ES transfusions and *A. baumannii-related* BSIs (p=0.069, Table 4). Only two BSIs were caused by S. aureus.

Conclusion

Prolonged ICU stays, frequent surgical interventions, comorbidities, advanced age, and gastrointestinal bleeding increase the need for transfusion in burn patients. Although ES transfusion is an integral component of burn management, it should not be considered life-saving due to its associated risks, including the increased likelihood of BSIs. We recommend a restrictive transfusion strategy in burn ICU patients to minimize transfusion-related reactions and BSI risk while ensuring optimal patient support. Further prospective, multicenter studies are necessary to establish clear transfusion thresholds in burn ICU setting.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee and was conducted in accordance with the principles of the Declaration of Helsinki. (Date: 24.01.2025, Decision No: 2025/010.99/12/23).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.K., S.Y., E.B., N.B., G.F., R.C.; Design: B.K., S.Y., E.B., N.B., G.F., R.C.; Supervision: B.K., S.Y., E.B., N.B., G.F., R.C.; Fundings: B.K., S.Y., E.B., N.B., G.F., R.C.; Materials: B.K., S.Y., E.B., N.B., G.F., R.C.; Data collection &/or processing: B.K., S.Y., E.B., N.B., G.F., R.C.; Analysis and/or interpretation: B.K., S.Y., E.B., N.B., G.F., R.C.; Literature search: B.K., S.Y., E.B., N.B., G.F., R.C.; Writing: B.K., S.Y., E.B., N.B., G.F., R.C.; Critical review: B.K., S.Y., E.B., N.B., G.F., R.C.

Conflict of Interest

None declared.

REFERENCES

1. Vlaar AP, Oczkowski S, de Bruin S, Wijnberge M, Antonelli M, Aubron C, et al. Transfusion strategies in non-bleeding critically ill adults: A clinical practice guideline from the European Society of Intensive Care Medicine. Intensive Care Med 2020;46:673–96. [CrossRef]
2. Cable CA, Razavi SA, Roback JD, Murphy DJ. RBC transfusion strategies in the ICU: A concise review. Crit Care Med 2019;47:1637–44. [CrossRef]
3. Du Y, Xia Y, You C, Wang Y, Duan D, Xu W, et al. Impact of red blood cell transfusion in massive burn: A multicenter cohort study. Sci Rep 2025;15:6196. [CrossRef]
4. Maxwell MJ, Wilson MJA. Complications of blood transfusion. CEACCP 2006;6:225–9. [CrossRef]
5. WHO. Health products policy and standards. Available at: https://www.who.int/teams/health-product-policy-and-standards/overview. Accessed Mar 1, 2025.
6. Raasveld SJ, de Bruin S, Reuland MC, van den Oord C, Schenk J, Aubron C, et al; InPUT Study Group. Red Blood Cell Transfusion in the Intensive Care Unit. JAMA 2023;330:1852–61.
7. ISBI Practice Guidelines Committee, Subcommittee A & Subcommittee S. ISBI practice guidelines for burn care, part 2. Burns J Int Soc Burn Inj 2018;44:1617–706.
8. Abda A, Ferli RR. Predicting burn patient mortality: A comparative analysis of the BOBI and R-baux scoring systems. Sriwijaya J Surg 2025;8:764–75. [CrossRef]
9. Mackie DP, Spoelder EJ, Paauw RJ, Knape P, Boer C. Mechanical ventilation and fluid retention in burn patients. J Trauma 2009;67:1233–8. [CrossRef]
10. Jeschke MG, vanBaar ME, Choudhry MA, Chung KK, Gibran NS, Logsetty S. Burn injury. Nat Rev Dis Primers 2020;6:11. [CrossRef]
11. Won P, Craig J, Choe D, Collier Z, Gillenwater TJ, Yenikomshian HA. Blood glucose control in the burn intensive care unit: A narrativereview of literature. Burns 2023;49:1788–95. [CrossRef]
12. Bittner EA, Shank E, Woodson L, Martyn JA. Acute and perioperative care of the burn-injured patient. Anesthesiology 2015;122:448–64. [CrossRef]
13. Coz Yataco AO, Soghier I, Hébert PC, Belley-Cote E, Disselkamp M, Flynn D, et al. Red blood cell transfusion in critically Ill adults: An American College of Chest Physicians Clinical Practice Guideline. Chest 2025;167:477–89. [CrossRef]
14. Lotterman S, Sharma S. Blood Transfusion. Treasure Island: StatPearls Publishing; 2025.
15. Vlaar APJ, Dionne JC, de Bruin S, Wijnberge M, Raasveld SJ, van Baarle FEHP, et al. Transfusion strategies in bleeding critically ill adults: A clinical practice guideline from the European Society of

Intensive Care Medicine. Intensive Care Med 2021;47:1368–92. [CrossRef]

16. Heard J, Ren Y, Taylor SL, Sen S, Palmieri T, Romanowski K, et al. burn ınjury severity in adults: Proposed definitions based on the National Burn Research Dataset. J Burn Care Res 2025;46:438–449. [CrossRef]
17. Tang CQ, Li JQ, Shou BM, Pan BH, Chen TS, Xiao YQ, et al. Epidemiology and outcomes of bloodstream infections in 177 severe burn patients from an industrial disaster: A multicentre retrospective study. Clin Microbiol Infect 2018;24:199.e1–199.e7. [CrossRef]
18. Nitsani Y, Michael T, Halpern D, Hasidim AA, Sher M, Givoli VR, et al. Blood stream ınfections in burns: A 14-year cohort analysis. Life (Basel) 2023;13:1357. [CrossRef]
19. Bergmann F, Jorda A, Sollner J, Sawodny R, Kammerer K, List V, et al. Prevalence and clinical implications of bloodstream infections in intensive care patients with or without burn injury: A retrospective cohort study. Eur J Clin Microbiol Infect Dis 2024;43:1731–40. [CrossRef]

Yanık Yoğun Bakım Ünitesinde Kısıtlayıcı Transfüzyon Bir Hayal mi?

Amaç: Yanık yoğun bakım ünitelerine (YBÜ) yatırılan hastalarda kan transfüzyonu ihtiyacını artırmaktadır. Uzun süreli yoğun bakımda kalmayla paralel olarak kan dolaşımı infeksiyonları (KDİ) riski de artmaktadır. Bu çalışma, transfüzyon ve BSI arasındaki ilişkiyi incelemeyi ve kısıtlayıcı transfüzyon uygulamasını teşvik etmeyi amaçlamaktadır.

Gereç ve Yöntem: Hastanemizin yanık yoğun bakım ünitesinde beş yıl boyunca ciddi yanıkları (toplam vücut yüzey alanının %20'sinden fazla) olan 158 hasta tedavi edildi. Restriktif transfüzyon için hemoglobin (Hb) eşiği 7 g/dL, liberal transfüzyon için ise 10 g/dL olarak belirlendi.

Bulgular: Çalışmaya dahil edilen 158 hastanın %17.7'si (n=28) kadındı. Hastaların yaş ortalaması 41±15 yıldı. Yanık toplam vücut yüzey alanı (TBSA) ortalaması %42.7±17 (aralığı: %20-92) idi. Yanık nedenleri %79.2'sinde (n=125) alev, %10.1'inde (n=16) elektrik, %7'sinde (n=11) kaynar su, birer hastada (n=0.6) sıcak yağ ve buhar ve %2.5'inde (n=4) kimyasal maddelerdi. Hastaların %11.4'ünde (n=18) kısmi kalınlıkta yanık, %69'unda (n=109) karışık derinlikte (kısmi/tam kalınlıkta) yanık ve %19.6'sında (n=31) tam kalınlıkta yanık mevcuttu. Toplam transfüzyon sayısı ile yanık yüzdesi, yanık yoğun bakım ünitesinde kalış süresi, gerçekleştirilen eskaratomi sayısı, son hemoglobin (Hb), beyaz kan hücresi (WBC) sayısı ve taze dondurulmuş plazma (TDP) ünitesi sayısı arasında istatistiksel olarak anlamlı bir ilişki bulunmuştur ($p<0.05$). Eritrosit süspansiyonu (ES) transfüzyonlarının %72.5-86.8'inde kısıtlayıcı transfüzyon uygulanmıştır. KDİ'ler arasında en sık izole edilen patojenler %28.5 (n=45) oranında koagülaz negatif stafilokok (KNS), %19.6 (n=31) oranında *A. baumannii* ve %12.7 (n=20) oranında *P. aeruginosa* olmuştur. Transfüzyon sayısı ile *KNS* ve *P. aeruginosa* izolatlarının varlığı arasında istatistiksel olarak anlamlı bir ilişki bulunurken ($p<0.05$), *A. baumannii* izolatları arasında böyle bir ilişki bulunmadı ($p>0.05$). Candida türlerinin neden olduğu BSI oranı %4.5 (n=7) idi.

Sonuç: Yanık yoğun bakım hastalarında transfüzyonla ilişkili reaksiyonları ve KDİ riskini en aza indirirken optimum hasta desteğini sağlamak için kısıtlayıcı bir transfüzyon stratejisi öneriyoruz.

Anahtar Sözcükler: Kan dolaşımı enfeksiyonları; kısıtlayıcı transfüzyon; yanıklar; yoğun bakım ünitesi.

SCIE DOI: 10.14744/scie.2025.62444
South. Clin. Ist. Euras. 2025;36(3):213-216

Original Article

Evaluation of Gram-Positive Growths in Blood Culture in the Pediatric Intensive Care Unit: Infection or Contamination?

Feyza İnceköy Girgin,[1] Ayten Saracoglu,[2] Nilüfer Yalındağ Öztürk[3]

[1]Department of Pediatric Intensive Care, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye
[2]Department of Anesthesiology, University of Florida School of Medicine, UF Health, Jacksonville, USA
[3]Department of Pediatric Intensive Care, Marmara University School of Medicine, Istanbul, Türkiye

Submitted: 20.06.2025
Revised: 20.06.2025
Accepted: 18.07.2025

Correspondence: Feyza İnceköy Girgin,
Department of Pediatric Intensive Care, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye
E-mail: feyzagirgin@hotmail.com

Keywords: Antibiotic therapy; gram positive culture result; pediatric intensive care unit.

ABSTRACT

Objective: Gram-positive organisms are commonly identified in cultures, either as a result of true infection or contamination. This research focused on examining the correlation between commonly used laboratory indicators and clinical results.This study aimed to evaluate the relationship between clinical outcomes and routine laboratory markers, along with antibiotic choices, in pediatric patients with gram-positive culture results in the pediatric intensive care unit (PICU).

Methods: A total of 179 PICU patients with gram-positive culture findings were retrospectively analyzed using hospital records from 2016 to 2019. Data collected included demographic information (age, sex), fever status, microbiological results, antibiotic therapy administered, laboratory values, and survival outcomes.

Results: The patients had a median age of 33.00 months (IQR: 8.00–66.00). Of the cohort, 109 (60.89%) were male and 70 (39.11%) were female. Positive culture findings were documented in 90 patients (50.3%). Vancomycin was prescribed to 59 patients (33%), while 31 patients (17.3%) received teicoplanin. A total of 34 patients (18.9%) died during hospitalization. The identified microorganisms included *Staphylococcus species* (n=56, 31.3%), *methicillin-resistant Staphylococcus epidermidis (MRSE)* (n=81, 45.3%), *Staphylococcus aureus (S.aureus)* (n=22, 12.3%), *Staphylococcus epidermidis (S.epidermidis)* (n=15, 8.4%), and methicillin-resistant *Staphylococcus aureus (MRSA)* (n=5, 2.8%). White blood cell (WBC) and platelet (PLT) counts were significantly higher among survivors compared to non-survivors (p=0.001 and p<0.001, respectively). No statistically significant associations were found between mortality and categorical variables assessed (p>0.05).

Conclusion: Gram-positive culture results are frequently encountered in pediatric intensive care units. By evaluating the clinical and laboratory parameters of the patient, it should be evaluated whether there is an infection or contamination, and infections should be treated.

INTRODUCTION

Background/rationale

Gram-positive culture results are frequently encountered in pediatric patients hospitalized in the pediatric intensive care unit (PICU), due to infection or contamination. Some laboratory parameters can guide us in the evaluation of infection. White blood cell (WBC), platelet (PLT) and C-Reactive Protein (CRP) are the most frequently evaluated and uncluded in many scoring systems for the diagnosis of sepsis in the PICU.[1-4]

S. aureus is a prominent pathogen known for causing severe infections, especially among critically ill individuals in intensive care settings. In the pediatric intensive care setting, infections caused by *S. aureus* are often associated with serious complications such as sepsis, ventilator-associated pneumonia, and infections at surgical sites or around indwelling medical devices.

Vancomycin and teicoplanin are glycopeptide antibiotics commonly employed in the treatment of gram-positive bacterial infections. They are especially valuable in managing infections caused by MRSA. Among their comparative advantages, teicoplanin has been reported to be less nephrotoxic than vancomycin.[5,6] By evaluating the clinical and laboratory parameters of the patient, it should be

evaluated whether there is an infection or contamination, and infections should be treated.

Objectives

This study aimed to examine changes in WBC, PLT and CRP levels in PICU patients, and to investigate the association of these parameters with clinical outcomes and mortality.

MATERIALS AND METHODS

Study design and setting

This study was carried out in the Department of Pediatrics, Pediatric Critical Care Division, using patient records collected between January 1, 2016, and January 1, 2019, from the hospital database. Ethical approval was secured from the institutional review board, and all methods adhered to the principles of the Declaration of Helsinki. (Approval Date: 12.06.2020, Decision No: 647).

Participants

Pediatric patients hospitalized in the PICU were enrolled in this study. Over the study period, 915 patients were hospitalized in the PICU, of whom 180 presented with positive culture results. One patient was excluded due to incomplete laboratory data, resulting in a final sample of 179 participants (Fig. 1).

Variables

The hospital's digital patient database was used to retrieve the relevant data.The primary outcome was in-hospital mortality (survival vs. death). Additional recorded variables included WBC (per microliter), PLT (per microliter), CRP (mg/L), presence of fever, source of the culture (blood or catheter), isolated microorganism, and the administered antibiotic.

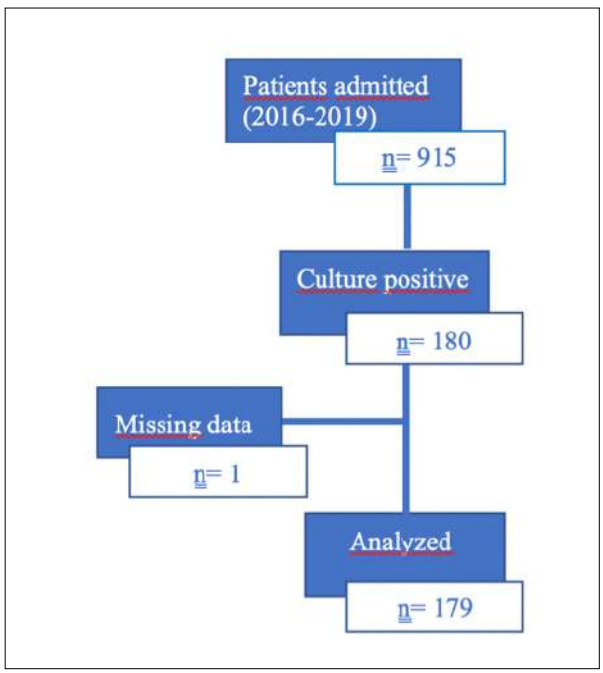


Figure 1. Participants of the study.

As per institutional protocol, patients with gram-positive culture results underwent a comprehensive evaluation that included clinical assessment (e.g., fever, perfusion, capillary refill time) and laboratory trends (WBC, CRP) to determine the need for antibiotic therapy.

Venous blood samples were collected at admission into anticoagulant tubes and analyzed via volume-conductivity-light scatter methodology. CRP levels were determined through immunoturbidimetric assay using the Beckman Coulter AU5800 system. All procedures followed the manufacturer's guidelines.

Catheter culture processing followed the Cleri et al.[7] method. Catheter tips were rolled onto blood agar, flushed with tryptic soy broth (TSB), and incubated to assess bacterial growth. Coagulase-negative staphylococci were identified per Kloos and Smith.[8]

Sample Size

The estimation of sample size was performed beforehand, considering mortality outcomes among three antibiotic regimens: None, vancomycin, and teicoplanin. Assuming a medium effect size (0.3), α=0.05, and 95% power, a minimum of 172 subjects was required.[9]

Statistical Methods

Data were analyzed using Jamovi. A threshold of $p<0.05$ was used to determine statistical significance.

RESULTS

Participants and Descriptive Data

A total of 179 children were evaluated, and the median age was 33 months (IQR: 8.00–66.00). The cohort included 109 males (60.89%) and 70 females (39.11%). There was no significant age difference by sex (p=0.415). Positive cultures were identified in 90 cases (50.3%). Antibiotics administered included vancomycin (n=59, 33%) and teicoplanin (n=31, 17.3%). Mortality occurred in 34 patients (18.9%). Predominant organisms included *Staph. spp.* (31.3%), methicillin-resistant *S. epidermidis* (45.3%), *S. aureus* (12.3%), *S. epidermidis* (8.4%), and MRSA (2.8%).

Outcome Data

No significant differences in WBC, PLT, or CRP were found based on gender or fever status. However, CRP levels were elevated in patients with confirmed infections. Survivors had significantly higher WBC and PLT counts than non-survivors. CRP levels varied significantly by antibiotic used, being highest in those receiving teicoplanin. Additionally, CRP levels were elevated in patients whose blood cultures yielded *S. aureus* or MRSA.

DISCUSSION

Key results

CRP was notably elevated in infections involving *S. aureus*, and both WBC and PLT were higher among survivors. Teicoplanin-treated patients and those with *S. aureus*-positive cultures had higher CRP levels.

Limitations

This retrospective study relied on protocol-based decisions by attending physicians, introducing potential variability. Inclusion of additional platelet indices (e.g., MPV, PDW) could have enhanced outcome prediction.

Interpretation

The nonspecific clinical presentation of febrile infants poses a significant challenge in distinguishing serious bacterial infections from benign viral illnesses.[10] Numerous investigations have sought to identify reliable screening biomarkers to aid clinicians in assessing the risk of bacterial infections among febrile children. One example is CRP, which is an acute-phase reactant that elevates swiftly during infectious or inflammatory processes.[11] Findings from the current study support the continued relevance of CRP as a diagnostic indicator for bacterial infections in critically ill children. This aligns with recent literature highlighting CRP's predictive value in identifying severe bacterial infections in febrile infants.[10]

Although prior research has demonstrated elevated white blood cell (WBC) counts in neonates with early-onset sepsis compared to their non-septic counterparts—persisting up to 24 hours post-admission[12] —our analysis did not find a significant association between WBC levels and variables such as sex, fever, infection status, antibiotic choice, culture results, or mortality. These findings are consistent with previous studies concluding that WBC alone lacks sufficient reliability to serve as a sole predictor of serious bacterial infections in febrile pediatric patients.[10,13]

The role of PLTs in sepsis has gained attention in recent literatüre.[14] During sepsis, PLTs contribute to hyperinflammation, intravascular coagulation, and thrombosis, potentially culminating in multi-organ dysfunction. In our study, survivors exhibited significantly higher WBC and PLT counts compared to non-survivors. The observed thrombocytopenia in deceased patients may reflect excessive platelet activation, resulting in increased consumption, immune-mediated destruction, and sequestration.[15,16] Appropriate antibiotic therapy remains fundamental to achieving favorable outcomes in critically ill patients. Inappropriate or delayed antimicrobial administration can contribute to treatment failure, prolonged hospitalization, and increased mortality.[17] Infections in the PICU setting require empiric antibiotic initiation based on local resistance patterns, followed by continuous clinical reassessment and de-escalation strategies as indicated.

MRSA is a frequent cause of severe infections, including bloodstream infections.[18] Vancomycin has traditionally been the first-line agent against MRSA, but concerns regarding nephrotoxicity have prompted consideration of alternatives.[19] Teicoplanin, a glycopeptide with similar antimicrobial efficacy, offers several advantages, including once-daily dosing, intramuscular administration, no requirement for drug-level monitoring, and a lower risk of renal impairment.[20] However, its higher cost remains a limitation. Patients treated with teicoplanin showed elevated CRP levels, which may indicate greater infection severity; however, mortality rates did not differ significantly among the antibiotic groups. These findings are supported by meta-analyses reporting comparable clinical and microbiological outcomes for vancomycin and teicoplanin.[21]

Conclusion

CRP remains a valuable biomarker for identifying bacterial infections and predicting clinical outcomes in pediatric intensive care settings. Platelet count may also serve as a useful prognostic indicator, with thrombocytopenia potentially reflecting underlying hyperinflammation, excessive consumption, or destruction. Finally, There was no meaningful difference detected in patient outcomes between vancomycin and teicoplanin, suggesting that both antibiotics are equally effective in managing severe gram-positive infections in the PICU.

Ethics Committee Approval

The study was approved by the Marmara University Clinical Research Hospital Ethics Committee (Date: 12.06.2020, Decision No: 647).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: F.I.G., N.Y.Ö.; Design: F.I.G., N.Y.Ö.; Supervision: F.I.G., A.S., N.Y.Ö.; Materials: F.I.G.; Data collection &/or processing: F.I.G., A.S.; Analysis and/or interpretation: F.I.G., A.S.; Literature search: F.I.G., A.S., N.Y.Ö.; Writing: F.I.G., A.S.; Critical review: F.I.G., A.S., N.Y.Ö.

Conflict of Interest

None declared.

REFERENCES

1. Waheed U, Williams P, Brett S, Baldock G, Soni N. White cell count and intensive care unit outcome. Anaesthesia 2003;58:180–2. [CrossRef]
2. Zarychanski R, Houston DS. Assessing thrombocytopenia in the intensive care unit: The past, present, and future. Hematol Am Soc Hematol Educ Progr 2017;8:660–6. [CrossRef]
3. Gao L, Liu X, Zhang D, Xu F, Chen Q, Hong Y, et al. Early diagnosis of bacterial infection in patients with septicopyemia by laboratory analysis of PCT, CRP, and IL-6. Exp Ther Med 2017;13:3479–83. [CrossRef]
4. Sampedro GR, Bubeck WJ. Staphylococcus aureus in the Intensive

Care Unit: Are these golden grapes ripe for a new approach? J Infect Dis 2017;215:S64–70.
5. Cavalcanti AB, Goncalves AR, Almeida CS, Bugano DD, Silva E. Teicoplanin versus vancomycin for proven or suspected infection. Cochrane Database Syst Rev 2010;6:CD007022. [CrossRef]
6. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP; STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 2014;12:1495–9. [CrossRef]
7. Cleri DJ, Corrado ML, Seligman SJ. Quantitative culture of intravenous catheters and other intravascular inserts. J Infect Dis 1980;141:781–6. [CrossRef]
8. Kloos WE, Bannerman TL. Staphylococcus. In Balows A, Hausler WJ, Herrmann KL, Isenberg HD, Shadomy HJ, eds. Manual of Clinical Microbiology. Washington DC: American Society for Microbiology; 1991.
9. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 2007;39:175–91. [CrossRef]
10. Zarkesh M, Sedaghat F, Heidarzadeh A, Tabrizi M, Bolooki-Moghadam K, Ghesmati S. Diagnostic value of IL-6, CRP, WBC, and absolute neutrophil count to predict serious bacterial infection in febrile infants. Acta Med Iran 2015;53:408–11.
11. Hsiao AL, Baker MD. Fever in the new millennium: A review of recent studies of markers of serious bacterial infection in febrile children. Curr Opin Pediatr 2005;17:56–61. [CrossRef]
12. Abdollahi A, Shoar S, Nayyeri F, Shariat M. Diagnostic value of simultaneous measurement of procalcitonin, interleukin-6 and hs-CRP in prediction of early-onset neonatal sepsis. Mediterr J Hematol Infect Dis 2012;4:e2012028. [CrossRef]
13. Bachur RG, Harper MB. Predictive model for serious bacterial infections among infants younger than 3 months of age. Pediatrics 2001;108:311–6. [CrossRef]
14. De Stoppelaar SF, van 't Veer C, van der Poll T. The role of platelets in sepsis. Res Pract Thromb Haemost 2014;112:666–77. [CrossRef]
15. Ghosh TK, Khan N, Malik A. Platelet auto-antibodies in septicaemic patients. Indian J Pathol Microbiol 1999;42:31–5.
16. Greinacher A, Selleng K. Thrombocytopenia in the intensive care unit patient. Hematol Am Soc Hematol Educ Progr 2010;2010:135–43. [CrossRef]
17. Campion M, Scully G. Antibiotic use in the intensive care unit: Optimization and de-escalation. J Intensive Care Med 2018;33:647–55. [CrossRef]
18. Bubacz MR. Community-acquired methicillin-resistant staphylococcus aureus: An ever-emerging epidemic. AAOHN J 2007;55:193–4. [CrossRef]
19. Maclayton DO, Hall RG 2nd. Pharmacologic treatment options for nosocomial pneumonia involving methicillin-resistant staphylococcus aureus. Ann Pharmacother 2007;41:235–44. [CrossRef]
20. Wood MJ. Comparative safety of teicoplanin and vancomycin. J Chemother 2000;12:21–5. [CrossRef]
21. Wood MJ. The comparative efficacy and safety of teicoplanin and vancomycin. J Antimicrob Chemother 1996;37:209–22. [CrossRef]

Çocuk Yoğun Bakım Ünitesinde Kan Kültüründe Gram-pozitif Bakteri Üremesinin Değerlendirilmesi: Enfeksiyon mu, Kontaminasyon mu?

Amaç: Gram-pozitif mikroorganizmalar kan kültürlerinde sıklıkla saptanmakta olup, bu durum gerçek bir enfeksiyon ya da kontaminasyonu gösterebilir. Bu çalışma, çocuk yoğun bakım ünitesinde (ÇYBÜ) gram-pozitif kültür sonucu olan hastalarda rutin laboratuvar belirteçleri, klinik sonuçlar ve antibiyotik tedavisi arasındaki ilişkiyi incelemeyi amaçladı.

Gereç ve Yöntem: 2016-2019 yılları arasında gram-pozitif kültür sonucu saptanan 179 ÇYBÜ hastasının retrospektif olarak kayıtları analiz edildi. Demografik bilgiler, ateş durumu, mikrobiyolojik sonuçlar, uygulanan antibiyotik tedavileri, laboratuvar değerleri ve sağkalım sonuçları toplandı.

Bulgular: Hastaların medyan yaşı 33.00 ay (IQR: 8.00–66.00) olup, 109 (%60.9) erkek ve 70 (%39.1) kız hastaydı. Olumlu kan kültürü sonucu 90 hastada (%50.3) saptandı. Vancomycin 59 hastaya (%33), teikoplanin ise 31 hastaya (%17.3) verildi. Hastanede 34 hasta (%18.9) yaşamını yitirdi. İzole edilen mikroorganizmalar *Staphylococcus* türleri (%31.3), metisilin dirençli *Staphylococcus epidermidis (MRSE)* (%45.3), *Staphylococcus aureus* (%12.3), *Staphylococcus epidermidis* (%8.4) ve metisilin dirençli *Staphylococcus aureus (MRSA)* (%2.8) olarak tespit edildi. Beyaz kan hücresi (BKH) ve trombosit (PLT) sayıları, sağ kalanlarda kaybedenlere göre anlamlı olarak yüksekti (sırasıyla, p=0.001 ve p<0.001). Diğer kategorik değişkenler ile mortalite arasında anlamlı ilişki bulunmadı (p>0.05).

Sonuç: Gram-pozitif kültür sonuçları pediatrik yoğun bakım ünitelerinde sıkça karşılaşılmaktadır. Enfeksiyon ve kontaminasyonun ayrımını yapmak için klinik ve laboratuvar parametrelerinin dikkatle değerlendirilmesi ve enfeksiyon varlığında uygun tedavinin başlanması gerekmektedir.

Anahtar Sözcükler: Antibiyotik tedavisi; çocuk yoğun bakım ünitesi; gram-pozitif kültür sonucu.

SCIE DOI: 10.14744/scie.2025.37973
South. Clin. Ist. Euras. 2025;36(3):217-223

Original Article

Relationship Between Platelet Indices with Severity of Hemorrhage, Prognosis and Scoring Systems for Nonvariceal Upper GIS Bleeding

Osman Maviş,[1] Fazıl Burak Dilek,[1] Korhan Kapucu,[1] Banu Boyuk[2]

[1]Department of Internal Medicine, University of Health Science, GOP Education and Research Hospital, Istanbul, Türkiye
[2]Department of Internal Medicine, University of Health Science, Istanbul Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye

Submitted: 20.01.2025
Revised: 02.07.2025
Accepted: 18.08.2025

Correspondence: Banu Böyük , Department of Internal Medicine, University of Health Science, GOP Education and Research Hospital, Istanbul, Türkiye
E-mail: banuilk@gmail.com

Keywords: Blatchford scoring; non-variceal upper GIS hemorrhage; platelet indices; Rockall scoring.

ABSTRACT

Objective: We aimed to determine the place of platelet indices [platelet (PLT), platelet crit (PCT), mean platelet volume (MPV) and platelet distribution width (PDW)] in predicting the severity of hemorrhage and prognosis in non-variceal upper gastrointestinal system (GIS) bleeding.

Methods: The study included 210 patients hospitalized due to non-variceal upper GIS bleeding. Full blood count values were recorded when the patients were admitted to hospital, on the 5th day and at discharge. The Rockall and Blatchford scores were calculated according to the clinical and endoscopic findings of patients and Forrest classification was made.

Results: Blatchford and Rockall scores for patients whose hospitalization period is more than 5 days and who require transfusion was higher than the group without ($p<0.001$). When the groups with a hospital stay of more than 5 days and less than 5 days and the groups with and without transfusion were compared, no significant difference was found between PLT, PCT, MPV and PDW values ($p>0.05$). There was a very weak positive correlation between MPV at time of admission and MPV and PDW values at discharge with Blatchford score. There was a very weak positive correlation between MPV and PDW values at discharge with Rockall score. To predict the risk of admission of 5 days or more, forward selection logistic regression was performed and platelet indexes were not identified to be independent predictors.

Conclusion: It was observed that platelet indices were not independent predictors in determining bleeding severity and prognosis in upper GIS hemorrhage, but MPV and PDW were very weakly related to scoring systems.

INTRODUCTION

Upper gastrointestinal (GI) hemorrhage is one of the most frequent causes of emergency department visits and represents a significant clinical challenge, with mortality rates reported to be as high as 10% despite advances in diagnostic and therapeutic endoscopic methods.[1,2] The most common cause of GI bleeding is hemorrhage from the upper part of the GI tract, located proximal to the ligament of Treit.[3] The incidence of GI hemorrhage in males is approximately twice that in females.[4]

While GI bleeding risk scoring is generally based on treatment requirements, some scoring systems take into account the probability of mortality and recurrent hemorrhage. The Rockall score includes age, the presence of shock, comorbidities, endoscopic diagnosis, and signs of recent bleeding observed during endoscopy.[5] The Blatchford score uses levels of urea and hemoglobin, systolic blood pressure, pulse rate, and the presence of melena, syncope, hepatic disease, and heart failure to determine whether intervention is required to control the bleeding.[6] Early identification of this clinical problem, which is associated with high mortality and morbidity, and the assessment of bleeding severity and risk are important for deciding on hospitalization to continue treatment and managing patient costs. The use of low-cost and non-invasive parameters in daily practice to guide the management and clinical decision-making processes for patients with up-

per GI bleeding offers great advantages.[7,8] Platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW) —known collectively as platelet indices — meet these criteria and are routinely measured as part of a complete blood count.

In our study, we aimed to investigate the role of non-invasive, low-cost platelet indices (PLT, PCT, MPV, and PDW) in diagnosing GI bleeding and in predicting bleeding severity and prognosis. Furthermore, we evaluated the correlation between these platelet indices and the Rockall and Blatchford scores.

MATERIALS AND METHODS

This retrospective study included 210 patients admitted to the internal medicine clinic with a diagnosis of non-variceal upper GI hemorrhage between 2016 and 2019. The study protocol was approved by the Taksim Clinical Research Ethics Committee on 13 November 2019 (Decision No. 160) and was conducted in accordance with the principles of the Declaration of Helsinki. All patients were over 18 years of age, were non-pregnant, had no malignancy, and had undergone endoscopy. The patient medical histories, initial physical examination findings, medications, and comorbidities were retrieved from the hospital's SARUS system. At admission, urea and creatinine levels were measured using a Beckman Coulter AU2700 (Beckman Coulter, Inc., USA) autoanalyzer with spectrophotometric methods. Hemoglobin, PLT, PCT, MPV, and PDW levels were analyzed using an ABX Pentra DX120 analyzer (Horiba Medical, USA). These parameters were recorded at three time points: At admission, on the 5th day of hospitalization, and at discharge. Endoscopic findings and the amount of erythrocyte transfusion administered during hospitalization were retrieved for all patients. The Forrest classification was applied to patients with peptic ulcers. The Rockall and Blatchford scores were calculated for all patients included in the study.

Statistical Analysis

Quantitative variables were summarized as mean and standard deviation, while qualitative variables were summarized as frequency (percentage). The chi-square test was used to evaluate qualitative variables. The normality assumption for variables was assessed using the Kolmogorov-Smirnov test for sample sizes greater than 50 and the Shapiro-Wilk test for sample sizes less than 50. When the assumptions for parametric testing were met, differences between the means of two independent variables were analyzed using the Student's t-test. When these assumptions were not met, the Mann-Whitney U test was applied. The correlation between two variables was assessed using the Pearson test for normally distributed data and the Spearman correlation test for non-normally distributed data. Additionally, explanatory variables affecting the categorized length of hospital stay were analyzed using the logistic regression method. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 25.0, and a p-value of <0.05 was considered statistically significant.

Table 1. Demographic characteristics of patients

	n	%
Gender		
Female	72	34.28
Male	138	65.72
Total	210	100
Age (Mean± Standard deviation)	62.29±21.38	
Comorbidities	**Yes (%)**	**No (%)**
Diabetes	17%	83%
Hypertension	39%	61%
Coronary artery disease	25%	75%
Congestive heart failure	12%	88%
Atrial fibrillation	10%	90%
Neurological disorders	9%	91%
Chronic renal failure	9%	91%
Respiratory disease	9%	91%
Valvular heart disease	4%	96%
Thyroid disorders	6%	94%
Other	5%	95%
Drugs	**Yes (%)**	**No (%)**
Acetylsalicylic acid	16%	84%
Coumadin	14%	86%
Clopidogrel	5%	95%
NOAC	6%	94%
P2Y12 inhibitors	1%	99%
NSAID	16%	84%
Heparin	1%	99%
Beta blocker	12%	88%
Antibiotic	1%	99%
ACE inhibitor	9%	91%
ARB	4%	96%
Digoxin	2%	98%
Calcium channel blocker	6%	94%
Aldosterone	4%	96%
Diuretic	8%	92%
Statin	3%	97%
Nitrate	1%	99%
Neurological drugs	2%	98%
Oral antidiabetic	2%	98%
Insulin	1%	99%
Thyroid drugs	3%	97%

RESULTS

Our study included a total of 210 patients, of whom 34.28% were female (n=72) and 65.72% were male (n=138). The

Table 2. The relationship between the Rockall, Blatchford, and Forrest scoring systems and the platelet indices obtained at admission, on the 5th day of hospitalization, and at discharge

Platelet indices	Scoring variables					
	Forrest		Rockall		Blatchford	
	r	p	r	p	r	p
Admission						
Platelet	-0.102	0.298	0.051	0.459	0.009	0.911*
Plateletcrit	-0.087	0.371	0.044	0.527	0.027	0.694*
Mean platelet volume	0.043	0.658	0.062	0.375	0.143	0.038*
Platelet distribution width	0.021	0.831	0.076	0.273	0.121	0.080*
Day 5						
Platelet	-0.143	0.143	-0.082	0.239	-0.041	0.550*
Plateletcrit	-0.131	0.180	-0.050	0.469	-0.020	0.772*
Mean platelet volume	-0.001	0.992	0.115	0.096	0.133	0.055*
Platelet distribution width	0.071	0.466	0.103	0.139	0.095	0.156*
Discharge						
Platelet	-0.200	0.039	-0.047	0.494	-0.039	0.571*
Plateletcrit	-0.219	0.016	0.016	0.818	0.001	0.999*
Mean platelet volume	-0.029	0.764	0.154	0.025	0.159	0.021*
Platelet distribution width	0.038	0.697	0.145	0.035	0.144	0.037*

*The normality assumption was violated for all variables. The Spearman correlation coefficient was used.

mean age of the patients was 62.29±21.38 years. Among patients with chronic diseases, 39% had hypertension (HT), 25% ischemic heart disease (IHD), 17% diabetes mellitus (DM), 12% congestive heart failure (CHF), 10% atrial fibrillation (AF), 10% neurological disorders, 9% chronic renal failure (CRF), 9% respiratory diseases, 6% thyroid disorders, and 4% valvular heart disease. The most commonly used medications were acetylsalicylic acid (ASA) and nonsteroidal anti-inflammatory drugs (NSAIDs). Among the patients, 16% used aspirin, 16% used NSAIDs, 14% used warfarin, 6% used novel oral anticoagulants (NOACs), and 5% used clopidogrel (Table 1).

The correlations between the Blatchford, Rockall, and Forrest scores and platelet indices were examined at admission, on the 5th day of hospitalization, and at discharge. Since the score variables were not normally distributed, the Spearman correlation coefficient was used. For the Blatchford score, a very weak positive correlation was found with MPV at admission (r=0.143, p=0.038; 14.03%), with MPV at discharge (r=0.159, p=0.021; 15.90%), and with PDW at discharge (r=0.144, p=0.037; 14.40%). For the Rockall score, very weak positive correlations were also observed with MPV (r=0.154, p=0.037; 15.40%) and PDW at discharge (r=0.145, p=0.035; 14.50%). The Forrest score showed very weak negative correlations with PLT (r=-0.200, p=0.039; 20.00%) and PCT at discharge (r=-0.219, p=0.016; 21.90%) (Table 2).

Since platelet indices were not normally distributed, the Mann-Whitney U test was used to evaluate whether differences in mean platelet indices were statistically significant according to transfusion requirements. Comparing the groups with and without transfusion, no statistically significant differences were found in PLT, PCT, MPV, or PDW levels (p>0.05). In contrast, the differences in mean HGB levels were statistically significant: Patients who required transfusion had lower mean HGB levels compared to those who did not (Table 3).

The differences in laboratory values were examined in relation to the length of hospital stay. For this purpose, the independent two-sample Student's t-test was used for PLT, as it was normally distributed, while the Mann-Whitney U test was applied for PCT, MPV, PDW, and HGB, which did not follow a normal distribution. Comparing the patient groups by the length of hospital stay (<5 days vs. >5 days), no statistically significant differences were found in PLT, PCT, MPV, or PDW levels (p>0.05). Lower hemoglobin levels, advanced age, and the presence of comorbidities (CHF, valvular heart disease, AF, and CRF) were significantly associated with longer hospital stays (p<0.001). Patients hospitalized for more than 5 days had significantly lower HGB values compared to those hospitalized for less than 5 days (p<0.001). In addition, the patients with a hospital stay longer than 5 days had significantly higher mean Rockall and Blatchford scores compared to those with a hospital stay less than 5 days (p<0.001) (Table 4).

A forward selection logistic regression analysis was performed to identify the risk factors associated with hospitalization longer than 5 days compared to hospitalization shorter than5 days. According to the Hosmer-Lemeshow and Omnibus test results, the logistic regression model

Table 3. Comparison of platelet indices by transfusion requirement

Variables	Transfusion need		p-value
	No	Yes	
Admission			
Hemoglobin	9.34±2.11	7.98±1.46	<0.001*
Platelet	233.79±100.37	244.88±81.04	0.114*
Plateletcrit	0.21±0.08	0.22±0.07	0.190*
Mean platelet volume	9.31±1.13	9.24±1.19	0.511*
Platelet distribution width	16.07±1.95	15.75±1.6	0.158*
Day 5			
Hemoglobin	121.75±169.54	111.28±136.59	0.530*
Platelet	252.46±98.2	233.48±78.14	0.194*
Plateletcrit	0.23±0.08	0.22±0.07	0.179*
Mean platelet volume	9.32±1.16	9.46±1.29	0.598*
Platelet distribution width	16.16±2.04	16.03±1.6	0.582*
Discharge			
Hemoglobin	10.6±1.66	10.43±1.3	0.767*
Platelet	256.23±102.51	245.55±79.97	0.561*
Plateletcrit	0.23±0.08	0.23±0.07	0.601*
Mean platelet volume	9.29±1.15	9.63±1.87	0.368*
Platelet distribution width	15.98±1.88	16.18±1.73	0.503*

*The normality assumption was violated for all variables. The Mann-Whitney U test was used.

Table 4. Comparison of laboratory findings, scoring system results, and comorbidities by length of hospital stay

Variables	Length of hospital stay		p-value
	<5 days	>5 days	
Platelet	229.34±81.24	245.8±100.81	0.400*
Plateletcrit	0.21±0.07	0.23±0.08	0.202**
Mean platelet volume	9.2±1.13	9.35±1.17	0.225**
Platelet distribution width	15.79±1.94	16.06±1.7	0.264**
Hemoglobin	9.58±2.06	8.11±1.65	<0.001**
Rockall	3.30±1.83	5.04±2.074	<0.001**
Blatchford	7.14±3.65	11.56±3.231	<0.001**
Diabetes	12 (16)	24 (20)	0.138***
Hypertension	30 (35.4)	50 (44.6)	0.122***
Coronary artery disease	18 (22.7)	33 (28.3)	0.128***
Congestive heart failure	5 (10.7)	19 (13.3)	0.013***
Atrial fibrillation	5 (9.3)	16 (11.7)	0.044***
Neurological disorders	4 (8)	14 (10)	0.047***
Chronic renal failure	4 (8)	14 (10)	0.049***
Respiratory disease	7 (8)	11 (10)	0.616***
Valvular heart disease	1 (4)	8 (5)	0.039****
Thyroid disorders	4 (5.3)	8 (6.7)	0.423***
Other	2 (4.9)	9 (6.1)	0.071****

*Independent sample t-test, **Mann-Whitney U, ***Pearson chi-square, ****Fisher's exact test

was found to be statistically significant. The Nagelkerke R^2 value was calculated as 0.334. Examining the parameter estimates, HGB level, comorbidities, and BUN level were identified as independent risk factors (Table 5).

Table 5. Logistic regression results for predicting hospitalization of 5 days or more

Variables	Parameter Estimation	Standard Error	p	Hosmer Lemeshow Test		Omnibus Test		Nagelkerke R^2
				Test statistic	p	Test statistic	p	
Hemoglobin	-0.338	0.095	<0.001	7.234	0.512	60.016	<0.001	0.334
Comorbidities (0=None)	-0.711	0.340	0.037					
BUN	0.035	0.011	0.001					
Constant term	2.436	0.956	0.011					

DISCUSSION

Upper GI hemorrhage is a serious clinical condition with a mortality rate ranging from 2% to 10% and an annual incidence of 103 to 172 per 100,000, despite advances in diagnostic and therapeutic endoscopic methods.[9] Various risk factors, including advanced age, liver cirrhosis, heart failure, and the use of antiplatelet or anticoagulant agents, affect both the occurrence of bleeding and mortality.[10] The incidence is higher among men, individuals with low socioeconomic status, and the elderly.

Medication use plays a significant role in the etiology of upper GI hemorrhage. The increasing prevalence of comorbidities in elderly patients particularly contributes to increased medication use. Medications such as NSAIDs, ASA, and warfarin are well-known etiological factors. NSAIDs and ASA disrupt the gastrointestinal mucosal barrier by inhibiting the synthesis of prostaglandins through cyclooxygenase inhibition; additionally, they impair platelet function and are considered causative agents of GI bleeding.[11] Bor et al.[12] reported that among patients presenting with upper GI hemorrhage, 43.2% had used NSAIDs and aspirin, 7% had used steroids, and 6.6% had received anticoagulant therapy. A study by Paspatis et al.[13] found that half of the patients with GI hemorrhage had used ASA or NSAIDs. Similarly, Ateş et al.[14] reported that 27% of patients had used ASA, 23% NSAIDs, 5% oral anticoagulants, and 1% steroids. In our study, the most frequently used medications were ASA (16%), NSAIDs (16%), and coumadin (14%).

One of the factors affecting the mortality and morbidity of patients with GI bleeding is the presence of chronic diseases. In our study, the prevalence of chronic conditions was 39% for HT, 25% for IHD, 17% for DM, and 12% for CHF. A study by Erkuş et al.[15] reported HT (32.3%) as the most common comorbidity, with 19.1% of patients having chronic IHD, 14.1% having DM, and 9.1% having CHF. Okutur et al.[16] found that 46.2% of patients had HT, 22% had DM, and 16.5% had IHD in their study. Consistent with our study, HT was the most common comorbidity among patients with upper GI bleeding in the literature, and the most commonly used medications were ASA and NSAIDs, followed by warfarin.[10-17]

Patient scores were calculated using the Rockall and Blatchford scoring systems, which are utilized to predict the prognosis and severity of bleeding in cases of non-variceal upper GI hemorrhage. In our study, higher scores on both the Rockall and Blatchford scoring systems were significantly associated with longer hospitalization durations. Prolonged hospital stays were associated with poor prognosis. We also found that low hemoglobin levels, advanced age, and comorbidities (CHF, valvular heart disease, AF, and CRF) were associated with longer hospital stays and thus appeared to correlate with poor prognosis. Several studies have found that male gender, advanced age, and the use of antiplatelet and anticoagulant medications are associated with poor prognosis.[18-20]

A variety of scoring systems are used to identify high-risk patients and distinguish them from those at low risk. Risk factors include the need for erythrocyte transfusion, monitoring in the intensive care unit, endoscopic intervention, recurrent hemorrhage, and mortality. In the literature, there are many studies evaluating the predictive accuracy of these scoring systems in assessing such risk factors. The Rockall and Blatchford scoring systems are commonly used to assess the prognosis and severity of bleeding.[6,21] Our study is the first to examine the correlation between these scoring systems and platelet indices. PLT, PCT, MPV, and PDW levels were recorded on the first and fifth days of hospitalization and at discharge. In our study, elevated MPV levels at admission, as well as elevated MPV and PDW levels at discharge, showed a weak correlation with higher scores on both the Rockall and Blatchford scoring systems.

No significant correlation was found between hospitalization duration and the mean levels of these platelet indices in our study. In the literature, there are very few studies investigating the correlation between platelet indices (PLT, PCT, MPV, PDW) and the prognosis of GI hemorrhage. A study by Şenel et al.[22] found that elevated levels of these indices were associated with longer hospital stays and poor prognosis. Similarly, a study by Makay et al.[23] investigating the correlation between MPV and GI hemorrhage in patients with Henoch-Schönlein purpura found that mean MPV was significantly lower in patients with GI hemorrhage compared to those without hemorrhage. In another study, Tanoğlu et al.[24] found that higher MPV values were associated with increased erythrocyte transfusion requirements and longer hospital stays.

To assess the prognosis and severity of bleeding, the need for erythrocyte transfusion was evaluated. There are several studies in the literature investigating the predictive performance of scoring systems in estimating the need for erythrocyte transfusion.[25,26] In a study by Chen et al.,[27] the Blatchford scoring system was found to be superior to the Rockall scoring system in predicting the need for blood transfusion. In our study, the mean Blatchford and Rockall scores were significantly higher in patients who required transfusion compared to those who did not ($p<0.001$). The need for erythrocyte transfusion is considered an indicator of poor prognosis. However, no significant correlation was found between PLT, PCT, MPV, and PDW levels and the need for transfusion.

The Forrest classification is used to determine the severity of bleeding in patients. No significant correlation was observed between PLT, PCT, MPV, PDW, or HGB levels across the Forrest groups. Independent predictors of bleeding severity were found to be comorbidities, peak heart rate, and BUN levels. In our study, hospitalization duration was used as a marker of prognosis. The independent predictors of poor prognosis were identified as low HGB levels, comorbidities, and BUN levels. Previous studies have reported various independent predictors of poor prognosis, including hematemesis,[28,29] signs of hypovolemia,[29,30] low HGB and HCT levels,[28-30] hypoalbuminemia,[30] erythrocyte transfusion,[28] and prolonged hospitalization.[31]

Study Limitations

The limitations of our study include the unavailability of some data due to its retrospective design. In addition, being a single-center study limited the sample size. Larger-scale, multicenter, and comprehensive studies are needed to further investigate this topic.

Conclusion

In our study, we aimed to investigate the correlation between platelet indices and the prognosis and severity of upper GI hemorrhage. We used the Rockall and Blatchford scoring systems to assess patient prognosis. The relationships between scoring systems and platelet indices were examined. Higher MPV levels at initial presentation and elevated PDW and MPV levels after treatment showed weak correlations with both the Blatchford and Rockall scoring systems, which are commonly used to predict clinical outcomes.

A significant correlation was found between prolonged hospitalization and the need for erythrocyte transfusion using the prognostic scoring systems. When length of hospital stay and the need for erythrocyte transfusion were used as prognostic criteria, platelet indices did not appear to be significant prognostic predictors.

In our study, platelet indices were not identified as independent predictors of prognosis and severity of hemorrhage. Larger, multicenter studies are warranted to further elucidate the role of platelet indices in predicting the prognosis and severity of hemorrhage in non-variceal upper GI bleeding.

Ethics Committee Approval

The study was approved by the Taksim Training and Research Hospital Clinical Research Hospital Ethics Committee (Date: 13.11.2019, Decision No: 160).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.B.; Design: O.M.; Supervision: B.B.; Fundings: F.B.D.; Materials: F.B.D.; Data collection &/or processing: O.M.; Analysis and/or interpretation: K.K.; Literature search: F.B.D.; Writing: O.M., F.B.D.; Critical review: K.K.

Conflict of Interest

None declared.

REFERENCES

1. Feinman M, Haut ER. Upper gastrointestinal bleeding. Surg Clin North Am 2014;94:43–53. [CrossRef]
2. Nadler M, Eliakim R. The role of capsule endoscopy in acute gastrointestinal bleeding. Therap Adv Gastroenterol 2014;7:87–92. [CrossRef]
3. Adler DG, Leighton JA, Davila RE, Hirota WK, Jacobson BC, Qureshi WA, et al. ASGE guideline: The role of endoscopy in acute nonvariceal upper-GI hemorrhage. Gastrointest Endosc 2004;60:497–504. [CrossRef]
4. Rosen AM, Fleischer DE. Upper GI bleeding in the elderly: Diagnosis and management. Geriatrics 1989;44:26–28.
5. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996;38:316–21. [CrossRef]
6. Blatchford O, Murray WR, Blatchford M. A risk score to predict need for treatment for upper gastrointestinal haemorrhage. Lancet 2000;356:1318–21. [CrossRef]
7. Theivanayagam S, Lim RG, Cobell WJ, Gowda JT, Matteson ML, Choudhary A, et al. Administration of erythromycin before endoscopy in upper gastrointestinal bleeding: A meta-analysis of randomized controlled trials. Saudi J Gastroenterol 2013;19:205–10. [CrossRef]
8. Al Dhahab H, McNabb-Baltar J, Al-Taweel T, Barkun A. Tate-of-the-art management of acute bleeding peptic ulcer disease. Saudi J Gastroenterol 2013;19:195–204. [CrossRef]
9. Tham J, Stanley A. Clinical utility of pre-endoscopy risk scores in upper gastrointestinal bleeding. Expert Rev Gastroenterol Hepatol 2019 Dec;13:1161–7. [CrossRef]
10. Van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. Best Pract Res Clin Gastroenterol 2008;22:209–24. [CrossRef]
11. Pasa S, Bayan K, Kucukoner M, Tuzun Y, Altintas A, Cil T, et al. The effects of nonsteroidal anti-inflammatory drugs on platelet function and severity of upper gastrointestinal haemorrhage. J Thromb Thrombolysis 2009;28:83–9. [CrossRef]
12. Bor S, Dağlı Ü, Sarer B, Gürel S, Tözün N, Sıvrı B, et al. A retrospective study demonstrating properties of nonvariceal upper gastrointestinal bleeding in Turkey. Turk J Gastroenterol 2011;22:249–54. [CrossRef]

13. Paspatis GA, Matrella E, Kapsoritakis A, Leontithis C, Papanikolaou N, Chlouverakis GJ, et al. An epidemiological study of acute upper gastrointestinal bleeding in Crete, Greece. Eur J Gastroenterol Hepatol 2000;12:1215–20. [CrossRef]
14. Ateş F, Karıncaoğlu M, Aladag M. Evaluation of 524 cases of non-variceal upper gastrointestinal bleeding. İnönü Üniv Tıp Fak Derg 2008;15:93–98. [Article in Turkish]
15. Erkuş E, Helvacı A, Bodur Ö, Özsoy N. Assessment of 99 cases with upper gastrointestinal system bleeding. Okmeydanı Tıp Derg 2013;29:76–80. [Article in Turkish] [CrossRef]
16. Okutur SK, Alkım C, Bes C, Gürbüz D, Kınık Ö, Gültürk E, et al. Acute upper gastrointestinal bleeding: Analysis of 230 cases. Akad Gastroenterol Derg 2007;6:30–36. [Article in Turkish]
17. Olt S, Uslan I, Eminler AT, Tamer A, Akcay E, Bastemir A, et al. Evaluation of patients with upper gastrointestinal bleeding retrospectively. Sakarya Tıp Derg 2015;5:130–34. [Article in Turkish] [CrossRef]
18. Strate LL, Orav EJ, Syngal S. Early predictors of severity in acute lower intestinal tract bleeding. Arch Intern Med 2003;163:838–43. [CrossRef]
19. Jairath V, Thompson J, Kahan BC, Daniel R, Hearnshaw SA, Travis SPL, et al. Poor outcomes in hospitalized patients with gastrointestinal bleeding: Impact of baseline risk, bleeding severity, and process of care. Am J Gastroenterol 2014;109:1603–12. [CrossRef]
20. Telaku S, Kraja B, Qirjako G, Prifti S, Fejza H. Clinical outcomes of nonvariceal upper gastrointestinal bleeding in Kosova. Turk J Gastroenterol 2014;25:110–15. [CrossRef]
21. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. Gut 1996 Mar;38:316–21. [CrossRef]
22. Şenel T, Ates I, Demir BF, Arikan MF, Karaahmetoglu S, Altiparmak E, et al. The diagnostic and prognostic value of platelet indices in gastrointestinal bleeding. Am J Emerg Med 2019 Apr;37:657–63. [CrossRef]
23. Makay B, Türkyılmaz Z, Duman M, Ünsal E. Mean platelet volume in Henoch-Schönlein purpura: relationship to gastrointestinal bleeding. Clin Rheumatol 2009;28:1225–28. [CrossRef]
24. Tanoğlu A, Eroglu M, Yıldırım AO, Kara M, Yazgan Y. Increased mean platelet volume is associated with length of stay and transfusion requirements in upper gastrointestinal bleeding. Gulhane Med J 2015;57:16–20. [Article in Turkish] [CrossRef]
25. Bryant RV, Kuo P, Williamson K, Yam C, Schoeman MN, Holloway RH, et al. Performance of the Glasgow-Blatchford score in predicting clinical outcomes and intervention in hospitalized patients with upper GI bleeding. Gastrointest Endosc 2013;78:576–83. [CrossRef]
26. Stanley AJ, Dalton HR, Blatchford O, Ashley D, Mowat C, Cahill A, et al. Multicentre comparison of the Glasgow Blatchford and Rockall Scores in the prediction of clinical end-points after upper gastrointestinal haemorrhage. Aliment Pharmacol Ther 2011;34:470–75. [CrossRef]
27. Chen IC, Hung MS, Chiu TF, Chen JC, Hsiao CT. Risk scoring systems to predict need for clinical intervention for patients with nonvariceal upper gastrointestinal tract bleeding. Am J Emerg Med 2007;25:774–79. [CrossRef]
28. Fattahi E, Somi I, Moosapour M, Fouladi R. Acute upper gastrointestinal bleeding. Pak J Biol Sci 2011;14:849–53. [CrossRef]
29. Corley DA, Stefan AM, Wolf M, Cook EF, Lee TH. Early indicators of prognosis in upper gastrointestinal hemorrhage. Am J Gastroenterol 1998;93:336–40. [CrossRef]
30. Morsy KH, Ghaliony M, Mohammed HS. Outcomes and predictors of in-hospital mortality among cirrhotic patients with non-variceal upper gastrointestinal bleeding in upper Egypt. Turk J Gastroenterol 2014;25:707–13. [CrossRef]
31. González-González JA, Vazquez-Elizondo G, Garcia-Compean D, Gaytan-Torres JO, Flores-Rendon AR, Jaquez-Quintana JO, et al. Predictors of in-hospital mortality in patients with nonvariceal upper gastrointestinal bleeding. Rev Esp Enferm Dig 2011;103:196–203. [CrossRef]

Varis Dışı Üst Gis Kanamalarında Trombosit İndekslerinin Kanama Ciddiyeti, Prognoz ve Skorlama Sistemleri ile İlişkisi

Amaç: Trombosit indekslerinin [trombosit (PLT), trombositkrit (PCT), ortalama trombosit hacmi (MPV), trombosit dağılım genişliği (PDW)] varis dışı üst gastrointestinal sistem (GİS) kanamalarında kanama ciddiyeti ve prognozu öngörmedeki yerini belirlemeyi amaçladık.

Gereç ve Yöntem: Varis dışı üst GİS kanaması nedeniyle yatırılmış 210 hasta çalışmaya alındı. Hastaların başvuru anındaki, 5. gündeki ve taburculuklarındaki tam kan sayımı değerleri kaydedildi. Hastaların Rockall ve Blatchford skorları hesaplandı ve Forrest sınıflaması yapıldı.

Bulgular: Yatış süresi 5 gün üzeri ve transfüzyon ihtiyacı olan hastaların Blatchford ve Rockall skorları; olmayan gruba göre daha yüksekti ($p<0.001$). Yatış süresi 5 gün üzeri ve altında olan gruplar ve transfüzyon yapılan ve yapılmayan gruplar karşılaştırıldığında PLT, PCT, MPV ve PDW değerleri arasında anlamlı fark saptanmadı ($p>0.05$). İlk başvuru esnasındaki MPV ve taburculuk esnasındaki MPV ve PDW değerleri ile Blatchford skoru arasında aynı yönlü çok zayıf bir ilişki bulundu. Taburculuk esnasındaki MPV ve PDW değerleri ile Rockall skoru arasında aynı yönlü çok zayıf bir ilişki bulundu. Yatış süresinin 5 gün ve üzeri olması riskini öngörmede, ileriye doğru seçimli lojistik regresyon analizi yapıldığında trombosit indeksleri bağımsız prediktör olarak saptanmadı.

Sonuç: Üst GİS kanamalarında kanama ciddiyeti ve prognozu belirlemede trombosit indekslerinin bağımsız prediktor olarak yer almadığı, ancak MPV ve PDW nin skorlama sistemleri ile çok zayıf ilişkili olduğu gözlendi.

Anahtar Sözcükler: FBlatchford skorlama; Rockall skorlama; trombosit indeksleri; varis dışı üst GİS kanama.

SCIE DOI: 10.14744/scie.2025.03780
South. Clin. Ist. Euras. 2025;36(3):224-227

Original Article

Factors Affecting Success in Single-Dose Methotrexate Treatment in Ectopic Pregnancies and 10 Years of Clinical Experience

Emre Mat,[1] İsmail Bağlar,[2] Esra Keles,[1] Ahmet Özkul,[2] Lokman Tekin Ertekin[2]

[1]Department of Gynecologic Oncology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye
[2]Department of Obstetrics And Gynecology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye

Submitted: 08.07.2025
Revised: 31.07.2025
Accepted: 05.08.2025

Correspondence: Emre Mat, Department of Gynecologic Oncology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye

E-mail: emremat63@gmail.com

Keywords: Ectopic pregnancy; methotrexate; β-hCG.

ABSTRACT

Objective: The aim of this study was to evaluate the success rate of ectopic pregnancy cases treated with single-dose methotrexate in an advanced gynecology and obstetrics center over a 10-year period and the factors affecting the response to treatment.

Methods: A total of 120 patients who were diagnosed with ectopic pregnancy and treated with single dose systemic methotrexate between January 2014 and December 2024 were retrospectively included in the study. Demographic data, clinical findings, baseline β-hCG levels, treatment responses, and rates of conversion to surgery if necessary were analyzed.

Results: In the study, treatment success with a single dose of methotrexate was 78.3%. The rate of second dose methotrexate administration was 13.3% and the rate of surgical requirement was 8.3%. Baseline β-hCG level was found to be the most important factor affecting treatment success ($p<0.001$).

Conclusion: Single-dose methotrexate treatment is an effective and safe treatment option in cases of ectopic pregnancy with appropriate criteria. Careful patient selection based on baseline β-hCG level and ectopic mass characteristics may increase treatment success and decrease the need for surgery.

INTRODUCTION

Ectopic pregnancy is an obstetric emergency that occurs when the fertilized ovum implants outside the endometrial cavity and can have serious consequences, accounting for approximately 1.5-2% of pregnancies.[1] With the development of early diagnosis possibilities, medical treatment options have come to the forefront as an alternative to surgery. Among these options, the most commonly used method is single dose systemic methotrexate administration.[2]

Methotrexate is an antifolate agent that terminates pregnancy by stopping the proliferation of trophoblast cells. It is frequently preferred in clinical practice due to its ease of administration, low risk of complications and reduced hospital stay.[3]

However, some factors affecting the success of this treatment method are still controversial. In particular, β-hCG level at the time of diagnosis, gestational week and characteristics of the ectopic mass may directly affect the treatment response.[4] In this study, we evaluated the efficacy of single-dose methotrexate treatment administered in an advanced center in the last ten years and examined the factors affecting success.

MATERIALS AND METHODS

This retrospective descriptive study included ectopic pregnancy cases treated with single dose systemic methotrexate (MTX) at an advanced gynecology and obstetrics center between January 2014 and December 2024. Ethics committee approval was obtained (Approval No: 2025/010.99/15/25. Date: 30/04/2025) and the study was

conducted in accordance with the principles of the Declaration of Helsinki.

A total of 120 patients who were hemodynamically stable, without fetal cardiac activity, with a mass diameter of 4 cm and a β-hCG level below 5000 IU/L were included in the study. Patients with MTX contraindications, ruptured or unstable cases were excluded.

All patients received MTX 50 mg/m² intramuscularly according to body surface area. β-hCG levels were checked on days 4 and 7; ≥15% decrease was considered as success criteria. A second dose was administered to patients who were deemed necessary, and those who did not respond to treatment were taken to surgery.

Data were obtained from patient files and analyzed with SPSS 26.0 program. Numerical variables were presented as mean ± standard deviation, categorical data were presented as frequency and percentage. Appropriate statistical tests were used for intergroup comparisons; $p<0.05$ was considered significant.

RESULTS

In our study, 120 patients who were diagnosed with ectopic pregnancy and treated with single dose methotrexate in a 10-year period were retrospectively evaluated. The mean age of the patients was 30.6±4.9 years and the mean gestational age was 6.4±0.9 weeks. Fifteen percent of the patients (n=18) had a previous history of ectopic pregnancy. The mean serum baseline β- hCG level was 2340±1080 IU/L and the mean mass size was 26.8±6.2 mm on transvaginal ultrasonography. Sociodemographic findings of the patients are given in Table 1.

In the study, 94 patients (78.3%) were successfully treated with a single dose of methotrexate. 16 patients (13.3%) received a second dose of methotrexate because the decrease in β-hCG on days 4 and 7 was not sufficient. The remaining 10 patients (8.3%) underwent surgical intervention due to non-response to treatment or clinical deterioration. In successfully treated patients, the mean time to decrease in serum β-hCG level to <5 IU/L was 23.4±6.8 days. No patient developed complications after treatment. The patients' initial β-hCG levels and single-dose MTX treatment success levels are given in Table 2.

When the patients who successfully responded to single dose MTX treatment were compared with those who failed, the only variable that made a significant difference was baseline β-hCG level ($p<0.001$). There was no statistically significant difference in age, gestational week, transvaginal ultrasonography mass diameter and history of infertility.

In line with these data, our study concluded that the baseline β-hCG level is the strongest factor determining the success of single dose methotrexate treatment. Especially in cases with >3000 IU/L, the failure rate increases.

DISCUSSION

In this study, 78.3% treatment success rate was obtained in ectopic pregnancy cases treated with a single dose of systemic methotrexate. This result is consistent with the range of 64-94% reported in the literature.[5] The baseline serum β-hCG level, which is one of the most important determinants of success rate, was found to be significantly higher in the unsuccessful group in our study; this is in line with recent studies.[6,7]

Jurkovic et al.[8] showed that there was no difference between methotrexate and expectant management in patients with β-hCG levels <1500 IU/L, but methotrexate was more effective at higher levels. Similarly, studies by Papageorgiou D et al.[9] identified the baseline β-hCG level as the strongest prognostic factor.

In our study, we observed that hCG levels above 3000 IU/L increased the risk of failure, which supports Capozzi et al.[10] report of a 64% failure rate. Cases with a mass di-

Table 1. Demographic and clinical characteristics of the cases

Feature	Single dose MTXSuccessful (n=94)	Single dose MTX Failure (n=26)	p value
Age (years. mean ± SD)	30.2±4.6	31.4±5.2	0.18
Gestational week (weeks)	6.3±0.8	6.7±1.1	0.15
Baseline β-hCG (IU/L)	1925±890	3960±1110	<0.001
Ectopic mass diameter (mm)	25.6±5.4	29.8±7.1	0.07
History of ectopic pregnancy (%)	12 (12.8)	6 (23.1)	0.21
History of infertility (%)	14 (14.9)	6 (23.1)	0.37
History of pelvic surgery (%)	22 (23.4)	6 (23.1)	0.96
Time to reset β-hCG (days)	23.4±6.8	-	-
Need for second dose of methotrexate (n, %)	10 (10.6)	6 (23.1)	0.09
Rate of transition to surgery (n, %)	0	10 (38.4)	<0.001

MTX: Methotrexate, p value of <0.05 indicates a significant difference.

Table 2. Treatment success and failure rates according to baseline β-hCG level

Baseline β-hCG Level (IU/L)	Number of Patients (n)	With a single dose of MTX	With a single dose of MTX
		Successful Treatment (n, %)	Failed Treatment (n,%)
<500	10	10 (100)	0 (0)
500-999	16	15 (93.7)	1 (6.3)
1000-1499	18	16 (88.8)	2 (11.2)
1500-1999	20	17 (85.0)	3 (15.0)
2000-2499	16	13 (81.2)	3 (18.8)
2500-2999	12	9 (75.0)	3 (25.0)
3000-3499	10	5 (50.0)	5 (50.0)
3500-3999	8	3 (37.5)	5 (62.5)
4000-4499	6	2 (33.3)	4 (66.7)
≥4500	4	1 (25.0)	3 (75.0)

MTX: Methotrexate, p value of <0.05 indicates a significant difference.

ameter >3.5cm on transvaginal ultrasonography have also been associated with lower success rates.[11]

In failed cases, a second dose of methotrexate was sufficient in some patients, while other patients required surgical intervention. This shows that the second dose can be a safe and effective option.[12] However, it is emphasized that patient selection criteria should be determined more carefully to reduce this need.[13]

In the literature, the advantages of the single-dose protocol such as short hospitalization time and low cost are pointed out, but it is also stated that it may not be suitable for all patients and individualized patient selection gains importance.[14,15] In the systematic review by Tang et al.,[16] it was emphasized that low progesterone levels and mild clinical symptoms may also predict success.

No serious complications were reported in our study, supporting the safety of the protocol. Nevertheless, patients should be closely monitored due to rare hepatotoxicity and gastrointestinal side effects.[17,18]

In conclusion, early diagnosis, appropriate patient selection and regular β-hCG monitoring increase the success of single-dose methotrexate treatment and decrease the need for surgery. To reduce the risk of failure, β-hCG level, mass diameter and clinical findings should be evaluated together.[19,20]

The strengths of our study include the fact that it was based on 10 years of data, the number of patients was sufficient and the treatment protocol was standardized. However, its retrospective nature, lack of some clinical data, and single-center nature are factors that limit the generalizability of the results. These findings should be supported by multicenter, prospective studies.

Conclusion

Single dose methotrexate offers an effective and safe treatment option in appropriately selected cases of ectopic pregnancy. The 78.3% success rate obtained in our study is consistent with the literature. It has been observed that baseline β-hCG level, especially at values above 3000 IU/L, increases the risk of treatment failure. Therefore, this parameter should be one of the main determinants in patient selection. The absence of complications supports the safety of the protocol and the second dose is an effective alternative that reduces the need for surgery. Evaluation of hormonal and biochemical markers in further studies may further strengthen patient selection processes.

Ethics Committee Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of University of Health Sciences Turkey, Kartal City Hospital (Date: 30.04.2025, Decision No: 2025/010.99/15/26).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.M., İ.B., E.K., A.Ö.; Design: L.T.E., İ.B., E.K., A.Ö.; Supervision: E.M., E.K., A.Ö.; Fundings: E.M., E.K., İ.B., L.T.E.; Materials: İ.B., E.K.; Data collection &/or processing: E.K., İ.B.; Analysis and/or interpretation: A.Ö., E.K.; Literature search: E.K., A.Ö., L.T.E.; Writing: E.M., İ.B., L.T.E.; Critical review: E.M., E.K., İ.B.

Conflict of Interest

None declared.

REFERENCES

1. Jurkovic D, Memtsa M, Sawyer E, Donaldson ANA, Jamil A, Schramm K, et al. Single-dose systemic methotrexate vs expectant management for treatment of tubal ectopic pregnancy: A placebo-controlled randomized trial. Ultrasound Obstet Gynecol 2017;49:171–6. [CrossRef]
2. Yang C, Cai J, Geng Y, Gao Y. Multiple-dose and double-dose versus single-dose administration of methotrexate for the treatment of ectopic pregnancy: A systematic review and meta-analysis. Reprod Biomed Online 2017;34:383–91. [CrossRef]
3. Günay T, Yardımcı OD, Hocaoğlu M, Bör ED, Turgut A, Karateke A. Factors affecting success of single-dose methotreaxhate treatment in ectopic pregnancy. Kocaeli Med J 2019;8:189–94. [CrossRef]
4. Bachman EA, Barnhart K. Medical management of ectopic pregnancy: A comparison of regimens. Clin Obstet Gynecol 2012;55:440–7. [CrossRef]
5. Yildiz A, Dogan O. Efficacy of single dose methotrexate treatment in ectopic pregnancies: 5 Years of experience. Kafkas J Med Sci 2017;7:188–92. [CrossRef]
6. Sendy F, Al Shehri E, Al Ajmi A, Bamanie E, Appani S, Shams T. Failure rate of single dose methotrexate in managment of ectopic pregnancy. Obstet Gynecol Int 2015;2015:902426. [CrossRef]
7. Kılıç BŞ, Tüten A, Öncül M, Açıkgöz AS, Öcal PK. Identifying prognostic factors which affect the success of ectopic pregnancy treatment with a single dose methotrexate. Turk J Obstet Gynecol 2014;11:84–7. [CrossRef]
8. Jurkovic D, Knez J, Appiah A, Farahani L, Mavrelos D, Ross JA. Surgical treatment of Cesarean scar ectopic pregnancy: Efficacy and safety of ultrasound-guided suction curettage. Ultrasound Obstet Gynecol 2016;47:511–7. [CrossRef]
9. Papageorgiou D, Sapantzoglou I, Prokopakis I, Zachariou E. Tubal ectopic pregnancy: From diagnosis to treatment. Biomedicines 2025;13(6):1465. [CrossRef]
10. Capozzi VA, Roberto L, Gallinelli A, Pezzani A, Monica M, Berretta R. Predictors of methotrexate success and fertility outcomes in tubal ectopic pregnancy: A retrospective cohort study. Medicina (Kaunas) 2025;61:1058. [CrossRef]
11. Aka N, Dede S, Aydin C. Factors affecting success in single dose methotrexate treatment. J Turkish Soc Gynecol Obstet 2015;4:68–71.
12. Shirazi M, Pooransari P, Hajiha N, Shaker Z, Ghazi M, Davari Tanha F, et al. Effect of single-dose methotrexate treatment on ovarian reserve in women with ectopic pregnancy undergoing infertility treatment: A single-center experience. Int J Fertil Steril 2020;14:23–6.
13. Kyriacou C, Kim SH, Arianoglou M, Bobdiwala S, Pikovsky M, Parker N, et al. Maternal plasma microRNAs as potential biomarkers for triaging pregnancies of unknown location and ectopic pregnancy diagnosis. Noncoding RNA Res 2025;13:162–73. [CrossRef]
14. Vaswani PR. Predictors of success of medical management of ectopic pregnancy in a tertiary care hospital in United Arab Emirates. J Clin Diagn Res 2014;8:OC04–8. [CrossRef]
15. Alur-Gupta S, Cooney LG, Senapati S, Sammel MD, Barnhart KT. Two-dose versus single-dose methotrexate for treatment of ectopic pregnancy: A meta-analysis. Am J Obstet Gynecol 2019;221:95–108.e2. [CrossRef]
16. Tang L, Nie S, Ling L, Zhu Q. Predictors of treatment failure of tubal pregnancy with single-dose methotrexate regimen – a systematic review and meta-analysis. J Obstet Gynaecol 2025;45:2447997. [CrossRef]
17. Qiao L, Hu J, Ou D, Liu M, Shi X, Li X, et al. Comparison of the efficacy and safety of methotrexate injection and methotrexate tablets in active RA. Rheumatology (Oxford) 2025;64:3426–33. [CrossRef]
18. Deniz S, Ali B, Canan U, Yılmaz AH, Olcay I, Burcu D, et al. Evaluation of the parameters in predicting single-dose methotrexate therapy success for ectopic pregnancy. J Obstet Gynaecol Res 2024;50:856–63. [CrossRef]
19. Solangon SA, Van Wely M, Van Mello N, Mol BW, Ross JA, Jurkovic D. Methotrexate vs expectant management for treatment of tubal ectopic pregnancy: An individual participant data meta-analysis. Acta Obstet Gynecol Scand 2023;102:1159–75. [CrossRef]
20. Dooley WM, Chaggar P, De Braud LV, Bottomley C, Jauniaux E, Jurkovic D. Effect of morphological type of extrauterine ectopic pregnancy on accuracy of preoperative ultrasound diagnosis. Ultrasound Obstet Gynecol 2019;54:538–44. [CrossRef]

Ektopik Gebeliklerde Tek Doz Metotreksat Tedavisinde Başarıyı Etkileyen Faktörler ve 10 Yıllık Klinik Deneyim

Amaç: Bu çalışmada, ileri düzey bir kadın hastalıkları ve doğum merkezinde, 10 yıllık süreçte tek doz metotreksat ile tedavi edilen ektopik gebelik olgularının başarı oranı ile tedaviye yanıtı etkileyen faktörlerin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Çalışmaya Ocak 2014-Aralık 2024 tarihleri arasında ektopik gebelik tanısı konmuş ve tek doz sistemik metotreksat tedavisi uygulanan toplam 120 hasta retrospektif olarak dâhil edilmiştir. Hastaların demografik verileri, klinik bulguları, başlangıç β-hCG düzeyleri, tedavi yanıtları ve gerekirse cerrahiye geçiş oranları analiz edilmiştir.

Bulgular: Çalışmada tek doz metotreksat ile tedavi başarısı %78.3 olarak saptanmıştır. İkinci doz metotreksat uygulaması %13.3, cerrahi gereksinim oranı ise %8.3 olarak bulunmuştur. Başlangıç β-hCG düzeyinin tedavi başarısını etkileyen en önemli faktör olduğu tespit edilmiştir ($p<0.001$).

Sonuç: Tek doz metotreksat tedavisi, uygun kriterleri taşıyan ektopik gebelik olgularında etkili ve güvenli bir tedavi seçeneğidir. Başlangıç β-hCG düzeyi ve ektopik kitle özellikleri dikkate alınarak hasta seçiminin dikkatli yapılması, tedavi başarısını artırabilir ve cerrahiye olan gereksinimi azaltabilir.

Anahtar Sözcükler: Ektopik gebelik; metotreksat; β-hCG.

SCIE DOI: 10.14744/scie.2025.57224
South. Clin. Ist. Euras. 2025;36(3):228-232

Original Article

Clinical and Radiological Outcomes of Distal Femur Physeal Fractures

Ahmet Berkay Girgin, Ahmet Acar, Ömer Torun, Hakan Aslan, Evrim Duman, Osman Yağız Atlı, Hüseyin Bilgehan Çevik

Department of Orthopedics and Traumatology, Ankara Etlik City Hospital, Ankara, Türkiye

Submitted: 17.07.2025
Revised: 31.07.2025
Accepted: 10.08.2025

Correspondence: Ahmet Berkay Girgin,
Department of Orthopedics and Traumatology, Ankara Etlik City Hospital, Ankara, Türkiye
E-mail: abgirgin1995@gmail.com

Keywords: Genu valgum; growth disturbance; limb length discrepancy; pediatric fracture; physeal injury.

ABSTRACT

Objective: Fractures of the distal femoral physes usually occur after high energy trauma and they are serious injuries of pediatric population. This aim of this sudy is to examine distal femoral physeal fractures treated in a level I pediatric trauma center epidemiologically and to report the complications that occurred during follow-up.

Methods: Patients, <18 years of age, admitted to the emergency department with distal femoral physeal fractures were included in the study. Demographic data, medical history, preoperative findings, injury mechanisms, postoperative outcomes, complications during follow-up period of the patients were noted. Salter-Harris classification was used to categorize the fractures.

Results: In total, 21 patients, with a mean age of 12.3 years (range, 1-16 years), were included in the study. Male to female ratio was 2.5. 12 patients (57.2%) had Salter-Harris type 2 fractures and it was the most common type. 19 (90.5%) fractures were treated surgically with different fixation methods. Mean follow-up duration was 97 months (range, 72-133 months). Complications observed during follow-up were genu valgum (n=2, 9.5%), limb length discrepancy (n=2, 9.5%), reoperation (n=7, 33.3%) and joint stiffness (n=1, 4.8%).

Conclusion: Distal femoral physeal injuries are injuries with a high rate of complications and these complications, like growth disturbance, may cause serious problems in adulthood. Although this injury is relatively uncommon, patients should be treated appropriately and followed regularly until skeletal maturity for possible late complications.

INTRODUCTION

Fractures involving the distal femoral epiphyseal plate are relatively uncommon injuries, however, they are serious since their complication rates are known to be high.[1] This injury, initially referred to as "cartwheel injury", occurs when children's feet get stuck and the knee becomes hyperextended.[2] It is more common in adolescence period and as the incidence of high-energy trauma steadily increases, the frequency of distal femur fractures is also increasing accordingly.[3,4]

The distal femoral epiphysis is the epiphyseal plate that contributes most to lower extremity growth.[5,6] For this reason, there is a high probability of growth disturbance or angular deformities occurring with these injuries.[7] As a result, repeated operations may be required to correct deformities.

This study aimed to examine pediatric distal femur fractures extending to the physeal plate in a level I pediatric trauma center epidemiologically and to report the complications that occurred during the follow-up and the treatment modalities according to the complications.

MATERIALS AND METHODS

The study was conducted at a tertiary center and was approved by the Ankara Etlik City Hospital Ethical Review Board in accordance with the Declaration of Helsinki (Date: 16/07/2025, No: AESH-BADEK1-2025-271). Informed consent was taken from all patients' parents to use their data in the study.

Patients, <18 years of age, admitted to the emergency department with distal femur fractures between 2014 and 2019 were retrospectively analyzed. Patients with distal femur fractures which have epiphyseal involvement, follow-up longer than 24 months, good imaging quality, and sufficient clinical data were included in the study. Patients with distal femur fractures which do not have epiphyseal involvement, poor imaging quality, insufficient clinical data, and those who did not give consent to participate in the study and share data were excluded from the study. The

Table 1. Demographic and clinical data of patients

Case number	Age (years)	Sex	Mechanism of injury	Salter-Harris classification	Additional injury	Treatment	Follow-up duration (months)	ROM (12th month)	Complications
1	1	M	Fall from height	2	N/A	Long leg cast	119	133	N/A
2	2	M	Fall from height	4	N/A	Long leg cast	120	130	N/A
3	9	M	MVA	2	Ipsilateral tibia shaft (Floating knee)	CRPF (K-wire + cannulated screw)	99	132	Reoperation (implant removal)
4	11	F	MVA	4	Contralateral femur shaft	ORIF (Plate)	108	135	Reoperation (implant removal)
5	12	M	Sport-related	2	N/A	CRPF (Cannulated screw)	91	132	N/A
6	12	F	Sport-related	2	N/A	CRPF (Cannulated screw)	90	136	N/A
7	13	M	Sport-related	2	N/A	CRPF (K-wire)	81	140	N/A
8	13	M	MVA	4	N/A	ORIF (External fixator + plate)	133	130	Reoperation (implant removal)
9	13	M	MVA	3	N/A	ORIF (Plate)	94	135	N/A
10	14	F	MVA	2	Bilateral tibia shaft (Floating knee) +Contralateral medial malleol	CRPF (K-wire)	89	95	Valgus (20°) and flexion (10°) angulation+LLD (3cm)+ Reoperation (Corrective osteotomy)+Stiffness
11	14	M	MVA	4	Ipsilateral tibial plateau	ORIF (Cannulated screws)	72	133	Reoperation (implant removal)
12	14	M	Fall from height	2	N/A	ORIF (Cannulated screws)	92	134	N/A
13	14	F	MVA	3	N/A	ORIF (Cannulated screws)	91	138	N/A
14	14	M	MVA	4	Ipsilateral tibia shaft (Floating knee)	ORIF (Cannulated screws)	92	132	N/A
15	14	M	Sport-related	2	N/A	CRPF (Cannulated screws)	113	136	Reoperation (implant removal)
16	14	M	MVA	2	Contralateral tibia shaft	CRPF (Cannulated screws)	112	137	N/A
17	15	F	Sport-related	2	N/A	CRPF (Cannulated screws)	76	134	Valgus angulation (16°)+LLD (3cm)
18	15	M	MVA	2	N/A	ORIF (Plate)	72	136	N/A
19	15	F	MVA	4	N/A	ORIF (Cannulated screws)	123	138	N/A
20	15	M	Fall from height	4	N/A	ORIF (Cannulated screws)	88	133	Reoperation (implant removal)
21	16	M	MVA	2	N/A	ORIF (Plate)	82	132	N/A

M: Male; F: Female; MVA: Motor vehicle accident; N/A: Not applicable; ORIF: Open reduction-internal fixation; CRPF: Closed reduction-percutaneous fixation; K-wire: Kirschner wire; ROM: Range of motion; LLD: Limb length discrepancy.

patients' treatments were decided by the senior orthopedic surgeon on duty on the day they came to the emergency room.

Demographic data, medical history, preoperative findings, injury mechanisms, postoperative outcomes, complications during the follow-up period of the patients were noted. Fractures were classified according to the Salter-Harris classification.[8] Anteroposterior and lateral orthoroentgenograms and knee radiographs were examined for possible radiographic complications. For functional evaluation, knee joint range of motion measurements at every follow-up examination were made with a goniometer.

RESULTS

There were 48 patients <18 years of age who were treated for distal femur fractures in our center between 2014 and 2019. 21 patients were included in the study because 27 of these fractures did not extend to the distal femoral epiphysis. Thus, during the same period, 43.8% of distal femur fractures had epiphyseal extension.

There were 15 male (71.4%) and 6 female (28.6%) patients and the male to female ratio was 2.5. Mean age of the patients was 12.3 years (range, 1-16 years). According to the Salter-Harris classification, the fractures of 12 patients (57.2%) were type 2, 2 patients (9.5%) were type 3, and 7 patients (33.3%) were type 4. 4 fractures (19%) occurred due to falls, 5 (23.8%) occurred due to sport-related injuries and 12 (57.2%) occurred due to motor vehicle accidents. 6 patients (28.6%) had additional injuries along with the distal femur fracture. 3 patients (14.3%) had floating knee injury. Additional injuries are detailed in the Table 1. 2 (9.5%) of the fractures were treated conservatively with a long leg cast held for 6 weeks, while the remaining 19 (90.5%) fractures were treated surgically. Open reduction and internal fixation was performed in 11 (57.9%) patients, while closed reduction and percutaneous fixation was performed in 8 (42.1%) patients. Details about fixation methods were given in the Table 1.

Mean follow-up duration was 97 months (range, 72-133 months). Fracture union was complete in all patients after 6 months. Complications observed during the follow-up were genu valgum (n=2, 9.5%), limb length discrepancy (LLD, n=2, 9.5%), and reoperation (n=7, 33.3%).

The patients' average knee joint range of motion at 12 months was 132.4o (range, 95-140o). Only 1 (4.8%) patient had decreased knee range of motion (95o) and no improvement was observed in subsequent follow-up. Detailed clinical and demographic data of the patients were given in the Table 1.

DISCUSSION

The distal femoral physeal plate is responsible for 70% of femoral growth and 40% of lower extremity growth. It is the fastest growing physes and has an average growth of 1 cm per year.[9-11] Therefore, in case of distal femoral injury, it may lead to devastating complications like growth arrest, varus-valgus angulation and LLD and because of that, repeated operations to correct deformities become inevitable.[7,12] In this study, growth arrest occurred in 2 (9.5%) of the patients, followed by valgus angulation and LLD of 3cm. One of them underwent corrective distal femoral osteotomy for valgus angulation. In a meta-analysis conducted by Basener et al.,[7] although the definition of growth disturbance has not been made clearly, the rate of overall growth disturbance after distal femur physeal fracture was reported as high as 52% and the rate of LLD>1.5cm was reported as 22%.

Risk factors for growth disturbance have been investigated many times in the literature. Many studies have been conducted to predict the outcome of distal femoral physeal fractures and some risk factors were determined. Salter Harris classification, presence of displacement, degree and direction of displacement were found to be significant risk factors, while injury mechanism and age were not found to have an effect on growth disturbance.[7,11,13-15]

In this study, 43.8% of distal femur fractures occurred during the same period of time were found to be physeal fractures. Similar results were found in previous epidemiological studies.[4,16,17]

Salter-Harris classification is a valuable classification as it gives an idea about prognosis of physeal fractures.[7,8,11,12,18] The most common fracture type in the study was Salter-Harris type 2 fractures and this confirms the literature.[4,16-18] The highest complication rate was seen in Salter-Harris type 4 fractures, similar to the literature.[11,12,17]

Various fixation methods are used in the surgical treatment of distal femur physeal fractures.[3,19,20] The main purpose of treatment should be to prevent further damage to the physeal plate that has already been damaged because of the fracture. In this study, fracture fixation was performed with cannulated screws in more than half of the patients. Although the aim is to preserve the physeal plate, stable fixation of the fracture is also important. Fixation with smooth pins has been reported to cause less growth disturbances.[21,22]

Most of the patients included in the study had been exposed to high-energy trauma. For this reason, approximately 30% of patients had additional injuries along with the distal femur fracture. Ipsilateral tibial shaft fracture, called as floating knee, was observed in 3 patients. This injury is rarely seen in the pediatric population and associated with higher complication rates, but there is no consensus in the literature regarding its management.[23,24] Although it is a rare injury, floating knee should be kept in mind in the event of high-energy trauma and action should be taken accordingly.

None of the children included in the study had either neurological or vascular injuries pre or postoperatively. However, distal femoral physeal fractures may also be associated with vascular injuries especially in Salter-Harris

type I injuries when the epiphysis fragment is displaced posteriorly.[12] Posteriorly displaced fracture fragments may cause compression or direct injury to the popliteal vessels. A proper vascular assessment is mandatory in the emergency department when the patient first presents and after closed reduction. If vascular injury is suspected, this is a medical emergency and immediate intervention is required.[25] Because, if a vascular injury is missed or not treated properly as soon as possible, devastating consequences may occur. Since it is a rare condition, there are few cases of distal femur physeal fracture with vascular compromise reported in the literature.[25-27]

Although it was a study conducted in a Level I trauma center and had long follow-up durations, the study has some limitations. First of all, the study is designed retrospectively and the sample size is small because it is a relatively rare injury. In addition, only available data for functional evaluation of the patients was knee joint range of motion measurements. Using functional scores instead of just measuring range of motion could provide a more accurate functional assessment.

Conclusion

Distal femoral physeal injuries are uncommon injuries, however the incidence of these injuries is increasing every day because of the increased motor vehicle accidents. Since the complication rates of these injuries are high, they are serious injuries that require proper treatment. Growth disturbance is a common complication of these injuries. For this reason, following-up patients until they reach skeletal maturity is strongly recommended.

Ethics Committee Approval

The study was approved by the Ankara Etlik City Hospital Ethical Review Board in accordance with the Declaration of Helsinki (Date: 16.07.2025, Decision No: AESH-BADEK1-2025-271).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: A.B.G., A.A., Ö.T., H.B.Ç.; Design: A.B.G., A.A., H.B.Ç.; Supervision: E.D., H.A., O.Y.A., H.B.Ç.; Data collection &/or processing: A.B.G., A.A., Ö.T., E.D., H.B.Ç., H.A., O.Y.A.; Analysis and/or interpretation: A.B.G., H.B.Ç., E.D., H.A.; Literature search: A.B.G., H.B.Ç.; Writing: A.B.G.; Critical review: A.B.G., A.A., Ö.T. E.D., H.A., O.Y.A., H.B.Ç.

Conflict of Interest

None declared.

REFERENCES

1. Czitrom AA, Salter RB, Willis RB. Fractures Involving the distal epiphyseal plate of the femur. Int Orthop 1981;4:269–77. [CrossRef]
2. Hutchinson J. Lectures on injuries to the epiphyses and their results: Delivered at the Royal College of Surgeons. Br Med J 1894;1:669–73. [CrossRef]
3. Sepúlveda M, Téllez C, Villablanca V, Birrer E. Distal femoral fractures in children. EFORT Open Rev 2022;7:264–73. [CrossRef]
4. Engström Z, Wolf O, Hailer YD. Epidemiology of pediatric femur fractures in children: The Swedish Fracture Register. BMC Musculoskelet Disord 2020;21:796. [CrossRef]
5. Ladenhauf HN, Jones KJ, Potter HG, Nguyen JT, Green DW. Understanding the undulating pattern of the distal femoral growth plate: Implications for surgical procedures involving the pediatric knee: A descriptive MRI study. Knee 2020;27:315–23. [CrossRef]
6. Liu RW, Armstrong DG, Levine AD, Gilmore A, Thompson GH, Cooperman DR. An anatomic study of the distal femoral epiphysis. J Pediatr Orthop 2013;33:743–9. [CrossRef]
7. Basener CJ, Mehlman CT, DiPasquale TG. Growth disturbance after distal femoral growth plate fractures in children: A meta–analysis. J Orthop Trauma 2009;23:663–7. [CrossRef]
8. Salter RB, Harris WR. Injuries involving the epiphyseal plate. JBJS 1963;45:587–622. [CrossRef]
9. Pritchett JW. Longitudinal growth and growth-plate activity in the lower extremity. Clin Orthop Relat Res 1992:274–9. [CrossRef]
10. Edwards PH Jr, Grana WA. Physeal fractures about the knee. J Am Acad Orthop Surg 1995;3:63–9. [CrossRef]
11. Arkader A, Warner WC Jr, Horn BD, Shaw RN, Wells L. Predicting the outcome of physeal fractures of the distal femur. J Pediatr Orthop 2007;27:703–8. [CrossRef]
12. Young EY, Stans AA. Distal femoral physeal fractures. J Knee Surg 2018;31:486–9. [CrossRef]
13. Hooper N, Johnson L, Banting N, Pathy R, Schaeffer EK, Bone JN, et al. Risk factor analysis for growth arrest in paediatric physeal fractures-A prospective study. J Clin Med 2024;13.2946. [CrossRef]
14. Bellamy JT, Ward LA, Fletcher ND. Evaluation of pediatric distal femoral physeal fractures and the factors impacting poor outcome requiring further corrective surgery. J Pediatr Orthop B 2021;30:6–12. [CrossRef]
15. Hulbert MA, Chun L, Bryan TP, Souder CD, Pennock AT. Factors associated with premature physeal closure after distal femur physeal fracture. J Pediatr Orthop 2025;45:e413–e7. [CrossRef]
16. Mann DC, Rajmaira S. Distribution of physeal and nonphyseal fractures in 2,650 long-bone fractures in children aged 0-16 years. J Pediatr Orthop 1990;10:713–6. [CrossRef]
17. Yamamura MK, Carry PM, Gibly RF, Holmes K, Ogilvie B, Phillips A, et al. Epidemiology of physeal fractures and clinically significant growth disturbances affecting the distal tibia, proximal tibia, and distal femur: A retrospective cohort study. J Am Acad Orthop Surg 2023;31:e507–e15. [CrossRef]
18. Cepela DJ, Tartaglione JP, Dooley TP, Patel PN. Classifications in brief: Salter-Harris classification of pediatric physeal fractures. Clin Orthop Relat Res 2016;474:2531–7. [CrossRef]
19. Korobeinikov A, Popkov D. Use of external fixation for juxta-articular fractures in children. Injury 2019;50:s87–s94. [CrossRef]
20. Abdelgawad AA, Kanlic EM. Pediatric distal femur fixation by proximal humeral plate. J Knee Surg 2013;26:S45–9. [CrossRef]
21. Dahl WJ, Silva S, Vanderhave KL. Distal femoral physeal fixation: Are smooth pins really safe? J Pediatr Orthop 2014;34:134–8. [CrossRef]
22. Garrett BR, Hoffman EB, Carrara H. The effect of percutaneous pin fixation in the treatment of distal femoral physeal fractures. J Bone Joint Surg Br 2011;93:689–94. [CrossRef]

23. Anari JB, Neuwirth AL, Horn BD, Baldwin KD. Ipsilateral femur and tibia fractures in pediatric patients: A systematic review. World Journal of Orthopedics 2017;8:638. [CrossRef]
24. Baldwin K, Anari J, Shore B, Denning JR, Li Y, Spence D, et al. The pediatric "floating knee" injury: A state-of-the-art multicenter study. JBJS 2019;101:1761–7. [CrossRef]
25. McKenna SM, Hamilton SW, Barker SL. Salter Harris fractures of the distal femur: Learning points from two cases compared. J Investig Med High Impact Case Rep 2013;1:2324709613500238. [CrossRef]
26. Ambulgekar RK, Chhabda GK. A rare case of distal femur physeal fracture dislocation with positional vascular compromise in an adolescent male. J Orthop Case Rep 2022;12:101–6. [CrossRef]
27. Houass E, Elgaliou MR, Riache H, Boufettal M, Allah Bassir R. Open distal femur physeal fracture with positional vascular compromise and ipsilateral open tibia fracture: A rare case report. Vis J Emerg Med 2024;36:101970. [CrossRef]

Distal Femur Fizyel Kırıklarının Klinik ve Radyolojik Sonuçları

Amaç: Distal femoral fizyel yaralanmaları genellikle yüksek enerjili travmalardan sonra oluşur ve pediatrik popülasyonda görülen ciddi yaralanmalardır. Bu çalışmanın amacı, birinci seviye pediatrik travma merkezinde tedavi edilen distal femoral fizyel yaralanmaları epidemiyolojik olarak incelemek ve takip sırasında oluşan komplikasyonları bildirmektir.

Gereç ve Yöntem: Çalışmaya, acil servise distal femoral fizyel yaralanma ile başvuran, 18 yaş altı hastalar dahil edildi. Hastaların demografik verileri, tıbbi öyküleri, ameliyat öncesi bulguları, yaralanma mekanizmaları, ameliyat sonrası sonuçları, takip süresince gelişen komplikasyonlar kaydedildi. Kırıkları kategorize etmek için Salter-Harris sınıflaması kullanıldı.

Bulgular: Çalışmaya toplam 21 hasta alındı ve yaş ortalaması 12.3 yıl (dağılım, 1-16 yıl) idi. Erkek/kadın oranı 2.5 idi. 12 hastada (%57.2) Salter-Harris tip 2 kırık vardı ve bu en sık görülen tipti. 19 (%90.5) kırık farklı fiksasyon yöntemleri kullanılarak cerrahi olarak tedavi edildi. Ortalama takip süresi 97 ay (dağılım, 72-133 ay) idi. Takip sırasında gözlenen komplikasyonlar genu valgum (n=2, %9.5), ekstremite uzunluk farkı (n=2, %9.5), reoperasyon (n=7, %33.3) ve hareket kısıtlılığı (n=1, %4.8) idi.

Sonuç: Distal femoral fizyal yaralanmalar yüksek komplikasyon oranına sahip yaralanmalardır ve bu komplikasyonlar, büyüme duraklaması gibi, yetişkinlikte ciddi sorunlara yol açabilir. Bu yaralanmalar nispeten nadir görülse de, hastalar uygun şekilde tedavi edilmeli ve olası geç komplikasyonlar için iskelet maturitesine kadar düzenli olarak takip edilmelidir.

Anahtar Sözcükler: Büyüme duraklaması; ekstremite uzunluk eşitsizliği; fizyel yaralanma; gene valgum; pediatrik kırık.

SCIE DOI: 10.14744/scie.2025.54514
South. Clin. Ist. Euras. 2025;36(3):233-239

Original Article

An Examination of Conscientious Intelligence Based on Sociodemographic Aspects: A Study on Healthcare Professionals

Halim Ömer Kaşıkcı

Yalova Provincial Directory of Health, Yalova, Türkiye

Submitted: 14.08.2025
Revised: 15.08.2025
Accepted: 20.08.2025

Correspondence: Halim Ömer Kaşıkcı,
Yalova Provincial Directory of Health, Yalova, Türkiye
E-mail: okasikci@gmail.com

Keywords: Conscience; conscientious intelligence; intelligence.

ABSTRACT

Objective: Conscientious intelligence, unlike logical and emotional intelligence, can be defined as consulting one's conscience in making decisions, determining what is good and what is bad, and consciously choosing what is right. This study aimed to determine the differences in conscientiousness among healthcare professionals based on sociodemographic characteristics.

Methods: This study was designed as a descriptive, cross-sectional study. Data were obtained using the Personal Information Form and the Conscientious Intelligence Scale. The Personal Information Form consists of seven questions and 32 items regarding the demographic characteristics of employees. Developed by Aktı and colleagues in 2017, the scale consists of 32 items and 7 subfactors. The study was conducted at a private hospital in Istanbul. The study population consisted of 380 employees. A convenience sampling method was used. An attempt was made to reach all employees using the complete enumeration method during sampling. The study was conducted by reaching 277 individuals who agreed to participate in the study. Data were collected using a survey method from employees who volunteered to participate in the study. Data were analyzed using statistical techniques in SPSS.

Results: The Cronbach's alpha value for the conscientious intelligence scale was found to be 0.87. This result demonstrates the reliability of the scale for the study. Of the participants, 84.1% were female, 63.9% were married, 35.5% had no children, 41.3% were between the ages of 26 and 34, 40.1% were high school graduates, 51.5% had less than 5 years of service experience, and 43% were midwives and nurses. The mean conscientious intelligence score was 121.28, and the standard deviation was 12.8.

Conclusion: According to the research findings, the participants' mean conscience intelligence scores were found to be high. It was concluded that the mean conscience intelligence scores of healthcare workers did not differ according to their socio-demographic characteristics, gender, and marital status. The mean conscience intelligence scores of healthcare workers varied according to their socio-demographic characteristics, such as number of children, age, educational status, length of service, and title.

INTRODUCTION

Conscience is a spiritual power and divine ability bestowed upon humanity by God, used to distinguish between good and evil and to guide people toward goodness. Generally speaking, conscience is the level of "moral consciousness, an inner consciousness" present in all humans, enabling them to grasp what is morally right and wrong through the ability to judge one's actions in accordance with moral principles.[1] Conscience is a feeling within the human heart, a feeling that creates peace when good is done and unease when evil is done, and a structure that constantly makes judgments. The definitions of conscience, "Distinguishing between good and evil, tending toward good, and making judgments about people's actions," are common in terms of the functional roles of conscience and the provision of self-control.[2]

Intelligence is defined in the Turkish Language Association (TDK). This definition is as follows: "The totality of a person's abilities to think, reason, perceive objective facts,

judge, and draw conclusions; understanding, sagacity, intelligence, and foresight".[3] Intelligence is the mind's ability to learn, to make useful use of what it has learned, to adapt to new conditions, to offer new solutions, and to take action for a purpose, to think logically, and to adapt to its environment.[4]

The first studies on intelligence, which has been defined and tested in various ways up until now, were developed in 1911 by Binet and others to identify primary school students at risk of failure. It was believed that this test could measure human intelligence. Binet defined intelligence as understanding, judgment, and reasoning.[5]

In his work "Frameworks of the Mind," Gardner defined intelligence as a talent and skill unique to each individual, enabling them to live in a constantly changing world and adapt to these changes. He proposed the "theory of multiple intelligences," which he defined under eight areas of intelligence. These are: 1. Verbal Intelligence, 2. Logical Intelligence, 3. Physical Intelligence, 4. Musical Intelligence, 5. Visual Intelligence, 6. Social Intelligence, 7. Intrapersonal Intelligence, and 8. Existential Intelligence.[6]

Zohar and Marshall, who proposed Spiritual Intelligence as a new form of intelligence, used the term "human creativity," "the ability to change rules," and "the ability to soften rigid rules with compassion." They argued that in order to achieve wisdom in the information age, this should be called "conscientious" rather than "spiritual." They suggested that it should be considered conscientious intelligence.[7]

Conscientious intelligence, unlike logical and emotional intelligence, can be defined as consulting one's conscience in making decisions, determining good and evil, and consciously choosing what is morally good or right. Conscientious intelligence is crucial for understanding one's inner voice and recognizing one's internal and external responsibilities. Tarhan (2015) lists the values of conscientious intelligence as follows: Listening to one's inner voice, internal and external responsibilities, accountability, responsibilities to God, ethical values, moral reasoning, wisdom, humility, honesty, and principledness.

Throughout history, common human desires can be listed as world domination, self-actualization, and leaving a mark on history. The purpose of this desire for self-actualization is to question existence and non-existence, fulfill the desire for immortality, and seek the meaning of life. This search drives people to seek their Creator and creates a conscientious inner voice. This conscientious inner voice can be revealed through the teachings of Anatolian wisdom, such as those of Rumi, for the transformation from the information age to the age of wisdom.[7]

This study aimed to determine the differences in the conscientious characteristics of healthcare professionals according to sociodemographic characteristics.

MATERIALS AND METHODS

The study was approved by the Yalova University Ethics Committee (Date: 25/06/2025 , No: 2025/248) and was conducted in accordance with the principles of the Declaration of Helsinki.

Purpose, Method, Population, and Sample

The study aim is to determine the differences in conscientiousness among healthcare professionals based on sociodemographic characteristics.

Conscientiousness is not a field that has received sufficient research, both in our country and internationally. Conscientiousness scores are considered important among management and employees, especially in healthcare organizations with multidisciplinary and stressful work environments. This study aims to investigate the role of conscientiousness in a hospital environment with a diverse employee profile and to positively contribute to the manager-work environment-employee management relationship.

This study was designed as a descriptive and cross-sectional study. Data were collected using a Personal Information Form and the Conscientiousness Scale. The Personal Information Form consists of seven questions on employee demographics and 32 items from the scales.

Developed by Aktı and collegues in 2017, the scale consists of 32 items and 7 subfactors. These subfactors are Ethical Values, Moral Sensitivity, Responsibility Towards the Creator, Compassion, Conscious Awareness, Social Sensitivity, and Wisdom. As a result of statistical analyses, the scale was accepted as having high factor loadings (0.45-0.86) and had construct validity. Items 1, 2, 3, 4, and 5 of the scale were reverse coded. The scale was rated using a 5-point Likert-type scale. The scoring for all items was determined as follows: 1: Strongly disagree, 2: Disagree, 3: Neither agree nor disagree, 4: Agree, and 5: Strongly agree.

The study was conducted at a private hospital in Istanbul. The study population consisted of 380 employees. A convenience sampling method was used. All employees were reached using a complete enumeration method. The study was conducted by contacting 277 individuals who agreed to participate in the study. Data were collected from employees who volunteered to participate in the study via a survey between June 26 and July 16, 2025. Data were analyzed using statistical techniques in SPSS.

Research Hypotheses

H1: Conscientiousness varies according to sociodemographic characteristics.

RESULTS

Reliability

Cronbach's alpha was examined to determine the reliability of the scale used in the study.

Table 1. Sociodemographic characteristics

Variable	n	%
Sex		
Female	233	84.1
Male	46	15.9
Total	277	100
Marital Status		
Married	177	63.9
Single	100	36.1
Total	277	100
Number of Children		
0	97	35.5
1	93	34.1
2	52	19.0
3 or more	31	11.4
Total	273	100
Age		
18-25	90	33.2
26-34	112	41.3
35-45	69	25.5
Total	271	100
Education Level		
High School	111	40.1
Associate degree	32	11.6
Bachelor's degree	96	34.7
Maaster's degree	22	7.9
PhD	16	5.7
Total	277	100
Job Title		
Midwife-Nurse	119	43.0
Health Tech.	56	20.2
Admin Services	48	17.4
Doctor	18	6.4
Management	36	13.0
Total	277	100
Years of Service		
1-5 years	139	51.5
6-10 years	75	27.2
11-15 years	32	11.9
16 years or more	28	10.4
Total	270	100

The conscientiousness scale value was found to be 0.87. This result demonstrates the reliability of the scale for the study.

Results Regarding Sociodemographic Characteristics

Results regarding the sociodemographic characteristics of the participants were examined within the scope of the study. The frequencies and percentages for these variables are shown in Table 1.

Of the participants, 84.1% were female, 63.9% were married, 35.5% had no children, 41.3% were between 26 and 34 years of age, 40.1% were high school graduates, 51.5% had less than 5 years of experience, and 43% were midwives and nurses.

Descriptive Statistics

The mean conscientious intelligence score was 121.28, and the standard deviation was 12.8.

A t-test was used to determine whether employees' conscientious intelligence scores differed based on gender and marital status. The t-test results revealed no significant differences in terms of gender or marital status (Table 2).

An ANOVA test was conducted to determine whether conscientious intelligence scores differed significantly based on the number of children, and the difference was found to be significant ($F=7.701$, $p<0.001$) (Table 3). A Tukey multiple comparison test was used to determine the differences. Those with three or more children were found to have a higher mean and significantly different mean than those with others. These results suggest that the number of children is a factor affecting conscientious intelligence scores.

The ANOVA test, conducted to determine whether conscientious intelligence scores differed by age, found the difference to be significant ($F=5.772$, $p<0.01$). A Tukey multiple comparison test was used to determine the differences. The mean score for employees aged 26-34 was found to be higher than that for employees aged 18-25. Accordingly, age appears to be a factor influencing conscientious intelligence scores.

An ANOVA test was conducted to determine whether conscientious intelligence differed based on length of

Table 2. Differences in conscientious intelligence scores by gender and marital status

	n	x	s.s	t value	p value
Sex					
Female	233	120.64	12.80	-0.1705	0.089
Male	46	124.48	14.40		
Marital Status					
Married	177	121.92	12.48	0.87	0.384
Single	100	120.32	14.40		

Table 3. Differences in conscientious ıntelligence scores by other sociodemographic variables

	N	x	s.s	F	p	Significant Differences
No of Children						
0 (A)	97	120.32	12.16	7.701	0.000	A<D
						B<D
						C<D
1 (B)	93	119.04	10.88			
2 (C)	52	120.64	16.31			
3+ (D)	31	131.84	11.84			
Age Group						
18-25 (A)	90	117.44	12.48	5.772	0.005	A<B
26-34 (B)	112	123.84	12.80			
35-45 (C)	69	121.60	14.40			
Years of Service						
1-5 years (A)	139	119.68	13.44	4.456	0.005	C<B
						C<D
6-10 years (B)	75	124.48	12.80			
11-15 years (C)	32	116.48	13.44			
16 years or more (D)	28	125.76	10.56			
	N	**Mean Rank**		**Chi-square**	**p**	**Significant Differences**
Educatioan Level						
High School (A)	111	124.08		23.737	0.000	B>A
						B>D
						B>E
Associate degree (B)	32	160.55				
Bachelor's degree (C)	96	133.71				
Maaster's degree (D)	22	104.50				
PhD (E)	16	103.40				
Job Title						
Midwife-Nurse (A)	119	126.13		21.624	0.000	C>A
						C>B
						C>D
						C>E
						A>D
Health Tech. (B)	56	106.22				
Admin Services (C)	48	168.24				
Doctor (D)	18	96.50				
Management (E)	36	116.25				

service, and the difference was found to be significant (F=4.456, p<0.01). A Tukey multiple comparison test was used to determine the differences. The mean difference between employees with 11-15 years of service was found to be lower and significantly different from the mean difference between employees with 6-10 years and 16 or more years of service. These results suggest that length of service is a factor affecting conscientious intelligence scores.

An ANOVA test was conducted to determine whether conscientious intelligence differed based on length of service, and the difference was found to be significant (F=4.456, p<0.01). A Tukey multiple comparison test was used to determine the differences. The mean difference between employees with 11-15 years of service was found to be lower and significantly different from the mean difference between employees with 6-10 years and 16 or more years of service. These results suggest that length of service is a factor affecting conscientious intelligence scores.

The Kruskal Wallis test, conducted to determine whether there were differences in conscientious intelligence based on title, found the difference to be significant (chi square=21.624, p<0.001). A Mann Whitney U test, con-

ducted to determine the differences, found that the mean for administrative workers was higher than the mean for all other groups, while the mean for midwives/nurses was higher than the mean for doctors. Accordingly, title appears to be a factor influencing conscientious intelligence scores.

DISCUSSION

According to the research findings, the participants' mean conscientious intelligence scores were found to be high. This finding is significant. This result demonstrates that employees with high conscientious intelligence possess moral sensitivity, empathy, and ethical decision-making skills. High levels of conscientious intelligence indicate that people can be more sensitive and responsible in relationships. Some studies have also found high levels of conscientious intelligence.[8-15] Other studies have found moderate levels of conscientious intelligence.[16] Studies conducted with healthcare workers in Türkiye have found high levels of conscientious intelligence.

The demographic results of the study appear to share similarities and differences with the literature. According to the demographic results of the study, gender did not create a significant difference. Research results from similar studies also indicate that conscientious intelligence, in particular, does not differ by gender.[8-17] In this context, considering both the findings of the current study and the results of similar studies in the literature, it can be concluded that gender is not a determining variable in conscientious intelligence. This supports the notion that conscientious intelligence is a construct based on universal and shared values among individuals and is shaped not by biological but rather by social and cognitive developmental processes.

In this context, according to the demographic results of the study, there is no significant difference between conscientious intelligence scores in terms of marital status. Studies showing similarly no differences are available in the literature.[12] Furthermore, there are studies in the literature that yield results different from our study. These studies suggest that single healthcare workers have higher conscientious intelligence levels than married individuals.[8,15,16] Furthermore, a study with results different from our study indicates that married individuals have higher mean conscientious intelligence levels than single individuals.[10] Based on the results of these studies, it cannot be concluded whether marital status has an impact on conscientious intelligence. These conflicting findings make it difficult to reach a definitive conclusion about the impact of marital status on conscientious intelligence. The impact of this variable should be evaluated in conjunction with other factors, such as the study's sample characteristics, participants' age groups, life experiences, or cultural context.

In this context, according to the demographic results of the study, there is a significant difference between conscientious intelligence scores based on the number of children variable. Healthcare workers with a higher number of children have higher conscientious intelligence scores. This suggests that healthcare workers behave more conscientiously after having children. This finding suggests that having children can strengthen components of conscientious intelligence such as empathy, responsibility, and moral sensitivity. Having a child creates a significant transformation in an individual's life; it can trigger processes such as prioritizing the needs of others, making sacrifices, and gaining emotional depth. In this context, healthcare workers are likely to exhibit more conscientious and sensitive attitudes after having children.

In this context, according to the demographic results of the study, there is a significant difference between conscientious intelligence scores in terms of the age variable. Considering the age criterion, it is concluded that age is a significant factor affecting conscientious intelligence scores. The average age of employees between 26 and 34 was found to be higher than that of employees between 18 and 25. In other words, it can be said that conscientious intelligence levels increase with age. Similar studies exist in the literature to this effect. Similar studies indicate increases in conscientious intelligence scores with age.[10,16,17] There are also studies that yield different results from our study. These studies found no difference by age. Researchers attribute this reason to the relatively similar age groups of the participants in the study.[9]

Another study found no difference between age groups.[8] The social, professional, and moral experiences individuals encounter with age may enable them to view events from a broader perspective and make more conscientious decisions. However, the existence of studies in the literature that fail to find significant differences by age demonstrates that this relationship is not always linear or universal. In such studies, methodological factors such as the close age groups or limited sample size may have prevented the age-conscientious intelligence relationship from becoming clear. Furthermore, individual differences, personality structure, and lifestyle are also important factors influencing this relationship.

In this context, according to the demographic results of the study, there is a significant difference between conscientious intelligence scores in terms of the length of service variable. This difference varies according to length of service. There are also studies that obtain similar results to our study.[15] There are also studies that obtain different results from our study. These studies do not show any difference according to length of service.[16] This suggests that the effect of length of service on conscientious intelligence may vary depending on the context, sample characteristics, and study methods. To more clearly understand the relationship between length of service and conscientious intelligence, comprehensive studies that take into account different demographic and occupational factors are necessary.

In this context, according to the demographic results of the study, there is a significant difference between consci-

entious intelligence scores in terms of educational background. The results indicate that those with an associate's degree had higher conscientious intelligence scores than other participants. This could be due to their thinking being more emotional and conscientious, rather than the professional and objective perspective that should result from their education. There are also studies that yield different results from ours. These studies found no differences based on educational background.[8,10,15,16] These differences may be due to various factors, such as sample structure, working conditions, or measurement tools. The impact of educational background on conscientious intelligence is complex and multifaceted; therefore, not only educational background but also an individual's personal and professional experiences should be considered.

In this context, according to the demographic results of the study, there is a significant difference between conscientious intelligence scores in terms of title. This difference depends on title. There are also studies that obtain similar results to our study.[10] There are also studies that obtain different results from our study. These studies do not show any difference based on length of service.[8] These differences may be due to differences in sample characteristics, fields of study, and measurement methods. Furthermore, the impact of title on conscientious intelligence should be evaluated in conjunction with factors such as individuals' professional experience, levels of responsibility, and work environment, and should be supported by more comprehensive analyses.

Limitations

The study's conduct in a private hospital in Istanbul can be considered a limitation in terms of scope. Therefore, it should not be generalized to healthcare professionals. The limitations of this study, due to its conduct in a single private hospital, impact the generalizability of the findings and limit the applicability of the results to other healthcare institutions or professional groups. The hospital's unique working style, cultural structure, and employee profile may hinder the broader validity of the findings. Therefore, applying these results to other healthcare institutions requires caution. However, focusing on a specific hospital provides a comparative reference for other institutions with similar characteristics and may guide future research.

Therefore, while the findings are valid for this specific sample, caution is advised when generalizing to broader populations. Within the scope of the study, it was assumed that the employees who responded to the surveys exhibited realistic and impartial attitudes. However, the fact that the employees responded under the influence of social recognition can be considered another limitation of the study due to the survey method used. Furthermore, the fact that the surveys and Likert-type scales did not fully reflect the variables is also considered a limitation.

Conclusion

According to the research results, levels of conscientious intelligence were found to be high among healthcare professionals. High levels of conscientious intelligence in healthcare settings can lead to improvements in the quality of healthcare services and patient care. This result demonstrates that employees with high conscientious intelligence possess moral sensitivity, empathy, and ethical decision-making skills. High levels of conscientious intelligence suggest that people can be more sensitive and responsible in relationships. This, in turn, will increase employee and patient satisfaction.

It was concluded that the mean conscience intelligence scores of healthcare workers did not differ based on socio-demographic characteristics, gender, and marital status. This supports the notion that conscientious intelligence is a universal construct based on shared values among individuals and is shaped by social and cognitive developmental processes rather than by biological or marital relationships.

It was concluded that the mean conscience intelligence scores of healthcare workers vary according to socio-demographic characteristics, such as the number of children, age, educational background, length of service, and title. After having children, healthcare workers exhibit more conscientious and sensitive attitudes. The social, professional, and moral experiences individuals encounter with age allow them to view events from a broader perspective and make more conscientious decisions. The difference was due to the relationship between length of service and age. The impact of education level on conscientious intelligence is complex and multifaceted. Therefore, it is not only education level but also an individual's personal and professional experiences that are influential. Furthermore, the impact of title on conscientious intelligence stems from its interaction with factors such as individuals' professional experience, level of responsibility, and work environment.

Because conscientious intelligence is a trait shaped by personal development and experience, a corporate culture should be established in healthcare institutions and organizations where the importance of ethical values and conscientious responsibility is emphasized, supported, and rewarded.

Given that variables such as age and length of service influence conscientious intelligence, training programs can be designed to enhance conscientious intelligence, particularly for young and inexperienced employees. These programs can aim to increase empathy, ethical decision-making, and a sense of responsibility.

Providing psychosocial support and professional development opportunities tailored to the needs of employees in different professional positions can be beneficial. This can strengthen employees' conscientious intelligence and encourage ethical behavior in the workplace.

Due to the varying and contradictory results found for some demographic variables in the study, it is recommended that the relationships between conscientious in-

telligence and demographic factors be examined through more comprehensive, multicenter studies.

Ethics Committee Approval

The study was approved by the Yalova University Hospital Ethics Committee (Date: 25.06.2025, Decision No: 2025/248).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Conflict of Interest

None declared.

REFERENCES

1. İmamoğlu A. Psychosocial analysis of the concept of conscience. J Acad Rev 2010;5:131.
2. Koç Z. Moral and theological foundations of conscience [Master's Thesis]. Ankara University; 2015.
3. Turkish Language Association. Dictionaries. Available at: http://sozluk.gov.tr/. Accessed Sep 5, 2025.
4. Mayer JD, Salovey P, Caruso DR. Emotional intelligence: Theory, findings, implications. Psychol Inq 2004;15:197–215. [CrossRef]
5. Yaylamaz S. Reading intelligence (RIQ). Hayat Publications.
6. Gardner H. Frames of mind: Theory of multiple intelligences (Kılıç E, trans). Alfa Publications.
7. Aktı Ü, Giderler C, Duran C, Behdioğlu S, Boz D. Validity and reliability study of the conscientious intelligence scale. J Islam Civ Stud 2017;2:329–49.
8. Arslanoğlu A, Tabur A. The effect of conscientious intelligence on the ability to manage patient expectations: Example from a university hospital. Med Sci 2019;8:1017–24. [CrossRef]
9. Şengül H, Bulut A. Analysis of conscientious intelligence levels of students studying at the faculty of health sciences of a foundation university. Turk Stud Soc 2020;15:3131–48.
10. Arslanoğlu A, Tütüncü D, Günay A, Bektemür G. The effect of the Covid-19 pandemic on the perception of conscientious intelligence in healthcare workers. Gumushane Univ J Health Sci 2021;10:667–77. [CrossRef]
11. Dur Ş, Göl İ, Erkin Ö. The effects of nursing students' conscientious intelligence on their cultural sensitivity levels. Perspect Psychiatr Care 2022;58:795–803. [CrossRef]
12. Bayer N, Şahin İ, Uzuntarla Y. The relationship between conscientious intelligence and organizational identification in nurses, Turkey. Era J Med Res 2021;8:108–15.
13. Polat H, Asi Karakaş S, Aslanoğlu E. Conscientious intelligence and job motivation in nurses working in psychiatric hospital: A descriptive study. Turk Klin J Nurs Sci 2022;14:868–75. [CrossRef]
14. Arslanoğlu A, Çengel Ö, Gemlik N, Yılmaz K, Maden Ö. The relationship between conscientious intelligence and human values: application in the field of health. Psychol Health Med 2025;30:1021–42. [CrossRef]
15. Tiryaki ŞH, Taşkıran EG, Çiftçioğlu G. A cross-sectional study of the relationship between missed nursing care and conscientious intelligence in hospital nurses. Int Nurs Rev 2025;72:e13024. [CrossRef]
16. Özden G, Parlar Kılıç S. Compassion in action: Exploring the relationship between nurse conscientious intelligence and palliative care. Nurs Crit Care 2024;29:695–705. [CrossRef]
17. Coban B, Karademir T, Acak M, Devecioğlu S. The emotional intelligence of students who are sitting a special-ability examination. Soc Behav Pers 2010;38:1123–34. [CrossRef]

Vicdani Zekanın Sosyodemografik Özelliklere Göre İncelenmesi: Sağlık Çalışanlarında Bir Uygulama

Amaç: Vicdani zekâ, mantıksal ve duygusal zekâdan farklı olarak karar aşamasında vicdana danışarak iyiyi ve kötüyü bulmak ve bilinçli olarak iyiyi, doğruyu seçmek şeklinde tanımlanabilir. Bu çalışmada, sağlık çalışanlarının vicdani özelliklerinin sosyodemografik özelliklere göre farklılıklarını belirlemek amaçlanmıştır.

Gereç ve Yöntem: Bu çalışma tanımlayıcı ve kesitsel tipte planlanmıştır. Veriler, Kişisel Bilgi Formu ve Vicdani Zekâ Ölçeği kullanılarak elde edilmiştir. Kişisel Bilgi Formu çalışanların demografik özellikleri yedi soru ve ölçekler kapsamındaki 32 maddeden oluşmaktadır. 2017 yılında Aktı ve arkadaşları tarafından geliştirilen Ölçek 32 maddeden ve 7 alt faktörden oluşmaktadır. Çalışmanın evrenini toplam 380 çalışan oluşturmaktadır. Örnekleme gidilirken tam sayım metoduyla tüm çalışanlara ulaşılmaya çalışılmıştır. Araştırmaya katılmayı kabul eden 277 kişiye ulaşılarak anket yapılmıştır. Veriler SPSS programında istatistiksel teknikler kullanılarak analiz edilmiştir.

Bulgular: Vicdani zekâ ölçeği Cronbach alpha değeri 0,87 olarak bulunmuştur. Bu sonuç, araştırma için ölçeğinin güvenilir olduğu göstermektedir. Katılımcıların %84.1'inin kadın olduğu, %63.9'unun evli olduğu, %35.5'inin çocuğu olmadığı, %41.3'ünün 26-34 arası yaşta olduğu, %40.1'inin lise mezunu olduğu, %51.5'inin 5 yıl altında hizmet süresine sahip olduğu, %43'ünün Ebe-hemşire meslek grubuna sahip olduğu görülmektedir. Vicdani zekâ ortalaması 121.28 ve standart sapması 12.8 olarak bulunmuştur.

Sonuç: Araştırma bulgularına göre katılımcıların vicdani zekâ puanı ortalamaları yüksek seviyede bulunmuştur. Sağlık çalışanlarının vicdan zekâ ortalama puanlarının sosyodemografik özelliklerinden cinsiyet ve medeni durum değişkenlerine göre farklılık göstermediği sonucuna ulaşılmıştır. Sağlık çalışanlarının vicdani zekâ ortalama puanlarının sosyodemografik özelliklerinden çocuk sayısı, yaş, öğrenim durumu, hizmet süresi ve unvan değişkenlerine göre farklılık gösterdiği sonucuna ulaşılmıştır.

Anahtar Sözcükler: Vicdan; vicdani zekâ; zekâ.

SCIE DOI: 10.14744/scie.2025.76500
South. Clin. Ist. Euras. 2025;36(3):240-246

Original Article

Relationship Between Electronic Health Literacy and Quality of Life in Women with PCOS: A Web-Based Cross-Sectional Study

Sahra Sultan Kara,[1] Esra Keleş,[2] İsmail Bağlar[1]

[1]Department of Obstetrics and Gynecology, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye
[2]Department of Gynecologic Oncology, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye

Submitted: 01.06.2025
Revised: 26.06.2025
Accepted: 03.07.2025

Correspondence: Sahra Sultan Kara, Department of Obstetrics and Gynecology, University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital, Istanbul, Türkiye
E-mail: sahracavusoglu@gmail.com

Keywords: eHealth literacy; polycystic ovary syndrome; quality of life; women's health.

ABSTRACT

Objective: To investigate the association between electronic health literacy (eHealth literacy) and health-related quality of life in women with polycystic ovary syndrome (PCOS).

Methods: A cross-sectional web-based survey was conducted among women with PCOS. Participants completed validated Turkish versions of the eHealth Literacy Scale (eHEALS) and the PCOS Quality of Life Questionnaire-50 (PCOSQ-50). Spearman's correlation and multiple linear regression analyses were employed to assess associations between eHealth literacy and HRQoL, adjusting for covariates including age, BMI, education level, and marital status.

Results: A total of 399 women participated in the study. The mean age was 28.5±6.5 years, and the mean body mass index (BMI) was 27.1±9.1 kg/m². A moderate positive correlation was observed between eHEALS scores and overall PCOSQ-50 scores (ρ=0.315, p<0.001). The strongest correlations were found with the emotional subdomain (ρ=0.326, p<0.001), followed by coping (ρ=0.239, p<0.001) and hirsutism (ρ=0.240, p<0.001). Regression analysis identified eHEALS as a significant positive predictor of quality of life (β=0.282, p<0.001). Higher BMI was negatively associated (β=-0.353, p<0.001).

Conclusion: Enhanced eHealth literacy is associated with improved quality of life in women with PCOS, particularly in emotional and coping domains. Targeted interventions to improve digital health literacy may optimize symptom management and psychosocial outcomes in this population.

INTRODUCTION

Polycystic ovary syndrome (PCOS), a common endocrine disorder affecting 5–15% of reproductive-aged women, is characterized by hyperandrogenism, oligo-anovulation, and polycystic ovarian morphology.[1-3] Beyond its metabolic and reproductive sequelae, PCOS imposes a significant psychosocial burden, with patients reporting elevated rates of anxiety, depression, and body image dissatisfaction.[4-6] Symptoms such as hirsutism, obesity, and infertility exacerbate emotional distress, underscoring the need for holistic management strategies that address both physical and mental health.[7,8]

The digital transformation of healthcare has positioned electronic health (eHealth) literacy, defined as "the ability to seek, comprehend, and apply electronic health information", as a critical determinant of self-management in chronic conditions.[9,10] Prior studies suggest that higher eHealth literacy correlates with improved glycemic control in diabetes, enhanced self-efficacy in hypertension, and reduced psychological distress in chronic pain populations.[11-13] However, its role in mitigating the multidimensional burden of PCOS remains underexplored.

This study aimed to evaluate the relationship between eHealth literacy and HRQoL in women with PCOS. We hypothesized that greater eHealth literacy would correlate with improved symptom management and quality of life, mediated through enhanced access to reliable health information and self-care behaviors.

MATERIALS AND METHODS

Study Design and Ethical Approval

A cross-sectional web-based survey was conducted from December 2024 to February 2025 under ethical approval from a tertiary healthcare institution (No: 2024/010.99/9/20, Date: 25/10/2024). The protocol adhered to the Declaration of Helsinki. Participants provided electronic informed consent prior to enrollment.

Participants and Recruitment

Women aged 18–55 years with PCOS were recruited in the study through two different enrollment methods. The first group comprised patients attending the outpatient gynecology clinic during routine clinical consultations. The second group was recruited via digital platforms, including social media networks (Instagram, Facebook) and PCOS-specific support groups, where a structured Google Forms questionnaire was disseminated. All participants completed the same version of the questionnaire. The study included a group of 399 participants with PCOS. The enrollment of study participants was presented in Figure 1.

Diagram illustrating participant recruitment methods. Outpatient clinic attendees accessed the Google Forms survey via QR code, while social media users (Facebook, Instagram, WhatsApp) participated through a direct survey link.

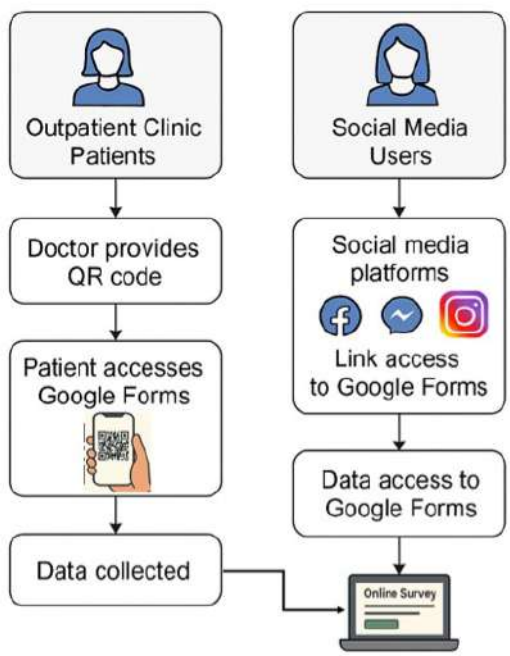


Diagram illustrating participant recruitment methods. Outpatient clinic attendees accessed the Google Forms survey via QR code, while social media users (Facebook, Instagram, WhatsApp) participated through a direct survey link.

Figure 1. Recruitment flow of study participants.

The questionnaire comprised three sections. The first section included questions related to sociodemographic information (age, body mass index (BMI), marital status, education, smoking, comorbidities, fertility history). The second section assessed eHealth literacy using the Turkish-validated eHealth Literacy Scale (eHEALS). The scale developed by Norman and Skinner, this 8-item Likert-scale instrument evaluates participants' ability to seek, interpret, and apply digital health information.[14] Responses range from 1 ("strongly disagree") to 5 ("strongly agree"), with total scores spanning 8–40. Higher scores denote superior eHealth literacy. The Turkish adaptation by Coşkun and Bebiş demonstrated strong internal consistency (Cronbach's α=0.88).[15]

The third section evaluated disease-specific quality of life using the Polycystic Ovary Syndrome Quality of Life-50 Scale (PCOSQ-50), a 50-item instrument developed by Nasiri-Amiri et al.[16] and validated in Turkish by Koyutürk et al.[17] The PCOSQ-50 assesses six domains: psychosocial/emotional well-being, fertility concerns, sexual function, obesity/menstrual irregularities, hirsutism, and coping mechanisms. Responses are scored on a 5-point Likert scale, with higher aggregate scores reflecting improved quality of life. The Turkish validation reported exceptional reliability (Cronbach's α=0.972), which remained robust in the current study (α=0.926).

Statistical Analysis

Analyses were performed in IBM SPSS v27. Descriptive statistics (mean ± SD, frequencies) characterized sociodemographics. Nonparametric methods were applied after Shapiro-Wilk and Kolmogorov-Smirnov tests indicated non-normal distributions. Bivariate correlations between eHEALS and PCOSQ-50 scores were assessed via Spearman's ρ. A multiple linear regression model, adjusted for age, BMI, education, and marital status, identified independent QoL predictors. Scale reliability was confirmed via Cronbach's α. Significance was set at $p<0.05$

Table 1. Baseline characteristics (n=399)

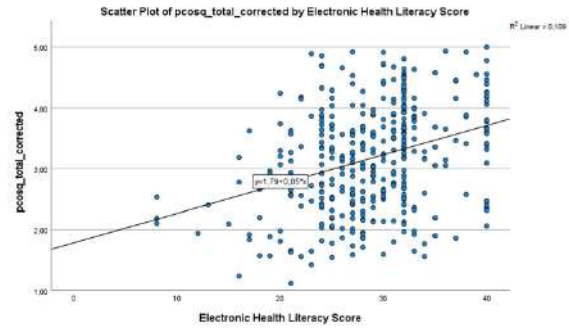
Variables	n (%)/Mean±SD
Age (years)	28.5±6.5
BMI (kg/m²)	27.1±9.1
Education Level	
Primary school	9 (2.3)
Middle school	54 (13.5)
High school	264 (66.2)
University or higher	72 (18.0)
Marital Status	
Single	173 (43.4)
Married	226 (56.6)

Values are presented as mean ± standard deviation or frequency (%), as appropriate.

Table 2. Correlation between eHEALS scores and PCOSQ-50 subdomains

PCOSQ-50 Subdomain	Spearman's ρ	p-value
Emotional	0.326	<0.001
Coping	0.239	<0.001
Hirsutism	0.240	<0.001
Obesity & Menstrual Problems	0.224	<0.001
Fertility	0.178	<0.001
Sexual Function	0.153	0.013

ρ: Spearman's correlation coefficient; PCOSQ-50: Polycystic Ovary Syndrome Quality of Life Questionnaire; eHEALS: eHealth Literacy Scale. *p<0.005.



Scatter plot showing the relationship between electronic health literacy (eHEALS) and overall quality of life (PCOSQ-50 total scores). Each circle represents one participant. The solid line indicates the fitted linear regression line.

Figure 2. Scatter Plot of eHEALS and PCOSQ-50 Total Scores

RESULTS

Baseline Demographic and Clinical Characteristics

The study group comprised 399 women with PCOS, with a mean age of 28.5±6.5 years, and a mean BMI of 27.1±9.1 kg/m². In terms of educational attainment, 66.2% had completed high school, 18.0% held university or postgraduate degrees, 13.5% had middle school education, and 2.3% reported primary school education. Regarding marital status, 56.6% of participants were married, and 43.4% were single (Table 1).

Association Between eHEALS and PCOSQ-50

A Spearman's rank-order correlation revealed a positive association between eHealth literacy and PCOS-related quality of life (ρ=0.315, p<0.001).

Spearman's rank correlation analysis also indicated statistically significant positive associations between eHEALS scores and all subdomains of the PCOSQ-50 (p<0.05). The strongest correlation was observed with the Emotional subdomain (ρ=0.326, p<0.001), followed by coping (ρ=0.239), hirsutism (ρ=0.240), obesity/menstrual problems (ρ=0.224), fertility (ρ=0.178), and sexual function (ρ=0.153) (all p<0.001 except Sexual Function, p= 0.013) (Table 2).

A scatter plot analysis was conducted to further illustrate the linear relationship between eHEALS and PCOSQ-50. As depicted in Figure 2, a positive association between eHEALS scores and PCOSQ-50 total scores were observed, indicating a 0.05-unit increase in quality of life per one-point rise in eHealth literacy.

Predictors of Quality of Life

Multiple linear regression analysis, adjusted for age, BMI, education level, and marital status, revealed significant predictors of PCOSQ-50 scores (overall model p<0.001, adjusted R^2=0.243). eHEALS scores were positively associated with PCOSQ-50 scores (B=0.041, SE=0.007, β=0.282, p<0.001), indicating that with each unit increase in eHEALS score associated with a 0.041-point improvement in PCOSQ-50 scores. BMI was inversely associated with PCOSQ-50 scores (B=–0.052, SE=0.007, β=–0.353, p<0.001), indicating a 0.052-point decline in PCOSQ-50 scores per unit increase in BMI. Age was also positively associated with quality of life (β=0.136, p= 0.010), while education level was inversely associated with PCOSQ-50 scores (β=-0.104, p= 0.028). Marital status did not reach statistical significance (β=0.086, p= 0.095) (Table 3).

Table 3. Multiple Linear Regression for PCOSQ-50 Total Score

Predictor Variable	B	SE	β (Beta)	t	p-value
Constant	3.055	0.341	–	8.953	<0.001
Age	0.018	0.007	0.136	2.581	0.010
BMI	–0.052	0.007	–0.353	–7.822	<0.001
Marital status	0.148	0.089	0.086	1.671	0.095
Education level	–0.139	0.063	–0.104	–2.203	0.028
Electronic Health Literacy Score	0.041	0.007	0.282	6.100	<0.001

B: Unstandardized regression coefficient; SE: Standard error; β: Standardized regression coefficient.

Table 4. PCOSQ-50 Scores by subgroup Education Level

Education Level	N	Mean Rank	Sum of Ranks	p-value (2-tailed)
High School	261	157.90	41,211.50	
University or higher	71	198.12	14,066.50	
Total	332	—	—	0.002

PCOSQ-50: Polycystic Ovary Syndrome Quality of Life Questionnaire.

Subgroup Analysis by Educational Attainment

To clarify the inverse association between education and quality of life in the regression model, a Mann-Whitney U test compared PCOSQ-50 scores between participants with university-level education or higher (n=71) and those with high school education (n=261). Results revealed significantly higher quality of life scores among university-educated participants (mean rank=198.12 vs. 157.90, U=7020.5, p=0.002), indicating higher quality of life among participants with greater educational attainment (Table 4).

This apparent contradiction, where subgroup comparison shows better QoL with higher education while regression analysis suggests a negative association, may reflect the differing statistical nature of these analyses. The Mann-Whitney U test directly compares groups without accounting for other influencing variables, whereas multiple linear regression adjusts for covariates such as age, BMI, and marital status. The observed reversal in the direction of association may result from complex interrelationships or collinearity among covariates included in the model, particularly if certain demographic or clinical characteristics are unevenly distributed across education levels. These findings highlight the importance of cautious interpretation when evaluating multivariable models in observational studies.

DISCUSSION

This study investigated the relationship between eHealth literacy and quality of life in women diagnosed with PCOS. The findings indicate that women with higher levels of eHealth literacy reported a better quality of life across various aspects affected by PCOS. Notably, the strongest correlation was observed with the Emotional subdomain of the PCOSQ-50, suggesting that the ability to effectively seek, comprehend, and apply electronic health information is particularly linked to improved emotional well-being in women managing this condition. Furthermore, the multiple linear regression analysis identified eHealth literacy as a significant positive predictor of overall quality of life, suggesting a woman's capacity to engage with online health resources plays a crucial role in her perceived quality of life when living with PCOS. In contrast, BMI emerged as a significant negative predictor of quality of life. A subsequent subgroup analysis comparing women with university-level education or higher to those with high school education revealed significantly higher quality of life scores in the more educated group.

The positive correlation between eHealth literacy and all quality of life domains implies a broad beneficial impact of this skill set on the multifaceted challenges faced by women with PCOS. This widespread effect suggests that eHealth literacy empowers women to navigate and utilize online health resources in ways that positively influence various dimensions of their condition, ranging from physical symptoms to emotional well-being and coping strategies. The strong correlation observed specifically within the emotional subdomain underscores the substantial psychosocial burden associated with PCOS.[18] It is plausible that women with higher eHealth literacy are better equipped to find and utilize online resources for emotional support, stress management techniques, and information related to mental health comorbidities often associated with PCOS, such as anxiety and depression.[19]

In the management of chronic conditions, such as PCOS, where women often experience a reduced quality of life, the positive role of eHealth literacy has also been highlighted in studies focusing on other long-term health issues. For instance, Xu et al.[20] reported that pregnant women with higher eHealth literacy exhibited better glycemic control in gestational diabetes mellitus. In a similar vein, Wang et al.[21] found that eHealth literacy had a positive impact on self-management efficacy and quality of life among individuals with hypertension. In patients experiencing chronic pain, Castarlenas et al.[22] observed that greater eHealth literacy was linked to lower levels of anxiety and depression and better psychological adjustment. In accordance with these findings, our study posits that women diagnosed with PCOS who exhibit higher levels of eHealth literacy are better equipped to manage their symptoms, thereby enhancing their quality of life.

The significant negative association observed between BMI and quality of life in our study aligns with a well-established body of research.[23] Obesity is a prevalent comorbidity in women with PCOS and is known to exacerbate various PCOS symptoms, including hyperandrogenism and insulin resistance, which can negatively impact overall well-being and quality of life.[24] The positive association between eHealth literacy and quality of life aligns with a growing body of evidence highlighting the benefits of eHealth literacy in the management of chronic conditions. Access to reliable online health information can empower individuals to better understand their condition, adhere to treatment plans, and adopt healthier lifestyle behaviors, ultimately leading to improved health outcomes and a higher quality of life.

Numerous systematic reviews and meta-analyses have consistently demonstrated that PCOS has a detrimental effect on quality of life, particularly in domains such as hirsutism and menstruation.[25] Our study builds upon this knowledge by suggesting that eHealth literacy may serve as a protective factor, potentially mitigating the negative impact of PCOS on quality of life. This is particularly relevant given the increasing recognition of digital health interventions for managing PCOS. Effective utilization of these digital tools often necessitates a certain level of eHealth literacy, implying that individuals with higher eHealth literacy may be better positioned to benefit from these interventions. The study therefore highlights a crucial intersection between the established challenges of PCOS and the potential of digital health engagement.

The enhancement in quality of life associated with higher eHealth literacy likely stems from the improved ability of women with PCOS to access a broader spectrum of reliable information concerning their condition.[26] This includes valuable insights into effective symptom management strategies, guidance on crucial lifestyle modifications such as diet and exercise, and awareness of available support networks and resources.[27] This readily available access to pertinent information can foster a greater sense of self-efficacy among women with PCOS , empowering them to actively participate in managing their symptoms and making well-informed decisions regarding their health, which in turn positively influences their overall quality of life. Furthermore, individuals with higher eHealth literacy may experience improved communication with their healthcare providers,[28] leading to more collaborative and effective management plans tailored to their specific needs and concerns. The findings of this study lend further support to the growing recognition of eHealth literacy as a significant determinant of health behavior and outcomes in the contemporary digital landscape.[29]

The subgroup analysis, which specifically compared university-educated participants with those holding a high school diploma, revealed significantly higher quality of life scores among the more educated group. This finding strongly suggests that higher educational attainment, particularly at the university level, is ultimately associated with better quality of life in women with PCOS. The benefits of higher education on quality of life may be partly explained by its ability to help people use online health resources effectively, as well as potentially higher socioeconomic status and improved access to healthcare services.[30]

Strengths and Limitations

This study possesses several notable strengths. The utilization of validated and disease-specific instruments, namely the eHEALS and PCOSQ-50, to assess eHealth literacy and quality of life in women with PCOS, enhances the rigor and relevance of our findings. The substantial sample size of 399 participants provides reasonable statistical power to detect meaningful associations. Furthermore, the inclusion of participants recruited through both clinic-based and digital platforms contributes to a more representative sample of women living with PCOS. The adjustment for relevant covariates in the multiple linear regression analysis strengthens the confidence in the independent effects of eHealth literacy and BMI on HRQoL.

However, certain limitations should be acknowledged. The cross-sectional study design inherently limits our ability to establish causal relationships between eHealth literacy and HRQoL. The reliance on self-reported data for all study variables may introduce the potential for recall bias or social desirability bias, which could influence the accuracy of the reported information. The study was conducted within a specific geographic location, and therefore, the generalizability of our findings to other populations with different cultural contexts, healthcare systems, and levels of digital literacy may be limited. Clinicians and policymakers should prioritize the development of accessible, evidence-based digital resources tailored to this population. Future interventions integrating eHealth literacy training with multidisciplinary care may optimize both physical and psychosocial outcomes in PCOS management.

Conclusion

Enhanced eHealth literacy is associated with improved quality of life in women with PCOS, particularly in emotional and coping domains. Our findings also support the negative impact of BMI on quality of life in this population. In addition, the subgroup analysis showed that higher education, especially at the university level, is linked to better quality of life. These findings highlight the growing importance of eHealth literacy for women with PCOS in managing their condition and enhancing well-being in a digital healthcare environment. Our study shows the need to consider eHealth literacy in the management of women with PCOS.

Ethics Committee Approval

The study was approved by the University of Health Sciences, Kartal Dr. Lütfi Kırdar City Hospital Hospital Ethics Committee (Date: 25.10.2024, Decision No: 2024/010.99/9/20).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: S.S.K., E.K., İ.B.; Design: S.S.K., E.K., İ.B.; Supervision: S.S.K., E.K., İ.B.; Fundings: S.S.K., E.K., İ.B.; Materials: S.S.K., E.K., İ.B.; Data collection &/or processing: S.S.K., E.K., İ.B.; Analysis and/or interpretation: S.S.K.; Literature search: S.S.K., E.K., İ.B.; Writing: S.S.K., E.K., İ.B.; Critical review: S.S.K., E.K., İ.B.

Conflict of Interest

None declared.

REFERENCES

1. Azziz R. Polycystic ovary syndrome. Obstet Gynecol 2018;132:321–36. [CrossRef]
2. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril 2016;106:6–15. [CrossRef]
3. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19–25. [CrossRef]
4. Teede HJ, Tay CT, Laven J, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 International Evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fertil Steril 2023;120:767–93.
5. Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: Pathophysiology, presentation, and treatment with emphasis on adolescent girls. J Endocr Soc 2019;3:1545–73. [CrossRef]
6. Brutocao C, Zaiem F, Alsawas M, Morrow AS, Murad MH, Javed A. Psychiatric disorders in women with polycystic ovary syndrome: A systematic review and meta-analysis. Endocrine 2018;62:318–25. [CrossRef]
7. Cooney LG, Lee I, Sammel MD, Dokras A. High prevalence of moderate and severe depressive and anxiety symptoms in polycystic ovary syndrome: A systematic review and meta-analysis. Hum Reprod 2017;32:1075–91. [CrossRef]
8. Bazarganipour F, Ziaei S, Montazeri A, Foroozanfard F, Kazemnejad A, Faghihzadeh S. Health-related quality of life in patients with polycystic ovary syndrome (PCOS): A model-based study of predictive factors. J Sex Med 2014;11:1023–32. [CrossRef]
9. Yin X, Ji Y, Chan CLW, Chan CHY. The mental health of women with polycystic ovary syndrome: A systematic review and meta-analysis. Arch Womens Ment Health 2021;24:11–27. [CrossRef]
10. Azziz R, Ehrmann D, Legro RS, Whitcomb RW, Hanley R, Fereshetian AG, et al. Troglitazone improves ovulation and hirsutism in the polycystic ovary syndrome: A multicenter, double blind, placebo-controlled trial. J Clin Endocrinol Metab 2001;86:1626–32. [CrossRef]
11. Norman CD, Skinner HA. eHEALS: The eHealth literacy scale. J Med Internet Res 2006;8:e27. [CrossRef]
12. Stellefson M, Hanik B, Chaney B, Chaney D, Tennant B, Chavarria EA. eHealth literacy among college students: A systematic review with implications for eHealth education. J Med Internet Res 2011;13:e102. [CrossRef]
13. Mitsutake S, Shibata A, Ishii K, Oka K. Associations of eHealth literacy with health behavior among adult internet users. J Med Internet Res 2016;18:e192. [CrossRef]
14. Norman CD, Skinner HA. eHealth literacy: Essential skills for consumer health in a networked world. J Med Internet Res 2006;8:e9. [CrossRef]
15. Coşkun S, Bebiş H. Adolesanlarda e-sağlık okuryazarlığı ölçeği: Türkçe geçerlik ve güvenirlik çalışması. Gulhane Med J 2015;57:378–84. [Article in Turkish]
16. Nasiri-Amiri F, Ramezani Tehrani F, Simbar M, Montazeri A, Mohammadpour RA. Health-related quality of life questionnaire for polycystic ovary syndrome (PCOSQ-50): Development and psychometric properties. Qual Life Res 2016;25:1791–801. [CrossRef]
17. Koyutürk G, Külünkoğlu BA. Polikistik Over Sendromu Yaşam Kalitesi-50 Ölçeği'nin Türkçe uyarlamasının geçerlik ve güvenirliği. Saglik Yasam Bilim Derg 2023;5:63–70. [Article in Turkish] [CrossRef]
18. Bazarganipour F, Taghavi SA, Montazeri A, Ahmadi F, Chaman R, Khosravi A. The impact of polycystic ovary syndrome on the health-related quality of life: A systematic review and meta-analysis. Iran J Reprod Med 2015;13:61–70.
19. Begum RF, Vellapandian C, Mohan S. Examining symptom and quality of life in polycystic ovarian syndrome: A web-based cross-sectional study. Future Sci OA 2024;10:2430878. [CrossRef]
20. Xu J, Chen Y, Zhao J, Wang J, Chen J, Pan X, et al. Current status of electronic health literacy among pregnant women with gestational diabetes mellitus and their perceptions of online health information: A mixed-methods study. BMC Pregnancy Childbirth 2024;24:392. [CrossRef]
21. Wang C, Lang J, Xuan L, Li X, Zhang L. The effect of health literacy and self-management efficacy on the health-related quality of life of hypertensive patients in a western rural area of China: A cross-sectional study. Int J Equity Health 2017;16:58. [CrossRef]
22. Castarlenas E, Sánchez-Rodríguez E, Roy R, Tomé-Pires C, Solé E, Jensen MP, et al. Electronic health literacy in individuals with chronic pain and its association with psychological function. Int J Environ Res Public Health 2021;18:12528. [CrossRef]
23. Jones GL, Hall JM, Balen AH, Ledger WL. Health-related quality of life measurement in women with polycystic ovary syndrome: A systematic review. Hum Reprod Update 2008;14:15–25. [CrossRef]
24. Ching HL, Burke V, Stuckey BG. Quality of life and psychological morbidity in women with polycystic ovary syndrome: Body mass index, age and the provision of patient information are significant modifiers. Clin Endocrinol (Oxf) 2007;66:373–9. [CrossRef]
25. Behboodi Moghadam Z, Fereidooni B, Saffari M, Montazeri A. Measures of health-related quality of life in PCOS women: A systematic review. Int J Womens Health 2018;10:397–408. [CrossRef]
26. Garad R, Lim S, Moran L. Lifestyle in polycystic ovary syndrome. In: Kovacs GT, Fauser B, Legro RS, editors. Polycystic ovary syndrome. Cambridge: Cambridge University Press; 2022. p. 92–101. [CrossRef]
27. Avery J, Ottey S, Morman R, Cree-Green M, Gibson-Helm M. Polycystic ovary syndrome support groups and their role in awareness, advocacy and peer support: A systematic search and narrative review. Curr Opin Endocr Metab Res 2020;12:98–104. [CrossRef]
28. Guo Y, Liu Y, Ding R, Yan X, Tan H, Wang Y, et al. A structural equation model linking health literacy, self-efficacy, and quality of life in patients with polycystic ovary syndrome. BMC Womens Health 2023;23:98. [CrossRef]
29. Hua Z, Yuqing S, Qianwen L, Hong C. Factors influencing eHealth literacy worldwide: Systematic review and meta-analysis. J Med Internet Res 2025;27:e50313. [CrossRef]
30. Jansen T, Rademakers J, Waverijn G, Verheij R, Osborne R, Heijmans M. The role of health literacy in explaining the association between educational attainment and the use of out-of-hours primary care services in chronically ill people: A survey study. BMC Health Serv Res 2018;18:394. [CrossRef]

Polikistik Over Sendromlu Kadınlarda Elektronik Sağlık Okuryazarlığı ile Yaşam Kalitesi Arasındaki İlişki: Web Tabanlı Kesitsel Bir Çalışma

Amaç: Bu çalışmanın amacı, polikistik over sendromu (PKOS) tanısı alan kadınlarda elektronik sağlık okuryazarlığı ile sağlık ilişkili yaşam kalitesi arasındaki ilişkiyi değerlendirmektir.

Gereç ve Yöntem: Çalışma, PKOS'lu kadınlar arasında yürütülen kesitsel, web tabanlı bir anket araştırmasıdır. Katılımcılar, elektronik Sağlık Okuryazarlığı Ölçeği (eHEALS) ve PKOS Yaşam Kalitesi Ölçeği-50'nin (PCOSQ-50) Türkçe'ye valide edilmiş ölçeklerini doldurmuştur. Elektronik sağlık okuryazarlığı ile yaşam kalitesi arasındaki ilişkiyi değerlendirmek üzere Spearman korelasyon analizi ve yaş, beden kitle indeksi (BKİ), eğitim düzeyi ve medeni durum gibi kovaryantlar için düzeltilmiş multiple lineer regresyon analizi uygulanmıştır.

Bulgular: Çalışmaya toplam 399 kadın katılmıştır. Katılımcıların yaş ortalaması 28.5±6.5 yıl, ortalama BKİ değeri ise 27.1±9.1 kg/m²'dir. eHEALS puanları ile PCOSQ-50 toplam puanları arasında orta düzeyde pozitif bir korelasyon saptanmıştır (ρ=0.315, p<0.001). En güçlü ilişki duygusal alt boyutta gözlenmiştir (ρ=0.326, p<0.001), bunu baş etme (ρ=0.239, p<0.001) ve hirsutizm (ρ=0.240, p<0.001) alt boyutları izlemiştir. Regresyon analizinde, eHEALS skoru yaşam kalitesinin anlamlı bir pozitif yordayıcısı olarak bulunmuştur (β=0.282, p<0.001); BKİ ise yaşam kalitesiyle negatif yönde ilişkili çıkmıştır (β=-0.353, p<0.001).

Sonuç: PKOS'lu kadınlarda daha yüksek düzeyde elektronik sağlık okuryazarlığı, özellikle duygusal iyilik hali ve baş etme stratejileri olmak üzere yaşam kalitesinin pek çok yönüyle olumlu şekilde ilişkilidir. Dijital sağlık okuryazarlığını geliştirmeye yönelik hedeflenmiş müdahaleler, bu hasta grubunda semptom yönetimi ve psikososyal iyilik halini artırmada etkili olabilir.

Anahtar Sözcükler: Elektronik sağlık okuryazarlığı; kadın sağlığı; polikistik over sendromu; yaşam kalitesi.

SCIE DOI: 10.14744/scie.2025.69370
South. Clin. Ist. Euras. 2025;36(3):247-252

Original Article

A Retrospective Analysis of Factors Associated with Prolonged (≥ 30 Days) Stay at the Pediatric Intensive Care Unit: A Single Center Experience

Feyza İnceköy Girgin,[1] Betül Ayaz Seçil,[1] Ayten Saracoglu,[2] Nilüfer Yalındağ Öztürk[3]

[1]Department of Pediatric Intensive Care, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye
[2]Department of Anesthesiology, University of Florida School of Medicine UF Health, Jacksonville, USA
[3]Department of Pediatrics, Marmara University School of Medicine Division of Pediatric Critical Care, Istanbul, Türkiye

Submitted: 18.06.2025
Revised: 11.07.2025
Accepted: 25.07.2025

Correspondence: Feyza İnceköy Girgin, Department of Pediatric Intensive Care, Marmara University Pendik Training and Research Hospital, Istanbul, Türkiye

E-mail: feyzagirgin@hotmail.com

Keywords: Chronic diseases; epidemiology; health resources; length of stay; pediatric intensive care unit.

ABSTRACT

Objective: This study aims to analyze the clinical and demographic characteristics of patients with prolonged pediatric intensive care unit (PICU) stay, focusing on medical and social factors that prolong stay.

Methods: To assess factors that prolong hospitalization, we reviewed medical records of patients hospitalized for at least 30 days in the PICU between January 1, 2017, and May 1, 2025.

Results: A total of 328 patients with prolonged PICU stay were identified. The mean age was 4.3 years (range, 1 months to 17.8 years), and the mean length of PICU stay was 92 days (range 30-920 days). The most common condition at admission was respiratory failure (68.9%). The vast majority of patients (71.6%) had underlying chronic conditions, the most common being central nervous system diseases (30.2%) followed by chronic respiratory diseases (23%). Two hundred fourteen patients (65.2%) required tracheostomy, 72 (22%) gastrostomy, and 328 (100%) mechanical ventilation. Mortality occurred in 34 patients (14.8%), with 21 cardiac (13.4%) and 13 (1.4%) brain deaths. In patients requiring tracheostomy, the PICU stay was considerably prolonged due to causes other than the clinical condition of the patient.

Conclusion: Patients admitted for social reasons had longer lengths of stay, with higher rates of tracheostomy, chronic ventilation support and underlying chronic diseases. Social reason-based admissions were increased after the pandemic. Developing different solutions for this group, which significantly uses intensive care resources, will help alleviate the burden on PICU's.

INTRODUCTION

A long-stay patient in the intensive care unit refers to a patient who has survived an acute critical illness but cannot be discharged due to the need for continuous monitoring or support.[1] Long-stay patients contribute to increased utilization of intensive care resources and medical costs, thereby exacerbating capacity issues in intensive care units.[2] Although research indicates that the proportion of long-stay patients is less than 10% of all admissions, they account for one-third of intensive care bed days. With the rising global costs of critical care, access to specialized acute care resources and the availability of intensive care beds have become ongoing challenges.[3] To ensure the effective use of these important beds, it is essential to draw attention to this area and propose solutions. Advances in medicine have transformed many pediatric conditions, previously associated with poor prognoses, into chronic and

Table 1. Clinical and Demographic Characteristics of Patients (n=328)

Characteristics	Number (%)	Medical (%)	Social (%)
	328	112(34.1)	216(65.9)
Male/ Female, n (%)	182/146 (55.5/44.5)	58/54 (51.8/48.2)	118/98 (54.6/45.4)
Age, mean (range)	4.3 (1 month to 17.8 years)	4.6 (1 month to 15.2 years)	4.1 (1 month to 17.8 years)
PRISM scores	12.1	22.4	9.8
Length of Stay (days), mean (range)	92 (30-920)	62 (30-154)	163 (30-920)
Indications for PICU admission, n (%)			
Respiratory failure	226 (68.9)	39 (62.9)	146 (89.5)
Shock/ multi organ failure	46 (14.0)	11 (17.7)	4 (2.5)
Postoperative care	23 (7.0)	5 (8.1)	9 (5.5)
Trauma	33 (10.1)	7 (11.3)	4 (2.5)
Underlying Chronic Diseases, n (%)			
Present	235 (71.6)	69 (61.6)	166 (76.9)
Absent	93 (28.4)	43 (76.9)	50 (23.1)
Chronic central nervous system diseases	71 (30.2)	17 (24.6)	54 (32.5)
Chronic respiratory diseases	54 (23.0)	19 (27.5)	35 (21.1)
Muscle diseases	48 (20.4)	22 (31.9)	26(15.7)
Central nervous system tumors	24 (10.2)	6 (8.7)	18 (10.9)
Metabolic diseases	19 (8.1)	2 (2.9)	17 (10.2)
Heart diseases	12 (5.1)	2(2.9)	10(6.0)
Hematologic – oncologic diseases	7(3.0)	1(1.5)	6(3.6)
Place of referral			
Emergency service	117 (35.7)	51 (45.5)	66 (30.6)
Clinical ward	141 (43.0)	46 (41.1)	95 (44.0)
Operating room	43 (13.1)	11 (9.8)	32 (14.8)
Foreign health center	27 (8.2)	4 (3.6)	23 (10.6)
Chronic device use			
Tracheostomy	214 (65.2)	93 (43.5)	159 (74)
Gastrostomy	72 (22.0)	39 (54.2)	33 (45.8)
Mechanical ventilation	328 (100)	112 (100)	216 (100)
İnvaziv	276 (84.1)	98 (87.5)	178 (82.4)
Noninvaziv	52 (15.9)	14 (12.5)	38 (17.6)
Treatments & interventions during PICU stay			
Antibiotic therapy	302 (92.1)	103 (92)	199 (92.1)
Central venous catheters	143 (43.6)	61 (54.5)	82 (38)
Dialysis	18 (5.5)	11 (9.8)	7 (3.2)
Plasmapheresis	12 (3.7)	8 (7.1)	4 (1.9)
Treatment for liver failure	38 (11.6)	23 (20.5)	15 (6.9)
ECMO	8 (2.4)	5 (4.5)	3 (1.4)
Cardiopulmonary resuscitation	98 (29.9)	46 (41.1)	52 (24.1)
Patient outcome			
Tranfer to clinical ward	244 (74.4)	89 (79.5)	155 (71.8)
Discharged home	28 (8.5)	13 (11.6)	15 (6.9)
Tranfer to palliative intensive care unit	22 (6.7)	8 (7.1)	14 (6.5)
Cardiac death	21 (6.4)	9 (8.0)	12 (5.6)
Brain death	13 (4)	4 (3.6)	9 (4.2)
Covid-19 Pandemic			
Yes	142 (43.3)	59 (52.7)	83 (38.4)
No	186 (56.7)	53 (47.3)	133 (61.6)

PICU – Pediatric intensive care unit, ECMO - Extracorporeal membrane oxygenation, PRISM – Pediatric Risk of Mortality.

often complex situations. This not only extends hospitalization periods but also contributes to longer stays for social reasons. This study conducts a retrospective analysis of long-stay patients, highlighting those whose hospitalization is extended for non-medical reasons. Given the inevitable presence of long-stay patients, this research aims to contribute to the literature by exploring different approaches to improve resource utilization in pediatric intensive care units (PICU), considering the reasons for hospitalization.

MATERIALS AND METHODS

The study was approved by the Marmara University Medical Faculty Clinical Research Ethics Committee (Date: 17/05/2024, Decision No: 05.2024.659) and was conducted in accordance with the principles of the Declaration of Helsinki.

We retrieved medical records of patients who were admitted 30 days or longer at the PICU between January 1, 2017, and May 1, 2025. Data included age, gender, underlying diseases, indications for PICU admission, interventions, device use, length of PICU stay, reasons for death, and Pediatric Risk of Mortality (PRISM) scores. The use of interventions and treatments during the PICU stay were assessed, including antibiotic therapy, inotropic agents, mechanical ventilation, central venous catheters, dialysis, cardiopulmonary resuscitation (CPR), plasmapheresis, and extracorporeal membrane oxygenation (ECMO). The study was approved by the institutional review board (05.2024.659).

Statistical Analysis

Data were processed using the SPSS 26.0 (Statistical Program for Social Sciences) package. For quantitative descriptive statistics, mean and standard deviation were used for normally distributed data, while median and interquartile ranges were used for non-normally distributed data. The chi-square test was used for comparisons of categorical data. The Mann-Whitney U-test was used for comparison of non-normally distributed quantitative variables between two independent groups, while Student's t-test was used for normally distributed variables. All statistical calculations were evaluated at a 95% confidence interval, with a significance level of $p<0.05$.

RESULTS

During the study period, a total of 328 patients required PICU stay of 30 days or longer, including 182 (55.5%) males and 146 (44.5%) females (Table 1). The mean age was 4.3 years (range 1 month to 17.8 years). The mean length of PICU stay was 92 days (range 30-920 days). The most common indications for admission were respiratory failure (68.9%), shock (14%), trauma (10.1%) and postoperative care (7%).

Of the patients, 235 (71.6%) had underlying chronic conditions. The average PRISM score was 9.8. One hundred seventeen patients (35.7%) were admitted through emergency service, 141 (43%) from the clinical ward, 43 (13.1%) from the operating room, and 27 (8.2%) from foreign health center. Two hundred fourteen patients (65.2%) had tracheostomy, 72 (22%) with gastrostomy, and 328 (100%) required mechanical ventilation. The average duration of mechanical ventilation was 3200 hours (768-9160 hours). Two hundred forty four patients (64.8%) were transferred to clinical wards, 28 (16.9%) were discharged directly, and 22 (3.5%) were transferred to palliative intensive care unit. Thirty-three patients (10.4%) were dead, with 21 deaths (6.4%) due to cardiac death and 13 (4%) due to brain death. Of the patients, 302 (92.1%) received antibiotic therapy, 143 (43.6%) had central venous catheters, 18 (5.5%) underwent dialysis, 12 (3.7%) had plasmapheresis, 38 (11.6%) required treatment for liver failure, and 8 (2.4%) received ECMO therapy. Cardiopulmonary resuscitation (CPR) was performed on 98 patients (29.9%) an average of 2 times. When evaluating the primary diagnoses, chronic central nervous system disorders were the most common, observed in 161 patients (49.1%). Respiratory diseases were present in 76 patients (23.2%), followed by central nervous system tumors in 46 patients (14%) and muscular disorders in 48 patients (14.6%). Additionally, 35 patients (10.7%) were diagnosed with metabolic diseases, while 28 patients (8.5%) had cardiac conditions.

Factors Influencing Length of Stay in the Pediatric Intensive Care Unit

The summary values related to the findings are presented in Table 2. Over an 8-year period, a total of 3,714 patients were admitted to PICU of whom 316 (8.5%) were foreign nationals. Among these patients, 328 (8.8%) had a prolonged PICU stay exceeding 30 days. Of the long-stay cohort, 112 (34.1%) were admitted for medical reasons, while 216 (65.9%) were admitted due to social circumstances. Foreign nationals comprised 9.8% (n=32) of the long-stay group.

Male patients had an average length of stay 6 days longer than females, and those referred from other PICUs stayed approximately 20 days longer. The most significant medical contributors to prolonged stay were chronic central nervous system (CNS) diseases and neuromuscular disorders. Patients with tracheostomies stayed an average of 66 days longer, a statistically significant difference ($p<0.05$).

Of the 48 patients (14.6%) diagnosed with neuromuscular disorders, 42 (12.8%) had spinal muscular atrophy. In these patients, chronic respiratory failure necessitated tracheostomy placement to facilitate stepwise discharge to ward care and eventually home. This procedure required informed consent, which could not be obtained in 21 cases; in these, tracheostomy was performed following a court order. The average time to obtain the court decision was 26 days. Among patients who underwent tracheostomy, 17 (5.2%) could not be discharged due to lack of access to home ventilators—largely attributable to their foreign national status and lack of insurance coverage.

Table2. Factors Influencing Length of Stay in the Pediatric Intensive Care Unit

Factors	Finding	Significant p-value
Gender	Male patients stayed on average 6 days longer than females	p<0.05
Tracheostomy	Associated with an average of 66 days longer stay	p<0.05
Neuromuscular disorders	14.6% of long-stay patients; SMA most common (12.8%)	
Lack of home ventilator (foreign nationals)	17 patients could not be discharged	p<0.05
COVID-19 pandemic effect	Increase in patients without chronic disease: 44.2% → 84%	p<0.05
	Tracheostomy rate increase: 50% → 68.8%	p<0.05
	Long-term ventilator need: 84% → 98%	p<0.05
Admission Reason: Social vs. Medical	Tracheostomy more frequent: 74% (social) vs. 43.5% (medical)	p<0.05
	CNS tumors more common in medical group: 23% vs. 8%	p<0.05
	Chronic CNS disorders more common in social group: 10% vs. 4%	p<0.05
	Social admissions stayed 66 days longer on average	p<0.05
	Medical admissions decreased: 59.3% → 40.7	p<0.05
PRISM score	Lower in socially admitted patients	p<0.05
Length of Stay (Social vs. Medical)	Social admissions stayed 66 days longer on average	p<0.05

CNS – Central nervous system. SMA – Spinal muscular atrophy. PRISM – Pediatric Risk of Mortality.

Impact of the COVID-19 Pandemic

The COVID-19 pandemic significantly altered PICU admission patterns. The proportion of patients without chronic conditions rose from 44.2% pre-pandemic to 84% post-pandemic (p<0.05). Tracheostomy prevalence increased from 50% to 68.8%, and the need for long-term ventilator support rose from 84% to 98% (p<0.05).

Comparison by Admission Reason

Tracheostomy was more frequent in patients admitted for social reasons (74%) compared to those with medical indications (43.5%) (p<0.05). CNS tumor prevalence was higher in the medical group (23%) versus the social group (8%), whereas chronic CNS disorders were more frequent in social admissions (10% vs. 4%). Following the pandemic, the rate of medical admissions decreased from 59.3% to 40.7%, while social admissions increased from 39.6% to 60.4% (p<0.05).

PRISM scores were significantly lower in socially admitted patients. Moreover, their average length of stay was 66 days longer than that of medically admitted patients (p<0.05). This group was also more likely to be referred from emergency departments or other PICUs.

DISCUSSION

This study highlights the burden imposed by long-stay patients admitted for social reasons. Although these patients are often clinically stable, discharge is delayed due to factors such as dependence on chronic devices or lack of home care resources. Previous studies reported average PICU stays of 64 days and 107±124 days.[4,5] In our study, 37% of long-stay cases were due to social reasons, with a significantly longer average stay than those admitted for medical reasons, consistent with the literature. Prolonged mechanical ventilation is a well-known factor contributing to extended PICU stays.[6-9] Tracheostomy, commonly performed in pediatric intensive care units, is primarily indicated for prolonged intubation due to cardiopulmonary and neurological conditions, aiming to ensure a secure airway, improve ventilation, and reduce hospital stay.[10] In our cohort, tracheostomy was performed in 43.5% of medically admitted and 74% of socially admitted patients, all of whom required chronic ventilator support.

Long ICU stays are associated with resource overutilization, bed shortages, and increased infection risk. Facilitating discharge through home mechanical ventilation programs could reduce PICU burden.[11] Families of long-stay patients are often better adapted to ICU care, which may facilitate transition to home settings.[12] However, the lack of a structured home care system and caregiver hesitancy—due to concerns over medical management, family dynamics, economic stress, and isolation—pose barriers.[13]

Following the COVID-19 pandemic, there was a marked shift in admission dynamics. Graciano et al.[14] reported a 70% decline in PICU admissions. In our study, medical admissions dropped while social admissions increased, likely due to increased caregiver anxiety during the pandemic.

Chronic conditions are frequently observed in PICU patients. Reported rates include 25.5%, 47.2%, and 46.9%.[15-17] Our study found a 71.6% rate among long-stay patients. This suggests the need for dedicated intermediate care units for patients with chronic conditions.

Neurologic disorders are the most frequent chronic diagnoses in these patients. One study reported that 296 out of 378 patients requiring home ventilation had neurologic disorders. Another identified technology-dependent neurologic conditions as the most common among patients

receiving home health services. In our cohort, chronic CNS disorders were more prevalent in socially admitted patients (32.5%) compared to medically admitted ones (24.6%). Establishing palliative rehabilitation centers for such patients may help reduce ICU burden.[18]

Limitations

The main limitations of this study are its retrospective design and single-center setting. Despite this, the findings underline a significant issue in pediatric critical care and offer insights into potential interventions.

Conclusion

Long-stay patients in the PICU consume a disproportionate share of resources. This study emphasizes the impact of social factors on prolonged hospitalization. These patients often have stable clinical status but cannot be discharged due to chronic device dependency and insufficient home care infrastructure. Expanding home care programs, establishing intermediate care units, and developing palliative rehabilitation centers are essential strategies to reduce PICU strain and maintain capacity during public health crises such as the COVID-19 pandemic.

Ethics Committee Approval

The study was approved by the Marmara University Medical Faculty Clinical Research Hospital Ethics Committee (Date: 17.05.2024, Decision No: 05.2024.659).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: F.I.G.; Design: F.I.G., B.A., M.N.Y.; Supervision: F.I.G., B.A., M.N.Y.; Materials: F.I.G., B.A.; Data collection &/or processing: F.I.G., B.A.; Analysis and/or interpretation: F.I.G., B.A., A.S.; Literature search: F.I.G., B.A., A.S.; Writing: F.I.G., B.A; Critical review: F.I.G., B.A.

Conflict of Interest

None declared.

REFERENCES

1. Temsah MA, Al-Eyadhy AA, Al-Sohime FM, Hassounah MM, Almazyad MA, Hasan GM, et al. Long-stay patients in pediatric intensive care units. Five-years, 2-points, cross-sectional study. Saudi Med J 2020;4:1187–96. [CrossRef]
2. Knaup E, Nosaka N, Yorifuji T, Tsukahara K, Naito H, Tsukahara H, et al. Long-stay pediatric patients in Japanese intensive care units: Their significant presence and a newly developed, simple predictive score. J Intensive Care 2019;7:38. [CrossRef]
3. Van de Riet L, Otten MH, van Karnebeek CD, van Woensel JBM. Long stay and frequent readmission in the pediatric intensive care in the Netherlands; 15-year time trends. Crit Care Explor 2022;4:e0798. [CrossRef]
4. Oktem S, Ersu R, Uyan ZS, Cakir E, Karakoc F, Karadag B, et al. Home ventilation for children with chronic respiratory failure in Istanbul. Respiration 2008;76:76–81. [CrossRef]
5. DeWitt PK, Jansen MT, Ward SL, Keens TG. Obstacles to discharge of ventilator-assisted children from the hospital to home. Chest 1993;103:1560–5. [CrossRef]
6. Matsumoto N, Hatachi T, Inata Y, Shimizu Y, Takeuchi M. Long-term mortality and functional outcome after prolonged paediatric intensive care unit stay. Eur J Pediatr 2019;178:155–60. [CrossRef]
7. Ping Kirk AH, Sng QW, Zhang LQ, Ming Wong JJ, Puthucheary J, Lee JH. Characteristics and outcomes of long-stay patients in the pediatric intensive care unit. J Pediatr Intensive Care 2018;7:1–6.
8. Miura S, Fukushima M, Kurosawa H, Kimura S. Epidemiology of long-stay patients in the pediatric intensive care unit: Prevalence, characteristics, resource consumption and complications. Z Gesundh Wiss 2022;30:111–9. [CrossRef]
9. Geoghegan S, Oulton K, Bull C, Brierley J, Peters M, Wray J. The experience of long-stay parents in the ICU: A qualitative study of parent and staff perspectives. Pediatr Crit Care Med 2016;17:e496–501. [CrossRef]
10. Ayvaz OD, Celayir A, Çakmak MH. Tracheostomy experiences in 37 children during 12 years: A retrospective study. South Clin Ist Euras 2023;34:91–6. [CrossRef]
11. Henderson CM, Raisanen JC, Shipman KJ, Jabre NA, Wilfond BS, Boss RD. Life with pediatric home ventilation: Expectations versus experience. Pediatr Pulmonol 2021;56:3366–73. [CrossRef]
12. Shipman KJ, Mercer AH, Raisanen JC, Jabre NA, Vo HH, Miles A, et al. "What would give her the best life?": Understanding why families decline pediatric home ventilation. J Palliat Med 2023;26:930–40. [CrossRef]
13. Vo HH, Mercer AH, Jabre NA, Henderson CM, Boss RD, Wilfond BS. Parent perspectives on the child experience of pediatric home ventilation via tracheostomy. Hosp Pediatr 2023;13:1124–33. [CrossRef]
14. Graciano AL, Bhutta AT, Custer JW. Reduction in paediatric intensive care admissions during COVID-19 lockdown in Maryland, USA. BMJ Paediatr Open 2020;4:e000876. [CrossRef]
15. Konca Ç, Tekin M, Karakoç F. Çocuk yoğun bakım ünitesinde yatan 770 hastanın değerlendirilmesi: Tek merkez deneyimi. Turk J Pediatr Dis 2015;9:90–5. [Article in Turkish]
16. Poyrazoğlu H, Dursun İ, Güneş T, Akçakuş M, Konuşkan B, Canpolat M, et al. Evaluation and outcome analysis of patients in pediatric intensive care unit. J Clin Pract Res 2008;30:232–7.
17. Kılıç FZ, Çoban Y, Davutoğlu M, Dalkıran T. Çocuk yoğun bakım ünitesinde izlenen hastaların geriye dönük analizi ve mortaliteyi etkileyen faktörlerin incelenmesi. J Pediatr Emerg Intensive Care Med 2016;3:140–5. [Article in Turkish]
18. Harputluoğlu N, Çelik T, Karaarslan U, Uysal S. Çocuklarda evde sağlık hizmetleri ile çocuk palyatif bakım ünitesinin birlikte çalışmasının önemi. J Pediatr Emerg Intensive Care Med 2021;8:83–7. [Article in Turkish]

Pediatrik Yoğun Bakım Ünitesinde Uzamış (≥30 Gün) Yatışla İlişkili Faktörlerin Retrospektif Analizi: Tek Merkez Deneyimi

Amaç: Bu çalışmanın amacı, çocuk yoğun bakım ünitesinde (ÇYBÜ) uzun süre kalan hastaların klinik ve demografik özelliklerini, yatış süresini uzatan tıbbi ve sosyal nedenlere odaklanarak analiz etmektir.

Gereç ve Yöntem: ÇYBÜ'de 1 Ocak 2017 ile 1 Mayıs 2025 tarihleri arasında 30 günden fazla yatan hastaların tıbbi kayıtları yatış süresini uzatan nedenler açısından retrospektif olarak incelendi.

Bulgular: Toplam 328 uzamış ÇYBÜ yatışı olan hasta çalışmaya dahil edildi. Hastaların ortalama yaşı 4.3 yıl (dağılım: 1 ay – 17.8 yıl), ortalama ÇYBÜ yatış süresi 92 gün olarak saptandı (dağılım: 30–920 gün). En sık başvuru nedeni solunum yetersizliği idi (%68.9). Hastaların %71.6'sında altta yatan kronik hastalık mevcuttu. Bu hastalıkların en yaygın olanları santral sinir sistemi hastalıkları (%30.2) ve kronik solunum sistemi hastalıklarıydı (%23). Toplamda 214 hastaya (%65.2) trakeostomi işlemi uygulanırken, 72 hastada (%22) gastrostomi açılması gerekli olmuştur. Tüm hastalar (%100) mekanik ventilasyon desteği aldı. Mortalite, toplam 34 hastada (%14.8) gözlendi; bu ölümlerin 21'i (%13.4) kardiyak nedenlere, 13'ü (%1.4) ise beyin ölümüne bağlıydı. Trakeostomi uygulanan hastalarda, ÇYBÜ'de kalış süresi çoğunlukla hastanın klinik durumundan bağımsız, klinik dışı nedenlerle uzamıştı.

Sonuç: Sosyal nedenlerle ÇYBÜ'ne kabul edilen hastalarda, yatış süresi anlamlı düzeyde daha uzun bulunmuş; bu hastalarda trakeostomi uygulama oranı, kronik ventilasyon desteği ihtiyacı ve altta yatan kronik hastalık prevalansı daha yüksek saptanmıştır. COVID-19 pandemisi sonrası süreçte, sosyal nedenli yoğun bakım kabul oranlarında artış saptanmıştır. Yoğun bakım kaynaklarını belirgin şekilde tüketen bu hasta grubuna yönelik alternatif bakım modellerinin geliştirilmesi, ÇYBÜ üzerindeki yükün azaltılmasına katkı sağlayabilir.

Anahtar Sözcükler: Çocuk yoğun bakım ünitesi; epidemiyoloji; kalış süresi; kronik hastalıklar; sağlık kaynakları.

SCIE DOI: 10.14744/scie.2025.98853
South. Clin. Ist. Euras. 2025;36(3):253-257

Original Article

Prognosis and Associated Factors in Patients Transferred from a Tertiary Intensive Care Unit to the Pulmonology Ward

Berrin Zinnet Eraslan, Nesrin Kıral, Yusuf Furkan Aydınlı, Ali Fidan, Sevda Şener Cömert

Department of Chest Diseases, Dr. Lütfi Kırdar City Hospital University of Health Sciences, Istanbul, Türkiye

Submitted: 10.07.2025
Revised: 28.07.2025
Accepted: 29.07.2025

Correspondence: Berrin Zinnet Eraslan, Department of Chest Diseases, Dr. Lütfi Kırdar City Hospital University of Health Sciences, Istanbul, Türkiye
E-mail: berzinbalta@yahoo.com

Keywords: Intensive care; mortality; patient transfer; prognosis.

ABSTRACT

Objective: The transfer of patients from the intensive care unit (ICU) to general wards is a clinically challenging process. A carefully considered decision to transfer and close monitoring on the ward may reduce mortality and the need for ICU readmission. This study aimed to evaluate prognostic factors associated with one-month mortality in patients transferred from a tertiary intensive care unit to a pulmonary medicine ward.

Methods: This retrospective observational study included patients who were transferred from a tertiary ICU to the pulmonary medicine ward between January 2024 and July 2024. Demographic, clinical, and laboratory data, as well as discharge status and one-month mortality outcomes, were evaluated.

Results: A total of 114 patients were included in the study. The one-month mortality rate was 23.7% (27 patients). Patients who died had significantly lower levels of albumin and hemoglobin, as well as a higher mean heart rate upon admission to the ward. Additionally, ICU readmission and the presence of malignancy were significantly associated with mortality in univariate analysis. However, in multivariate logistic regression, only ICU readmission remained an independent predictor of mortality (p=0.032), while malignancy and elevated heart rate were not statistically significant (p=0.297 and p=0.092, respectively)

Conclusion: Patients transferred from a tertiary ICU to a pulmonary medicine ward are at high risk for short-term mortality. ICU readmission was identified as an independent prognostic factor. Moreover, high heart rate, low albumin and hemoglobin levels, and the presence of malignancy may help in identifying high-risk patients. Early identification and close monitoring of these patients may reduce mortality and ICU readmissions.

INTRODUCTION

Patients may become vulnerable to medical errors and adverse events during the transition from the intensive care unit (ICU) to general wards.[1,2] This transitional period is considered one of the most critical phases of hospitalization. The ICU provides continuous monitoring and multidisciplinary care, whereas such resources are more limited on general wards. Moreover, the healthcare team responsible for the patient's care changes during this transition. For these reasons, post-ICU care demands rigorous monitoring and standardized protocols.[3]

Among hospital wards, pulmonary medicine units hold a distinctive position. These wards commonly manage patients with acute or chronic respiratory conditions and are equipped to provide close respiratory monitoring—such as continuous oxygen saturation monitoring—and Non-invasive ventilation support. This makes them particularly well-suited for post-ICU patients with ongoing respiratory needs.

Patients transferred from the ICU to the ward often include individuals who have received treatment for severe infections, respiratory failure, sepsis, or multiple organ dysfunction. Even after discharge from the ICU, these patients remain at risk of complications and clinical deterioration.[4] This may lead to unfavorable outcomes such as ICU readmission or mortality.[5] Therefore, close monitoring of patients in the post-ICU period and early identification of high-risk individuals are essential.

Several clinical parameters have been identified as being associated with in-hospital mortality during the post-ICU period. These include advanced age, altered mental status, hypoxia, need for mechanical ventilation, and elevated

blood urea levels.[6,7] However, studies focusing specifically on patients transferred to pulmonary medicine wards remain limited.[8] Early assessment of prognosis in this patient group is crucial for optimizing clinical management.

The aim of this study is to evaluate one-month mortality and identify prognostic factors in patients transferred from a tertiary ICU to a pulmonary medicine ward.

MATERIALS AND METHODS

This retrospective cohort study was conducted at a tertiary care hospital in Istanbul, Türkiye. The study included adult patients who were transferred from the hospital's third-level general ICU to the pulmonary medicine ward between January 2024 and July 2024. Medical records were reviewed retrospectively through the hospital's electronic database.

Data collected for each patient included demographic characteristics, primary diagnoses and comorbidities, laboratory parameters at the time of ICU-to-ward transfer, need for mechanical ventilation and history of endotracheal intubation, and microbiological culture results obtained from blood, sputum, urine, or tracheal aspirates. Information regarding the length of ICU stay and subsequent ward stay, ICU readmission status, discharge outcomes, and one-month post-discharge mortality were also recorded.

Patients were eligible for inclusion if they were aged 18 years or older, were transferred from the ICU to the chest diseases ward within the specified study period, had complete medical and follow-up data, and remained in the ward for at least 24 hours after transfer. Patients were excluded if they were discharged to another hospital or department directly from the ICU, if their medical or follow-up records were incomplete, or if they left the hospital against medical advice.

Total serum calcium levels were used without correction for albumin.

Data regarding one-month mortality following transfer to the pulmonary medicine ward were obtained through the hospital's electronic medical record system.

The primary outcome of the study was one-month mortality following transfer to the pulmonary medicine ward. Secondary outcomes included identification of clinical factors associated with mortality and need for ICU readmission.

The study protocol was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (No: 2025/010.99/16/8, Date: 27/05/2025). All procedures were conducted in accordance with the principles of the Declaration of Helsinki.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 25.0. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. The Mann–Whitney U test was used for comparisons of non-normally distributed continuous variables. Categorical variables were analyzed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

To identify factors associated with one-month mortality, univariate analyses were initially performed. Variables found to be statistically significant in univariate analysis were included in a multivariate logistic regression model. In this model, the variables included were "presence of malignancy," "whether ICU readmission occurred during ward follow-up," and "heart rate measured during ward stay." A p-value of <0.05 was considered statistically significant in the regression analysis.

RESULTS

Baseline Characteristics

A total of 114 patients who were transferred from a tertiary ICU to the pulmonary medicine ward between January and July 2024 were included in this study. The mean age of the patients was 71.7±15.1 years, and 53.5% (n=61) were male. The most common comorbidities were hypertension (65.8%), diabetes mellitus (35.1%), and heart failure (20.2%). Additionally, 21.9% (n=25) of the patients had malignancy. Of the patients, 40.4% (n=46) were intubated. The median ICU length of stay was 9 days (IQR: 5–17), while the median length of stay on the pulmonary ward was 10 days (IQR: 6–16). During follow-up, 14.0% (n=16) of patients required readmission to the ICU (Table 1).

Mortality Rate and Comparison Between Groups

Among the 114 patients included, 23.7% (n=27) died within one month after discharge from the pulmonary medicine ward. Comparison between survivors and non-survivors revealed that the mean age was significantly higher in the mortality group (78.8±10.3 vs. 71.0±14.1 years, p=0.013).

Table 1. Baseline characteristics of 114 patients

Variables	Value
Age, mean±SD (years)	71.7±15.1
Male sex, n (%)	61 (53.5)
COPD, n (%)	49 (43)
Hypertension, n (%)	75 (65.8)
Diabetes Mellitus, n (%)	40 (35.1)
Heart failure, n (%)	23 (20.2)
Malignancy, n (%)	25 (21.9)
Intubation, n (%)	46 (40.4)
ICU length of stay, median (IQR), days	9 (5-17)
Pulmonary ward stay, median (IQR), days	10 (6-16)
Readmission to ICU, n (%)	16 (14.0)

COPD=Chronic obstructive pulmonary disease, ICU=Intensive care unit, IQR=Interquartile range.

Table 2. Comparison between survivors and non-survivors

Variable	Survivors (n=87)	Non-Survivors (n=27)	p-value
Age, mean±SD (years)	71.0±14.1	78.8±10.3	0.013
Malignancy, n (%)	16 (18.6)	13 (48.1)	0.001
ICU readmission, n (%)	6 (6.9)	9 (33.3)	0.001
Heart rate, median (IQR) (bpm)	88	101	0.005
CRP, mean±SD (mg/L)	67.4±87.2	84.0±61.8	0.010
WBC count, mean±SD (10^3/μL)	9.71±4.69	11.15±3.94	0.019
Serum albumin, mean±SD (g/dL)	3.01±0.43	2.67±0.44	0.001
Hemoglobin, mean±SD (g/dL)	12.21±2.10	9.93±1.74	0.020
Hematocrit, mean±SD (%)	34.15±6.34	30.45±4.72	0.018
Calcium, mean±SD (mg/dL)	8.44±0.60	8.12±0.75	0.044
Potassium, mean±SD (mmol/L)	3.90±0.57	4.00±0.49	0.035

CRP: C-reactive protein; WBC: White blood cell; ICU: Intensive care unit; SD: Standard deviation; bpm: beats per minute.

Table 3. Clinical outcomes of patients transferred from ICU to pulmonary ward

Outcome	n	Percentage (%)
Discharged home	87	76.3
Died in the pulmonary ward	1	0.9
Transferred back to ICU	22	19.3
Transferred to another department	4	3.5
Total	114	100.0

Other parameters significantly associated with mortality were as follows:

- The presence of malignancy was more frequent in the mortality group (48.1% vs. 18.6%, p=0.001).
- ICU readmission was significantly more common among non-survivors (33.3% vs. 6.9%, p=0.001).
- Median heart rate measured on the ward was higher in non-survivors (101 vs. 88 bpm, p=0.005).
- C-reactive protein (CRP) and white blood cell (WBC) counts were significantly elevated in the mortality group (p=0.010 and p=0.019, respectively).
- Serum albumin was significantly lower in non-survivors (p=0.001).
- Hemoglobin, hematocrit, and calcium levels were also lower in the mortality group, whereas potassium levels were significantly higher (p=0.020, p=0.018, p=0.044, and p=0.035, respectively) (Table 2).

Clinical Outcomes

Among the 114 patients included, 23.7% (n=27) died within one month after discharge from the pulmonary medicine ward. A total of 16 patients (14.0%) required readmission to the ICU, and 4 patients (3.5%) were transferred to other departments for further management (Table 3).

Logistic Regression Analysis

Logistic regression analysis revealed that ICU readmission was an independent prognostic factor for mortality (p=0.001, OR=5.85, 95% CI: 1.95–17.54) (Table 4).

DISCUSSION

In this study, we evaluated the one-month mortality rate and associated prognostic factors in patients transferred from a tertiary ICU to a pulmonary medicine ward. The one-month mortality rate was found to be 23.7%. One-month mortality after ICU discharge has been reported to range from 10% to 25% in previous studies.[9-11] Our result (23.7%) is near the upper end of this range. This may be because our hospital does not have an intermediate care

Table 4. Multivariate logistic regression analysis of 1-month mortality

Variable	B	SE	Wald	P	OR (Adjusted)*	OR 95% CI
Malignancy (vs no malignancy)	–0.576	0.553	1.086	1.201	1.78	0.562 (95% CI: 0.190–1.661)
ICU readmission (vs no	–1.767	0.548	10.394	0.001	5.85	0.171 (95% CI: 0.058–0.500)
Heart rate (per bpm)	0.027	0.016	2.833	0.092	1.027	1.027 (95% CI: 0.981–1.076)
Constant	–1.912	1.744	1.201	0.273	-	-

*Adjusted ORs were calculated as 1/Exp(B) due to reverse coding in the logistic regression model. B: Regression coefficient; SE: Standard error; Wald: Wald chi-square test statistic, P: p-value; OR: Odds ratio; CI: Confidence interval; ICU: Intensive care unit; bpm: Beats per minute.

unit, so patients with more serious conditions are transferred directly to the pulmonary ward. Therefore, our patient group may have had more severe illnesses compared to those in hospitals with step-down care.

Several laboratory parameters were significantly associated with mortality in our study, including hemoglobin, hematocrit, WBC, international normalized ratio (INR), calcium, albumin, and potassium levels. These findings suggest that patients were transferred with ongoing systemic inflammation, nutritional deficiencies, organ dysfunction, or coagulation abnormalities.

Hemoglobin levels were significantly lower in the mortality group (mean 9.9 g/dL). In a large-scale study by Lin et al.,[12] a hemoglobin level below 10 g/dL within the first week was associated with a 26-34% increase in one-year mortality risk. This supports the potential prognostic significance of anemia in critically ill patients post-ICU.

Similarly, INR was significantly higher in non-survivors (mean 1.26). Benediktsson et al.[13] reported that in patients with sepsis, each unit increase in PT-INR upon ICU admission increased in-hospital mortality by 42% (HR=1.422). Our findings are in line with these data, indicating that elevated INR may reflect coagulopathy and poor prognosis.

In our study, serum calcium levels were also significantly lower in the mortality group (mean 8.11 mg/dL, p=0.013). Hypocalcemia is frequently observed in ICU patients and may contribute to complications involving the cardiovascular, neuromuscular, and coagulation systems. This is consistent with the findings of Iqbal et al.,[14] who reported the common occurrence of hypocalcemia among ICU patients.

Serum albumin levels were significantly lower in the mortality group (mean 2.6 g/dL, p=0.001). Hypoalbuminemia is considered a marker of inflammation and malnutrition and has been strongly associated with increased mortality in critically ill patients. A large meta-analysis by Vincent et al.,[15] which included acutely ill patients, confirmed that hypoalbuminemia is an independent predictor of poor outcomes, even in ICU populations.

In addition to laboratory parameters, clinical variables such as heart rate and ICU readmission were also associated with increased mortality in our study. Patients in the mortality group had significantly higher heart rates at the time of ward admission. Tachycardia may reflect ongoing physiological stress, unresolved systemic inflammation, or underlying cardiovascular dysfunction. Previous studies have suggested that abnormal vital signs—particularly heart and respiratory rate—at the time of ICU discharge may serve as consistent but not yet well-validated indicators of ICU readmission risk.[16]

Moreover, ICU readmission emerged as the only independent predictor of one-month mortality in our multivariate analysis. ICU readmission is widely recognized as a marker of clinical deterioration and has been associated with increased in-hospital mortality. In a meta-analysis including over two million ICU discharges, Hosein et al.[11] reported that among every 100 patients discharged alive from the ICU, approximately 4 to 6 were readmitted, and 3 to 7 died before hospital discharge. These findings emphasize the prognostic value of ICU readmission and highlight the importance of structured discharge planning and close monitoring during the post-ICU period.

Limitations

This study has several limitations. First, as a single-center retrospective study, the generalizability of the findings may be limited. Additionally, the relatively small sample size may have reduced the statistical power to detect significance in some variables during multivariate analysis. Important prognostic indicators such as functional scoring systems (e.g., APACHE, SOFA) could not be evaluated. Laboratory parameters such as CRP, albumin, and calcium were available only as single measurements at the time of transfer, and were not analyzed, which may have limited the assessment of disease progression. These limitations highlight the need for future multicenter prospective studies to validate and expand upon our findings.

Conclusion

This study highlights that patients transferred from a tertiary intensive care unit to the pulmonary medicine ward have a substantial short-term mortality risk, with a 1-month mortality rate of 23.7%. ICU readmission was identified as an independent predictor of mortality. Although elevated heart rate, low serum albumin and hemoglobin levels, and presence of malignancy were not independently associated with mortality in multivariate analysis, they were significantly different in univariate analysis and may still warrant clinical attention. These findings emphasize the importance of early risk stratification and close monitoring of patients following ICU discharge. Future multicenter, prospective studies with larger cohorts and inclusion of dynamic clinical scores and follow-up data are warranted to validate these findings and improve post-ICU care strategies.

Ethics Committee Approval

The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Hospital Ethics Committee (Date: 27.05.2025, Decision No: 2025/010.99/16/8).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: B.Z.E., N.K., A.F.; Design: N.K., A.F.; Supervision: S.C., N.K., B.Z.E.; Materials: N.K., S.C., A.F.; Data collection &/or processing: B.Z.E., Y.F.A.; Analysis and/or interpretation: A.F., Y.F.A.; Literature search: B.Z.E., Y.F.A.; Writing: B.Z.E., N.K.; Critical review: S.C., N.K., A.F.

Conflict of Interest

None declared.

REFERENCES

1. World Health Organization. Transitions of care: Technical series on safer primary care. Available at: https://apps.who.int/iris/handle/10665/252272. Accessed Aug 11, 2025.
2. Hervé MEW, Zucatti PB, Lima MADS. Transition of care at discharge from the intensive care unit: A scoping review. Rev Latino-Am Enfermagem 2020;28:e3325. [CrossRef]
3. Hosein FS, Bobrovitz N, Berthelot S, Zygun D, Ghali WA, Stelfox HT. A systematic review of tools for predicting severe adverse events following patient discharge from intensive care units. Crit Care 2013;17:R102. [CrossRef]
4. Lee J, Cho YJ, Kim SJ, Yoon HI, Park JS, Lee CT, et al. Who dies after ICU discharge? Retrospective analysis of prognostic factors for in-hospital mortality of ICU survivors. J Korean Med Sci 2017;32:528–33. [CrossRef]
5. Ponzoni CR, Corrêa TD, Filho RR, Serpa Neto A, Assunção MSC, Pardini A, et al. Readmission to the intensive care unit: Incidence, risk factors, resource use, and outcomes. A retrospective cohort study. Ann Am Thorac Soc 2017;14:1312–9. [CrossRef]
6. E Silva LGA, de Maio Carrilho CMD, Talizin TB, Cardoso LTQ, Lavado EL, Grion CMC. Risk factors for hospital mortality in intensive care unit survivors: A retrospective cohort study. Acute Crit Care 2023;38:68–75. [CrossRef]
7. Keegan MT, Gajic O, Afessa B. Severity of illness scoring systems in the intensive care unit. Crit Care Med 2011;39:163–9. [CrossRef]
8. Santhosh L, Lyons PG, Rojas JC, Ciesielski TM, Beach S, Farnan JM, et al. Characterising ICU-ward handoffs at three academic medical centres: Process and perceptions. BMJ Qual Saf 2019;28:627–34. [CrossRef]
9. Goldhill DR, Sumner A. Outcome of intensive care patients in a group of British intensive care units. Crit Care Med 1998;26:1337–45. [CrossRef]
10. Moreno R, Miranda DR, Matos R, Fevereiro T. Mortality after discharge from intensive care: The impact of organ system failure and nursing workload use at discharge. Intensive Care Med 2001;27:999–1004. [CrossRef]
11. Hosein FS, Roberts DJ, Turin TC, Zygun D, Ghali WA, Stelfox HT. A meta-analysis to derive literature-based benchmarks for readmission and hospital mortality after patient discharge from intensive care. Crit Care 2014;18:715. [CrossRef]
12. Lin IH, Liao PY, Wong LT, Chan MC, Wu CL, Chao WC. Anaemia in the first week may be associated with long-term mortality among critically ill patients: Propensity score-based analyses. BMC Emerg Med 2023;23:32. [CrossRef]
13. Benediktsson S, Frigyesi A, Kander T. Routine coagulation tests on ICU admission are associated with mortality in sepsis: An observational study. Acta Anaesthesiol Scand 2017;61:790–6. [CrossRef]
14. Iqbal M, Rehmani R, Hijazi M, Abdulaziz A, Kashif S. Hypocalcemia in a Saudi intensive care unit. Ann Thorac Med 2008;3:57–9. [CrossRef]
15. Vincent JL, Dubois MJ, Navickis RJ, Wilkes MM. Hypoalbuminemia in acute illness: Is there a rationale for intervention? A meta-analysis of cohort studies and controlled trials. Ann Surg. 2003;237:319–34. [CrossRef]
16. Rosenberg AL, Watts C. Patients readmitted to ICUs* : A systematic review of risk factors and outcomes. Chest 2000;118:492–502. [CrossRef]

Üçüncü Basamak Yoğun Bakım Ünitesinden Göğüs Hastalıkları Servisine Devredilen Hastalarda Prognoz ve İlişkili Faktörler

Amaç: Yoğun bakım ünitesinden (YBÜ) servise hasta transferi, klinik açıdan zorlu bir süreçtir. Devir kararının titizlikle verilmesi ve serviste yakın izlem sağlanması, mortaliteyi ve yoğun bakıma tekrar yatış gereksinimini azaltabilir. Bu çalışmanın amacı, üçüncü basamak yoğun bakım ünitesinden göğüs hastalıkları servisine devredilen hastalarda bir aylık mortalite ile ilişkili prognostik faktörleri değerlendirmektir.

Gereç ve Yöntem: Bu retrospektif gözlemsel çalışmaya, Ocak 2024-Temmuz 2024 tarihleri arasında üçüncü basamak yoğun bakım ünitesinden göğüs hastalıkları servisine devredilen hastalar dahil edilmiştir. Hastalara ait demografik, klinik ve laboratuvar bulgular ile taburculuk durumu ve bir aylık mortalite verileri değerlendirilmiştir.

Bulgular: Çalışmaya toplam 114 hasta dahil edildi. Bir aylık mortalite oranı %23.7 (27 hasta) idi. Mortalite gelişen hastalarda albümin ve hemoglobin düzeyleri anlamlı olarak daha düşük, servise yatış sırasında ortalama kalp atış hızı ise daha yüksekti. Ayrıca, tek değişkenli analizde yoğun bakım ünitesine yeniden yatış ve malignite varlığı mortalite ile anlamlı şekilde ilişkiliydi. Ancak çok değişkenli lojistik regresyon analizinde yalnızca yoğun bakım ünitesine yeniden yatış, mortalitenin bağımsız bir öngörücüsü olarak kaldı (p=0.032); malignite ve yüksek kalp atış hızı ise istatistiksel olarak anlamlı bulunmadı (sırasıyla, p=0.297 ve p=0.092).

Sonuç: Üçüncü basamak yoğun bakım ünitesinden göğüs hastalıkları servisine devredilen hastalarda kısa dönem mortalite riski yüksektir. Bu çalışmada, yoğun bakıma yeniden yatışın bir aylık mortalitenin bağımsız bir öngöstergesi olduğu gösterilmiştir. Ayrıca, yüksek nabız sayısı istatistiksel olarak sınırda anlamlılık göstermiştir. Bu parametreler, yüksek riskli hastaların belirlenmesinde klinik açıdan dikkate alınmalı; bu hastaların erken tanımlanması ve yakından izlenmesi, klinik sonuçları iyileştirmeye katkı sağlayabilir.

Anahtar Sözcükler: Hasta transferi; mortalite; prognoz; yoğun bakım.

SCIE DOI: 10.14744/scie.2025.29577
South. Clin. Ist. Euras. 2025;36(3):258-266

Original Article

Natural History of Cervical Intraepithelial Neoplasia During Antepartum and Postpartum Periods in Pregnant Women with High-Risk HPV Positivity and Abnormal Cervical Cytology

İlkan Kayar,[1] Ferhat Çetin,[2] Özer Birge[3]

[1]Department of Obstetrics and Gynecology, Osmaniye State Hospital, Osmaniye, Türkiye
[2]Department of Obstetrics and Gynecology, Private Osmaniye Park Hospital, Osmaniye, Türkiye
[3]Department of Gynecological Oncology, Eskisehir City Hospital, Eskisehir, Türkiye

Submitted: 07.04.2025
Revised: 15.05.2025
Accepted: 16.05.2025

Correspondence: Özer Birge, Department of Gynecological Oncology, Eskisehir City Hospital, Eskisehir, Türkiye
E-mail: ozer.birge@saglik.gov.tr

Keywords: Antenatal period; cervical cytology; colposcopy; human papillomavirus; postpartum period.

ABSTRACT

Objective: The colposcopic evaluation of the high-risk human papillomavirus positive and abnormal cervical cytological test results from cervix uteri cancer screening tests taken during pregnancy and comparison of the cytological and histopathological results in the antenatal and postpartum periods were aimed.

Methods: The study included 32 pregnant women over the age of 25 who had HPV positive and abnormal cytological results in cervix uteri cancer screening tests conducted during routine antenatal follow-ups between 2022-2025. Our study includes cases of women who presented during pregnancy, where HPV and cervicovaginal smear tests were conducted during the initial assessment and whose results showed high-risk HPV positive and/or abnormal cytological changes.

Results: Upon examination of the overall results of our study. According to the smear cytology conducted at the 6th month postpartum, the NILM or healing rates were higher in the group without dysplasia compared to the group with dysplasia, 46% versus 11%, and a statistically significant difference was observed between the two groups (p:0.038). When the colposcopic evaluation and biopsy results conducted at the 6th week postpartum were compared with the colposcopic evaluation and biopsy results taken during the antenatal period, it was observed that 9% of all cases progressed, 63% persisted, and 28% regressed. Upon examining the impact of the delivery method on histopathological results and associated rates, it was observed that there were regression rates of 38% in 6 cases in normal spontaneous vaginal delivery and 19% in 3 cases in caesarean delivery, and that the regression rates after normal delivery were significantly high.

Conclusion: Based on the results of high-risk HPV positivity and/or abnormal cytological tests conducted during pregnancy, alongside colposcopic evaluation, only conservative approach during pregnancy and a colposcopy and biopsy approach in the postpartum period are readily implementable.

INTRODUCTION

1-3% of women diagnosed with cervical uterine cancer are in the antenatal or postpartum period at the time of diagnosis.[1] Cervical uterine cancer is among the most common malignancies observed during pregnancy, with estimated incidences ranging from 0.8 to 1.5 per 10,000 births.[2] Most cases are diagnosed at an early stage of the disease due to frequent routine prenatal screenings.[3] Despite low pregnancy rates, particularly in advanced disease cases, the progression and prognosis of cervical cancer detected during pregnancy are similar to those of non-pregnant women for disease-free survival and overall survival.[3] Among women diagnosed with abnormal cervical cytopathology, the rate of development of high-risk HPV types is approximately 90%.[4]

Cervical lesions may be detected or palpated during a speculum examination at almost every week of gestation. Vigilance is necessary regarding ectropion, decidual alter-

ations, cyanosis, erythema, a sensitive cervical structure with fragile bleeding, vascular congestion in the pelvic area, cervical stromal oedema, cervical softening, prominence of vaginal rugae, fatal pressure, sensations of pressure from pregnancy products, and cervical maturation, which are typical physiological changes often seen during pregnancy. Screening and diagnostic tests should be conducted by proficient specialists in reputable facilities. It may lead to challenges and false positive results, particularly in the objective physiological evaluation of colposcopy.[5,6] In general, the management of pregnant women with abnormal cervical cytology is the same as for non-pregnant women. Nonetheless, conization by diagnostic excisional procedure including expedited treatments like LEEP, is unacceptable without prior colposcopy. Furthermore, endocervical curettage and endometrial biopsy should not be conducted as part of colposcopic evaluation. The endocervical canal can be gently sampled with a cytobrush.[5]

Conflicting reports exist regarding the natural history of cervical intraepithelial neoplasia (CIN) in pregnant women. Origoni et al.[6] reported that high-grade cervical intraepithelial lesions (HGSIL/CIN2-3) are exceedingly uncommon, with a rate of progression to invasive cervical cancer of 0.4%. Coppolillo et al.,[7] on the other hand, found that high-grade intraepithelial lesions of the cervix may progress at a rate of 13.3%, with a rate of progression to microinvasive cancer in four out of every 30 women.

In a separate study, spontaneous regression was observed in 16.7-69.3% of pregnant women with CIN 2/3 who did not receive any treatment after delivery.[8] To this end, there is evidence that the overexpression of sex hormones during pregnancy may promote cervical carcinogenesis by inducing squamous metaplasia in the transformation zone and modifying the local immune system. The enhanced regression may be attributed to the decrease in sex hormones following delivery.[9] The impact of the standard spontaneous vaginal delivery or the operative delivery method is not yet definitive.[10]

The objective of the study is to conduct a colposcopic assessment during the antenatal and postpartum phases in pregnant women with high-risk HPV positivity (type 16 and 18) and abnormal cervical cytopathological results, to meticulously analyse the histopathological findings, and to determine their impact on regression, persistence, or progression rates by comparing them with the postpartum period and mode of delivery.

MATERIALS AND METHODS

The study included 32 pregnant women who tested positive for HPV and exhibited abnormal cytological results in cervical uterine cancer screening conducted during routine antenatal follow-ups between 2022 to 2025. The data from the electronic archive system were retrospectively analysed in the study conducted with the approval of the Clinical Research Ethics Committee dated 18.04.2025 and numbered 4/5. In compliance with the Declaration of Helsinki, participants were apprised of the study, and informed consent was secured from all women for their participation.

Our study comprises cases of women who presented during pregnancy, had HPV and cervicovaginal smear tests at their first evaluation, and exhibited high-risk HPV positivity (type 16 and 18) and/or abnormal cytological changes. The study included cases over the age of 25 with HPV-positive, abnormal cytological results in cervical cancer screening tests conducted during pregnancy, who subsequently delivered via normal spontaneous vaginal delivery or caesarean section at term. Cases that were non-pregnant, exhibited normal cervical cytology, tested positive for low-risk HPV, and presented with invasive cancer histopathology, as well as those that were pregnant but experienced threatened abortion or vaginal bleeding, threatened premature birth or had a history thereof, displayed apparent benign or malignant mass lesions in the vulva, vagina, and cervix upon speculum examination, and declined follow-up or colposcopic evaluation were excluded from the study. Cases inaccessible for cytological and histopathological results during the postpartum period, together with those with insufficient birth information, were excluded from the study.

For individuals aged 25 and older who are pregnant, high-risk HPV positive, and exhibit abnormalities in smear cytology, a biopsy was performed on the most suspicious area of the cervix uteri using biopsy forceps when a suspicious lesion or significant finding indicative of invasion was identified during pregnancy via colposcopy. Colposcopic examination of 32 pregnant cases was performed in the gynecological lithotomy position. Since the active and original squamocolumnar junction and the transformation zone between the two regions were clearly observed in the cervix uteri examination of all cases, our colposcopic care was considered sufficient.

Cytological and pathological evaluations were conducted by pathologists specializing in gynaecological oncology. Subsequent treatment decisions were predicated on cytological data, HPV testing, and histological findings. Data from all pregnant women were gathered retrospectively. All cases were monitored every six weeks throughout the course of pregnancy. The decision concerning the birth method was made routinely based on the delivery methods of prior pregnancies or standard follow-up until the 40th week in first pregnancies. The initial follow-up occurred six weeks post-delivery.

The cervical cytology test was SurePathTM (BD SurePath™Liquid-Based Cytology test), while the HPV test was Hybrid capture 2 (digeneR Hybrid capture 2 HPV DNATest (QIAGE, Germantown, MD, USA). The Bethesda 2001 classification was employed to evaluate cytological evaluations.

Not all pregnant cases who underwent colposcopic ex-

aminations and biopsies underwent endocervical curettage (ECC). All cases were monitored until 37 weeks and above term delivery weeks and until 6 weeks postpartum. The study included cases of normal spontaneous vaginal delivery or caesarean delivery at term.

The study aimed to evaluate age, gravida, parity, gestational week at delivery, BMI, smoking history, alcohol consumption status, gestational weeks, HPV vaccination status, HPV types, smear cytology, delivery types, and colposcopic assessment, as well as to compare histopathological and cytological results during pregnancy and at six weeks postpartum.

The objective of this retrospective analysis was to compare pregnant women who were diagnosed with abnormal cytology and histopathology in the cervix based on various variables, such as pregnancy period, postpartum period, and delivery methods.

The term "regression of lesions" refers to the identification of a lower-grade lesion in the postpartum period (6 weeks after delivery) compared to the initial examination. Persistence was defined as the identification of a cervical intraepithelial neoplasia (CIN) lesion of the same grade as at the initial diagnosis during the postpartum histopathological evaluation. Histological evidence of a higher grade of CIN or cancer on colposcopic examination and biopsy at 6 weeks after delivery in comparison to the antenatal biopsy was used to define disease progression.

In all cases, the antenatal period and postpartum period were compared and the persistence, the persistence, regression, and progression rates were assessed based on the histological findings obtained from the biopsy samples. The colposcopic examination, biopsy, and cervical cytology test were conducted again after the sixth week postpartum to diagnose regression, progression, and persistence in the patients. The results were compared between the antenatal and postpartum periods. Furthermore, the objective was to conduct a cytological and histopathological comparison of the lesions in the cervix in accordance with the delivery methods.

Statistical Methods

Data analysis was performed using IBM SPSS Statistics 26. Categorical independent variables were presented as frequencies and percentages with cross-tables, and their distributions were compared using the "Chi-Square" test and "Fisher's Exact" test. The "Mc Nemar" test was used to determine whether there was a difference in terms of dependent categorical variables. The "Shapiro-Wilk" test was applied to continuous variables, and it was seen that they did not meet the "Normal Distribution" conditions. Comparisons of independent groups were performed using the nonparametric "Mann-Whitney U" test, and median min and max values were presented. In all statistical comparison tests, type-I error was determined as α=0.05 and two-tailed tests were performed.

RESULTS

The average age of the 32 cases in our study was 29.8±2.7 years, with the youngest participant being 26 years old and the oldest pregnant woman being 36 years old. The average body mass index (BMI) was 28.5±6.6, with values ranging from 18.3 to 41.2.

The most common HPV types are 16 and 18, accounting for around 68.7% of cases. According to the colposcopic examination and biopsy results of the cases with high-risk HPV positive and abnormal findings in smear cytology, dysplasia was detected in 23 cases in 72% (CIN3 in 6%, CIN2 in 19% and CIN1 in 47%). The colposcopic evaluation and biopsy conducted at six weeks postpartum revealed a dysplasia rate of 59% in 19 cases (25% CIN2, 34% CIN1), with no cases of CIN3 found, and a regression of dysplastic lesions was noted. Cervical cytology indicates that HGSIL and ASC-H lesions during the antenatal period have regressed compared to cytology obtained at six months postpartum (13% vs. 9% and 6% vs. 3%) (Table 1).

Upon comparing cases of varying degrees of cervical intraepithelial neoplasia (dysplasia) with cases without of dysplasia following colposcopic biopsy at six weeks postpartum, no statistically significant differences were found in age, BMI, gravida, parity, gestational weeks, and types of birth. In the dysplasia group, the BMI value was slightly elevated (30.2 compared to 28.6), but no statistically significant difference was noted (Table 2).

Upon comparison of the colposcopic biopsy results at the sixth postpartum week, it was shown that regression rates were higher in the group without dysplasia (38% vs. 21%), while progression rates were lower (0% vs. 16%). The smear cytology conducted at the sixth postpartum month indicated that the NILM (Negative Intraepithelial Lesion or Malignancy) or healing rates were much higher at 46% compared to 11% in the group without dysplasia, with a statistically significant difference detected between the two groups (p=0.038) (Table 3).

Upon comparison of the colposcopic biopsy results from the antenatal and postpartum periods, it was noted that 1 of 9 cases without dysplasia exhibited progression to CIN 1, 8 of 15 CIN 1 cases demonstrated persistence, 2 progressed, and 5 regressed. Additionally, 4 of 6 CIN 2 cases showed persistence while 2 regressed, and all CIN 3 cases regressed, subsequently categorizing them within the CIN 2 group (Table 4).

Upon comparing the cytological results collected during the antenatal period with those from cervical cytology obtained at six months postpartum, it was observed that 6 out of 12 ASCUS cases regressed to the negative (NILM) group, 5 cases persisted, and 1 case progressed to the LGSIL group. One case in the LGSIL group progressed to the HGSIL group; however, no invasive carcinoma progression was noted in the HGSIL and ASC-H groups, and 75% of the lesions regressed to low-grade lesions (Table 5). Upon comparing the colposcopic evaluation and biopsy

Table 1. Demographic, clinical and histopathological features of the cases

	Mean±SD	Median (Min-Max)
Age	29.8±2.7	30 (26-36)
BMI	28.5±6.6	29.5 (18.3-41.2)
Gravida	2.3±1.4	2 (1-5)
Parity	1±1.1	1 (0-4)
Pregnancy Week	14.7±8.2	11 (6-34)
Delivery Weeks	38.2±1.4	38 (36-42)
	N	%
Education		
University	1	3
High School	9	28
Primary School	19	59
Not	3	9
Co-morbidity		
Yes	3	9
No	29	91
Smoke		
Yes	14	44
No	18	56
Alcohol		
Yes	9	28
No	23	72
Abortion		
Yes	9	28
No	23	72
Delivery Type		
CS	16	50
NSVD	16	50
HPV Vaccination		
Not	32	100
HPV DNA		
HPV type 16	16	50
HPV type 18	6	18.7
Others	32	31.3
Colposcopy (Antenatal)		
Cin 3	2	6
Cin 2	6	19
Cin 1	15	47
No Dysplasia	9	28
Colposcopy (Antenatal)		
Dysplasia	23	72
No Dysplasia	9	28
Colposcopy (PP 6th Week)		
Cin 2	8	25
Cin 1	11	34
No Dysplasia	13	41
Colposcopy (PP 6th Week)		
Dysplasia	19	59
No Dysplasia	13	41
Recovery (PP 6th Week)		
Regression	9	28
Persistent	20	63
Progression	3	9
Cytology (Antenatal)		
ASCUS	12	38
LGSIL	14	44
HGSIL	4	13
ASC-H	2	6
Cytology (PP 6th Month)		
ASCUS	9	28
LGSIL	11	34
HGSIL	3	9
ASC-H	1	3
NILM	8	25
Cytology (PP 6th Month) NILM		
Yes	8	25
No	24	75
ECC (PP 6th Week)		
Chronic cervicitis	18	56
LGSIL	14	44

Table 2. Risk factors for dysplasia in colposcopic biopsy at 6th postpartum week

	Colposcopy (PP 6th Week)				
	Dysplasia		No Dysplasia		P*
	Median	(Min-Max)	Median	(Min-Max)	
Age	30	(26 - 36)	30	(26 - 35)	0.892
BMI	30.2	(19.2 - 38.5)	28.6	(18.3 - 41.2)	0.744
Gravida	2	(1 - 5)	2	(1 - 5)	0.952
Parity	1	(0 - 4)	1	(0 - 3)	0.745
Pregnancy Week	10	(6 - 33)	12	(8 - 34)	0.408
Delivery Weeks	38	(36 - 42)	38	(36 - 40)	0.567

Table 3. Risk factors for dysplasia in colposcopic biopsy at 6th postpartum week (continued)

	Colposcopy (PP 6th Week)				P*
	Dysplasia		No Dysplasia		
	N	%	N	%	
Comorbidity					
Yes	2	11	1	8	1.000
No	17	89	12	92	
Smoke					
Yes	11	58	3	23	0.112
No	8	42	10	77	
Alcohol					
Yes	6	32	3	23	0.704
No	13	68	10	77	
Abortion					
Yes	5	26	4	31	1.000
No	14	74	9	69	
Colposcopy (Antenatal)					
Cin 3	2	11	0	0	NA
Cin 2	6	32	0	0	
Cin 1	10	53	5	38	
No Dysplasia	1	5	8	62	
Colposcopy (Antenatal)					
Dysplasia	18	95	5	38	0.180[M]
No Dysplasia	1	5	8	62	
Delivery Type					
CS	9	47	7	54	1.000
NSVD	10	53	6	46	
Natural History (PP 6th Week)					
Regression	4	21	5	38	NA
Persistent	12	63	8	62	
Progression	3	16	0	0	
Cytology (Antenatal)					
ASCUS	3	16	9	69	NA
LGSIL	10	53	4	31	
HGSIL	4	21	0	0	
ASC-H	2	11	0	0	
Cytology (PP 6th Month)					
ASCUS	4	21	5	38	NA
LGSIL	9	47	2	15	
HGSIL	3	16	0	0	
ASC-H	1	5	0	0	
NILM	2	11	6	46	
Cytology (PP 6th Month) NILM					
Yes	2	11	6	46	**0.038**
No	17	89	7	54	
ECC (PP 6th Week)					
C. Cervicitis	8	42	10	77	0.112
LGSIL	11	58	3	23	

*Chi-Square or Fisher's Exact Test. M= McNemar TestHPV: Human papillomavirus; PP: Postpartum; NILM: Negative Intraepithelial Lesion or Malignancy; NSVD: Normal Spontaneous Vaginal Delivery; CIN: Cervical Intraepithelial Neoplasia; ASCUS: Atypical Squamous Cells of Udetermined Significance; LGSIL: Low-grade squamous intraepithelial lesion; HGSIL: High-grade squamous intraepithelial lesion; ASC-H: Atypical squamous cells; CS: Cesarean delivery.

Table 4. Comparison of antenatal and postpartum 6th week colposcopic biopsy results

	Colposcopy (Antenatal)									
	No Dysplasia		Cin 1		Cin 2		Cin 3		Overall	
	N	%	N	%	N	%	N	%	N	%
Colposcopy (PP 6th Week)										
No Dysplasia	8	89	5	33	0	0	0	0	13	41
Cin 1	1	11	8	53	2	33	0	0	11	34
Cin 2	0	0	2	13	4	67	2	100	8	25
Overall	9	100	15	100	6	100	2	100	32	100

CIN: Cervical Intraepithelial Neoplasia.

Table 5. Comparison of antenatal and postpartum 6th week cervical cytology results

	Cytology (Antenatal)									
	ASCUS		LGSIL		HGSIL		ASC-H		Overall	
	N	%	N	%	N	%	N	%	N	%
Cytology (PP 6th Month)										
NILM	6	50	2	14	0	0	0	0	8	25
ASCUS	5	42	3	21	1	25	0	0	9	28
LGSIL	1	8	8	57	2	50	0	0	11	34
HGSIL	0	0	1	7	1	25	1	50	3	9
ASC-H	0	0	0	0	0	0	1	50	1	3
Overall	12	100	14	100	4	100	2	100	32	100

HPV: Human papillomavirus; PP: Postpartum; NILM: Negative Intraepithelial Lesion or Malignancy; NSVD: Normal Spontaneous Vaginal Delivery; CIN: Cervical Intraepithelial Neoplasia; ASCUS: Atypical Squamous Cells of Udetermined Significance; LGSIL: Low-grade squamous intraepithelial lesion; HGSIL: High-grade squamous intraepithelial lesion; ASC-H: Atypical squamous cells.

Table 6. Comparison of postpartum 6th week natural history histological results according to delivery types

	Delivery Type					
	CS		NSVD		Overall	
	N	%	N	%	N	%
Natural history (PP 6th Week)						
Regression	3	19	6	38	9	28
Persistent	12	75	8	50	20	63
Progression	1	6	2	13	3	9
Overall	16	100	16	100	32	100

NSVD: Normal Spontaneous Vaginal Delivery; CS: Cesarean delivery.

results from the 6th week postpartum with those from the antenatal period, it was noted that 9% of cases progressed, 63% persisted, and 28% regressed. Upon examining the impact of the delivery method on histopathological results and associated rates, it was observed that the regression rate was 38% in 6 cases of normal spontaneous vaginal delivery and 19% in 3 cases of caesarean delivery, with significantly higher regression rates following normal delivery. Given the limited number of cases, it was noted that the persistence rates were elevated in caesarean deliveries compared to vaginal deliveries (75% vs. 50%), while the progression rates lowered (6% vs. 13%) (Table 6).

DISCUSSION

Upon examination of the overall findings of our study, the smear cytology performed at six months postpartum revealed that the NILM (Negative Intraepithelial Lesion or Malignancy) or healing rates were higher in the group without dysplasia compared to the group with dysplasia, at 46% versus 11%, and a statistically significant difference was observed between the two groups (p:0.038). Upon comparison of the colposcopic evaluation and biopsy data obtained at the sixth week postpartum with those from the antenatal period, it was noted that 9% of cases exhibited progression, 63% shown persistence, and 28% showed regression. Upon examining the impact of the delivery method on histopathological results and associated rates, it was observed that the regression rate was 38% in 6 cases of normal spontaneous vaginal delivery and 19% in 3 cases of caesarean delivery, and that the regression rates after normal delivery were significantly higher. Given the limited number of cases, it was observed that the persistence rates were higher in caesarean deliveries compared to vaginal deliveries (75% vs. 50%), while the progression rates were lower (6% vs. 13%).

In non-pregnant women, the diagnosis and treatment of HGSIL (CIN2/3) are well-defined; nonetheless, apprehensions persist due to a lack of data about diagnosis and treatment during the antenatal period. It is particularly stated in every study in the literature that it would be more appropriate to treat in the postpartum period, but that much more research is still required to facilitate the necessary diagnosis and treatment. In general, retrospective studies reveal that the regression rates of CIN2-3, particularly in the postpartum period, range from 16.7% to 69.3%, and the persistence rates range from 26.8% to 70%. However, these results are not highly consistent, and their lower and upper limits may vary depending on the demographic, cytological, and histopathological data of the population in which the studies were conducted.[8] In another cohort study examining pregnant and non-pregnant individuals, the spontaneous regression rates of CIN lesions were 56.9% in pregnant cases and 31.4% in non-pregnant cases, with no statistically significant difference detected between the two groups (p=0.144); however, regression rates were higher in pregnant cases.[11] In a systematic review study, it was stated that regression rates in clinical follow-up of CIN 2 lesions in non-pregnant women were as high as 60%, and especially in young women, regression rates were more common and higher under surveillance with conservative treatments, and progression rates were extremely rare. During the one-year follow-up after a CIN 2 diagnosis, the combined regression rates were around 46%, whereas progression rates were about 14%. It has been stated that progression rates are much lower in high-risk HPV negative cases and regression rates are lower at around 40% in high-risk HPV positive cases within 24 months.[12] In our study, the most common HPV types were 16 and 18, and all cases were positive for high-risk HPV types. Despite this, our persistence and progression rates were observed in accordance with the literature. In another study conducted on pregnant women, CIN2-3 was diagnosed in 46% of the antenatal period, and in their colposcopic evaluation and histopathological examination at the 8th week postpartum, regression was observed in 38%, progression in 1.6%, and persistence in 60%. And in a case with CIN 3 histopathology, microinvasive carcinoma was diagnosed in the conization pathology performed after caesarean delivery.[8]

Despite the fact that the natural history of CIN in pregnant women is not significantly different from that of non-pregnant women, there are several significant characteristics of CIN during pregnancy. It is exceedingly uncommon for CIN to progress to an invasive state during pregnancy. Most cases persist, while a significant number of them regress.[13] The overall regression rate for CIN during pregnancy has been estimated to be as high as 76% for low-grade squamous intraepithelial lesions (LSILs) and up to 59% for HSILs.[14-18] The regression rate of CIN during pregnancy is generally accepted to be significantly higher than that of non-pregnant women, despite the occurrence of some heterogeneous results.[16]

Regression rates are higher (63%-76%) for LSIL/CIN 1 that occurs during pregnancy, while progression rates are lower (6%-8%). The overall regression rate for HSIL (CIN 2/CIN 3) during pregnancy is 29%-59%.[14,18] CIN 2 exhibited a significantly higher regression rate relative to CIN 3 (59%-88% versus 21%-29%).[14,18] In our study, CIN 1 and CIN 3 lesions exhibited greater regression than CIN 2 lesions, in contrast, CIN 2 lesions shown to progress to CIN 3. Nonetheless, we would like to highlight that generalization is challenging due to the limited number of cases, and the results may vary with extended follow-up.

In a separate study, most regression in abnormal cytopathological lesions identified during the antenatal period tends to occur within the first two years post-birth. When we look at the rates, it was seen that the regression rates of the lesions were 68-70% in the first two years after CIN2 and 3 diagnosed during pregnancy.[17] The progression rates of cervical intraepithelial lesions, a biggest problem for women's health, to invasive cancer are approximately 1% and notably low during pregnancy; hence, more conservative treatment approaches may be favoured in the management of CIN, particularly during pregnancy.[16] In our study, the comparison of histopathology results from the antenatal period and the sixth week postpartum revealed regression rates of 28%, persistence rates of 63%, and progression rates of 9%. Although existing studies in the literature did not provide information about HPV status, it was observed that the rates of progression and persistence remained low, despite all cases in our study being positive for high-risk HPV.

High regression rates of HGSIL (CIN2-3) lesions have been reported during the antenatal period. It is stated that regression rates are notably higher following normal spontaneous vaginal delivery in comparison to caesarean delivery rates (67% vs. 13%). It is stated that physiological trauma

during normal labour, cervical ripening, inflammatory reaction in the cervix uteri epithelial structure and the reparative structure of the cytokines migrating here and the change in the cervical mucus structure help to renew the dysplastic cervix epithelial structure.[6,19] It has been proposed that ischemia alterations resulting from the pressure exerted by the fatal head and other pregnancy products on the cervix uteri during vaginal delivery may lead to the regression of dysplastic epithelium and the creation of a new epithelial structure.[6] There are studies that have discovered a high regression rate of 70% for HGSIL lesions, irrespective of the normal or operative delivery method. Consequently, there is no correlation between the delivery method and dysplastic epithelial regression.[11,20]

The mechanism of CIN regression, which is prevalent during pregnancy, is not yet completely comprehended. Pregnancy-induced immunological alterations, inflammatory processes, and cervical repair associated with delivery are among the hypotheses that have been proposed. Cervical trauma and subsequent repair during vaginal delivery have been posited to contribute to regression, with several studies supporting the fact that regression is more prevalent in vaginal deliveries.[14,21]

Our study indicates that the rates of CIN regression following normal delivery are twice as high as those following caesarean delivery. The persistence rates following both normal and caesarean deliveries align with existing literature, and we believe that progression rates are elevated in caesarean deliveries because to the limited number of cases. We could state that as the number of cases increases, these rates may also be consistent with the literature in favor of normal delivery.

Pregnant individuals with histologically proven CIN 2 or CIN 3 should undergo active surveillance with repeat colposcopy every 12 to 24 weeks. Postponing colposcopy till after delivery is permissible.[5] Histological treatment for HSIL is not advised. Diagnostic excisional procedures or repeat biopsies should be deferred until post-delivery unless carcinoma is detected.[5] Our study revealed no increase in the rates of progression, preinvasive, or invasive cancer diagnoses in antenatal and postpartum Pap smear testing and colposcopic biopsy results. This result indicates that patients should not hesitate to undergo vaginal speculum examinations, colposcopic evaluations, or biopsies during pregnancy due to concerns such as embarrassment, fear, or potential complications etc. It is advisable to adopt a conservative approach, relying solely on observation during pregnancy, and to conduct necessary invasive procedures six weeks postpartum.

The retrospective form of our study, coupled with a restricted number of patients and a brief follow-up time, shows its limitations. A further restriction is that pregnant women are more likely to take part in cytology screening programs compared to non-pregnant women. This may suggest that our HPV and cytological diagnosis rates surpass those of the non-pregnant routine female population, resulting in the detection of more early lesions.

Nonetheless, the presence of high-risk HPV positivity and abnormal smear cytology in all pregnant women, the comprehensive follow-ups conducted during antenatal and postpartum periods, the inclusion of all birth types, and the evaluation of cytology and histopathology by the same pathologist in a specialized gynaecologic oncology laboratory may exclude interobserver variability, thus underscoring a strength of our study. We believe that our findings possess clinical significance and can be interpreted in light of other studies reviewed in this report.

Conclusion

In summary, cervical cytology and/or HPV tests are essential components of routine prenatal care and remain a crucial aspect of cervical cancer screening in pregnant women. Once invasive cervical cancer is ruled out during the antenatal period, conservative treatment of all identified cervical intraepithelial neoplasia lesions is deemed safe; however, a thorough postpartum assessment is advised irrespective of the method of delivery.

Ethics Committee Approval

The study was approved by the Osmaniye Korkut Ata University Clinical Research Hospital Ethics Committee (Date: 18.04.2025, Decision No: 4/5).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: İ.K., F.Ç.; Design: F.Ç., Ö.B.; Supervision: Ö.B.; Funding: F.Ç.; Materials: İ.K., F.Ç.; Data collection &/or processing: F.Ç., Ö.B.; Analysis and/or interpretation: İ.K., Ö.B.; Literature search: F.Ç.; Writing: F.Ç., Ö.B.; Critical review: İ.K., Ö.B.

Conflict of Interest

None declared.

REFERENCES

1. Creasman WT. Cancer and pregnancy. Ann NY Acad Sci 2001;943:281–6. [CrossRef]
2. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: Results of linkage with the California cancer registry. Am J Obstet Gynecol 2003;189:1128–35. [CrossRef]
3. Kaplan KJ, Dainty LA, Dolinsky B, Rose GS, Carlson J, McHale M, et al. Prognosis and recurrence risk for patients with cervical squamous intraepithelial lesions diagnosed during pregnancy. Cancer 2004;102:228–32. [CrossRef]
4. Liu Y, Ang Q, Wu H, Xu J, Chen D, Zhao H, et al. Prevalence of human papillomavirus genotypes and precancerous cervical lesions in a screening population in Beijing, China: Analysis of results from China's top 3 hospital, 2009–2019. Virol J 2020;17:104. [CrossRef]
5. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, et al; 2019 ASCCP Risk-Based Management Consensus Guidelines Committee. 2019 ASCCP Risk-Based Management Consensus Guidelines for abnormal cervical cancer screening tests and cancer

precursors. J Low Genit Tract Dis 2020;24:102–31. [CrossRef]
6. Origoni M, Salvatore S, Perino A, Cucinella G, Candiani M. Cervical Intraepithelial Neoplasia (CIN) in pregnancy: The state of the art. Eur Rev Med Pharmacol Sci 2014;18:851–60.
7. Coppolillo EF, DE Ruda Vega HM, Brizuela J, Eliseth MC, Barata A, Perazzi BE. High-grade cervical neoplasia during pregnancy: diagnosis, management and postpartum findings. Acta Obstet Gynecol Scand 2013;92:293–7. [CrossRef]
8. Grimm D, Lang I, Prieske K, Jaeger A, Müller V, Kuerti S, et al. Course of cervical intraepithelial neoplasia diagnosed during pregnancy. Arch Gynecol Obstet 2020;301:1503–12. [CrossRef]
9. Serati M, Uccella S, Laterza RM, Salvatore S, Beretta P, Riva C, et al. Natural history of cervical intraepithelial neoplasia during pregnancy. Acta Obstet Gynecol Scand 2008;87:1296–300. [CrossRef]
10. Schuster S, Joura E, Kohlberger P. Natural history of squamous intraepithelial lesions in pregnancy and mode of delivery. Anticancer Res 2018;38:2439–42. [CrossRef]
11. Mailath-Pokorny M, Schwameis R, Grimm C, Reinthaller A, Polterauer S. Natural history of cervical intraepithelial neoplasia in pregnancy: Postpartum histo-pathologic outcome and review of the literature. BMC Pregnancy Childbirth 2016;16:74. [CrossRef]
12. Tainio K, Athanasiou A, Tikkinen KAO, Aaltonen R, Cárdenas J, Hernándes, et al. Clinical course of untreated cervical intraepithelial neoplasia grade 2 under active surveillance: Systematic review and meta-analysis. BMJ 2018;360:k499. [CrossRef]
13. Kim JY, Shim JY. Cervical intraepithelial neoplasia and cervical cytology in pregnancy. J Pathol Transl Med 2024;58:283–90. [CrossRef]
14. Stuebs FA, Mergel F, Koch MC, Dietl AK, Schulmeyer CE, Adler W, et al. Cervical intraepithelial neoplasia grade 3: Development during pregnancy and postpartum. Arch Gynecol Obstet 2023;307:1567–72. [CrossRef]
15. Dasgupta S. The fate of cervical dysplastic lesions during pregnancy and the impact of the delivery mode: A review. Cureus 2023;15:e42100. [CrossRef]
16. Chen C, Xu Y, Huang W, Du Y, Hu C. Natural history of histologically confirmed high-grade cervical intraepithelial neoplasia during pregnancy: Meta-analysis. BMJ Open 2021;11:e048055. [CrossRef]
17. Ehret A, Bark VN, Mondal A, Fehm TN, Hampl M. Regression rate of high-grade cervical intraepithelial lesions in women younger than 25 years. Arch Gynecol Obstet 2023;307:981–90. [CrossRef]
18. Han B, Yuan M, Gong Y, Qi D, Jiang T, Li J, et al. The clinical course of untreated CIN2 (HPV16/18+) under active monitoring: A protocol of systematic reviews and meta-analysis. Medicine (Baltimore) 2023;102:e32855. [CrossRef]
19. Massad LS, Einstein MH, Huh WK, Katki HA, Kinney WK, Schiffman M, et al; 2012 ASCCP Consensus Guidelines Conference. 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2013;17:S1–27. [CrossRef]
20. Yost NP, Santoso JT, McIntire DD, Iliya FA. Postpartum regression rates of antepartum cervical intraepithelial neoplasia II and III lesions. Obstet Gynecol 1999;93:359–62. [CrossRef]
21. Chung SM, Son GH, Nam EJ, Kim YH, Kim YT, Park YW, et al. Mode of delivery influences the regression of abnormal cervical cytology. Gynecol Obstet Invest 2011;72:234–8. [CrossRef]

Yüksek Riskli HPV Pozitifliği ve Anormal Servikal Sitolojisi Olan Gebe Kadınlarda Antepartum ve Postpartum Dönemde Servikal İntraepitelyal Neoplazinin Doğal Seyri

Amaç: Gebelik sürecinde alınan serviks uteri kanser tarama testlerinden yüksek riskli human papillomavirüs (HPV) pozitif ve anormal servikal sitolojik testi (CVS) sonuçlarının kolposkopik değerlendirmesi ve antenatal ve postpartum dönemde sitolojik ve histopatolojik sonuçlarının karşılaştırılması amaçlandı.

Gereç ve Yöntem: 2022-2025 yılları arasında rutin antenatal takiplerinde alınan serviks uteri kanser tarama testlerinde HPV pozitif ve anormal sitolojik sonuçları olan 25 yaş üzeri 32 gebe çalışmaya dahil edildi. Çalışmamız gebelik sürecinde başvuran kadınlardan ilk muayenede HPV ve servikovajinal smear testi alınan ve sonuçlarında high risk HPV pozitif ve/veya anormal sitolojik değişiklikler olan olgulardan oluşmaktadır.

Bulgular: Çalışmamızın genel sonuçlarına bakıldığında; postpartum 6. ayda alınan smear sitolojisine göre displazi izlenmeyen grupta displazi izlenen gruba göre NILM (Negative intraepitelyal lezyon veya malignite) yani iyileşme oranlarının %46 ya karşılık %11 gibi daha yüksek olduğu ve iki grup arasında istatistiksel anlamlı farklılık izlendi (p=0.038). Postpartum 6. haftada yapılan kolposkopik değerlendirme ve alınan biyopsi sonuçlarının antenatal dönemde yapılan kolposkopik değerlendirme ve biyopsi sonuçları ile karşılaştırıldığında; tüm olguların %9'unun progrese, %63'ünün persiste kaldığı ve %28'inin ise regrese oldukları izlendi. Özellikle doğum şeklinin histopatolojik sonuçlara etkisi ve buna bağlı oranlara bakıldığında ise normal spontan vajinal doğumda 6 olguda %38 ve sezaryen doğumda ise 3 olgu %19 oranında regresyon oranlarını olduğu ve normal doğum sonrası regresyon oranlarının anlamlı yüksek olduğu görüldü.

Sonuç: Gebelik sürecinde alınan ve yüksek risk HPV pozitif ve/veya anormal sitolojik test sonuçlarına göre olgulara kolposkopik değerlendirilmesinin yanı sıra gebelik sürecinde sadece konservatif yaklaşım ve postpartum dönemde kolposkopi ve biyopsi yaklaşımı rahatlıkla yapılabilir.

Anahtar Sözcükler: Antenatal dönem; human papillomavirüs; kolposkopi; postpartum dönem; servikal sitoloji.

SCIE DOI: 10.14744/scie.2025.22605
South. Clin. Ist. Euras. 2025;36(3):267-272

Original Article

Evaluation of The Patients Diagnosed with Urinary Stone Disease in Our Pediatric Nephrology Clinic

İrem Ünal,[1] Nuran Küçük,[2] Nahide Haykır Zehir,[2] Yasemin Akın[2]

[1]Department of Neonatology, Sancaktepe Prof. Dr. Ilhan Varank Training and Research Hospital, Istanbul, Türkiye
[2]Department of Pediatrics, Kartal Dr. Lutfi Kirdar City Hospital, Health Sciences University, Istanbul, Türkiye

Submitted: 14.05.2025
Revised: 28.06.2025
Accepted: 03.07.2025

Correspondence: İrem Ünal, Department of Neonatology, Sancaktepe Prof. Dr. Ilhan Varank Training and Research Hospital, Istanbul, Türkiye
E-mail: driremunal37@gmail.com

Keywords: Metabolic disorder; pediatric nephrology; urinary stone disease.

ABSTRACT

Objective: Our study aimed to evaluate the demographic characteristics, clinical presentations, metabolic disorders, radiological findings, and treatment outcomes of pediatric patients diagnosed with urinary stone disease in a pediatric nephrology outpatient clinic.

Methods: A retrospective, descriptive study was conducted involving 256 pediatric patients aged between 0-18 years, diagnosed with urinary stone disease from January to December 2016. Clinical data, laboratory results, radiological findings, and treatments were collected from patient files and analyzed statistically.

Results: Among the patients, 52.3% were male, and the median age was 39.5 [15.0-87.0] months. The most common reason for presentation was known urinary stone disease follow-up (21.5%), followed by abdominal pain and restlessness. A positive family history of urinary stone disease was noted in 61.3%, and parental consanguinity was observed in 5.5%. Metabolic abnormalities were detected in 57% of cases, most frequently hypocitraturia (34.4%), hypercalciuria (20.7%), and hyperoxaluria (17.9%). Hypocitraturia was more prevalent in older children, while hypercalciuria was more common in infants. Medical treatment was initiated in 70.7% of patients, primarily with potassium citrate (69.1%). Surgical interventions included extracorporeal shock wave lithotripsy (12.6%), percutaneous nephrolithotomy (2%), and open surgery (3.1%).

Conclusion: Pediatric urinary stone disease commonly presents with metabolic disturbances, particularly hypocitraturia, and frequently involves familial predisposition. Early diagnosis through appropriate imaging and metabolic screening, followed by targeted medical management, is essential for preventing renal complications and reducing the need for surgical interventions.

INTRODUCTION

Pediatric urinary stone disease (USD) is the formation of stones in the urinary tract in children, mainly in the kidneys, ureters, or bladder. This clinical condition is prevalent among the paediatric population. The global prevalence of USD in children has been rising yearly, with the most significant increase among adolescents aged 10 to 14.[1] Over the past 25 years, the annual incidence of pediatric USD has grown globally from 6% to 0%.[1,2] Urinary stone disease has been identified as an endemic disorder in Türkiye, affecting 10% to 20% of the pediatric population.[3]

Socioeconomic, climatic, and dietary factors have been identified as the primary contributors to the prevalence of kidney stones.[4] Genetic and underlying systemic diseases have also been implicated in paediatric populations.[1,3] While USD is observed in children of all ages, the mean age at diagnosis is reported to be between 4.2 and 9.4 years.[5] Hereditary factors should be considered in children diagnosed outside this age range.[6]

While the etiology of USD in children is often not discernible, metabolic causes have been reported with increased frequency in recent years. The underlying metabolic disorder is present in at least 10-70% of children with USD.[5]

The absence of clarity regarding the classical signs and symptoms of USD in children, when compared with adults, results in delayed diagnoses, which can potentially lead to growth retardation, chronic pyelonephritis, or even end-stage renal disease.[3] In contrast, the incidence of chronic renal failure is highest in idiopathic calcium oxalate stones, inherited metabolic disorders such as adenine phosphoribosyltransferase (APRT) deficiency, cystinuria, Dent disease, familial hypomagnesemia with hypercalciuria and

nephrocalcinosis (FHHNC), and primary hyperoxaluria (PH) all frequently cause chronic kidney disease (CKD) and may progress to end-stage renal disease (ESRD).[7] Therefore, early identification, accurate diagnosis, and close clinical monitoring of patients with these inherited metabolic disorders are essential to reduce morbidity and prevent long-term renal complications.

Our study aimed to examine pediatric patients with USD who were followed up in our clinic for one year and to evaluate the frequency and various features.

MATERIALS AND METHODS

Study Design

This is a retrospective, observational, descriptive study conducted at the pediatric nephrology outpatient clinic.

Study Population

Our study included pediatric patients between 0 and 18 years of age diagnosed with USD based on clinical symptoms and confirmed by ultrasonography or other radiological imaging methods, between January 2016 and December 2016. Patients with incomplete data, prior genitourinary surgeries, or systemic diseases affecting calcium or oxalate metabolism were excluded from the analysis.

Ethical Approval and Informed Consent

Our study was conducted according to the Declaration of Helsinki. Ethical approval was obtained from the Kartal Dr. Lütfi Kırdar Training and Research Hospital Ethics Committee (No: 2017/514/104/4, Date: 28/03/2017).

Data Collection and Variables

Demographic characteristics such as age and sex, family history of USD, parental consanguinity, presenting symptoms, laboratory findings, metabolic evaluation results, stone location, imaging modalities, and treatment approaches were extracted from hospital records using a standardized data abstraction form.

Metabolic evaluation included 24-hour urine analyses, including calcium, oxalate, citrate, uric acid, and spot urine tests corrected for creatinine. Hypercalciuria, hyperoxaluria, hyperuricosuria, hypocitraturia, and cystinuria were defined according to standard pediatric reference ranges. The stone location was categorized as unilateral or bilateral.

Statistical Analysis

All statistical analyses were performed using the Jamovi program (Version 2.6) [Computer Software]. The variables were investigated using a visual histogram and Shapiro-Wilk's test to determine whether or not they were normally distributed. Descriptive analyses were presented using median and interquartile range for non-normally distributed data. Categorical variables were analyzed using the chi-square test. The one-way ANOVA test was used to compare multiple groups. P-values were adjusted using the Bonferroni correction method. A p-value <0.05 was considered statistically significant.

RESULTS

Among the 256 patients included in the study, urinary tract anomalies were identified in 22 patients (8.6%). Most patients (66.8%, n=171) had no comorbid conditions. Prematurity (6.3%), congenital heart disease (3.5%), growth retardation (2.3%), undescended testes (2.0%), and hypothyroidism (2.0%) were the most frequently observed associated conditions. Other systemic diseases were reported in 13.7% of the cohort (Table 1).

The most common reasons for admission were follow-up of previously diagnosed USD (21.5%), abdominal pain (10.5%), restlessness (8.6%), and hematuria (5.5%). Other complaints included urinary tract infection (3.9%), red discoloration or visible stones in the diaper (3.5%), urinary symptoms such as dysuria or incontinence (5.9%), and a smaller number of patients presented with fever, flank pain, or constipation. A considerable proportion of patients (27.8%) were diagnosed incidentally through abdominal or urinary tract ultrasonography performed for unrelated complaints. A statistically significant difference was found in symptom distribution across age groups ($p<0.0001$), with restlessness predominating in the 0–2 age group, hematuria in the 2–5 age group, and abdominal pain in children older than 5 years (Table 1).

Renal stones were localized to the left side in 105 patients (41.5%), the right side in 57 (22.5%), and bilaterally in 68 (26.9%) (Table 2). Renal ultrasonography revealed macrocalculi in 162 patients (63.3%), microcalculi in 60 (23.4%), and medullary nephrocalcinosis in 34 (13.3%). There was a statistically significant difference in stone size distribution across age groups ($p<0.001$) (Table 3).

Metabolic evaluation revealed hypocitraturia in 109 patients (50.7%), hyperuricosuria in 56 (28.3%), hyperoxaluria in 59 (28.2%), hypercalciuria in 56 (23.3%), and cystinuria in 2 patients (0.89%). Multiple abnormalities were noted in a subset of patients. Additional laboratory findings included proteinuria in 70 patients (30.7%), elevated spot urine Na/K ratio in 31 (21.2%), pyuria in 34 (13.2%), hematuria in 32 (12.5%), and positive urine cultures in 18 (7.1%). There were no statistically significant differences between age groups regarding the presence of hypercalciuria ($p=0.227$), hypocitraturia, hyperoxaluria, or cystinuria ($p>0.05$) (Table 4). The etiology of USD could not be identified in 47.7% (n=122) of the patients.

Of all patients, 154 (60.1%) received medical therapy, with potassium citrate being the most commonly prescribed agent. Surgical intervention was required in 45 patients (17.6%), including extracorporeal shock wave lithotripsy (12.6%), percutaneous nephrolithotomy (2%), and open surgery (3.1%) (Table 5).

Table 1. Demographic and clinical characteristics of pediatric patients with urinary stone disease

	n=256
Demographics	
Gender, n (%)	
Female	122 (47.7)
Male	134 (52.3)
Age, median [IQR]	39.5 [15.0-87.0]
Mode of delivery, n (%)	
Vaginal	183 (71.8)
Cesarean	72 (28.2)
Neonatal History, n (%)	
Prematurity	16 (6.3)
NICU admission	47 (18.4)
Oxygen therapy	31 (12.1)
Antibiotic therapy	35 (13.7)
Vitamin and Supplement, n (%)	
Usage of vitamin D	255 (99.6)
Duration of vitamin D use	
One year	255 (99.6)
Two years	1 (0.4)
Additional vitamin use	16 (6.3)
Additional medical conditions, n (%)	
None	171 (66.8)
Congenital heart disease	9 (3.5)
Growth retardation	6 (2.3)
Undescended testis	5 (2)
Hypothyroidism	5 (2)
Hemangioma	4 (1.6)
Cerebral palsy	3 (1.2)
Hydrocephalus	3 (1.2)
Autism	3 (1.2)
MTHFR gene mutation	3 (1.2)
Epilepsy	2 (0.8)
Myelomeningocele	2 (0.8)
Retinopathy of prematurity	2 (0.8)
Food allergy	2 (0.8)
Other Nephrology Conditions, n (%)	
None	228 (89)
UPJ obstruction	4 (1.6)
Polycystic kidney disease	3 (1.2)
Neurogenic bladder	3 (1.2)
CKD	2 (0.8)
Hydronephrosis	2 (0.8)
RTA type 2	2 (0.8)
Hypoplastic kidney	2 (0.8)
Renal agenesis	2 (0.8)
AME syndrome	2 (0.8)
Ectopic kidney	1 (0.4)
Megaureter	1 (0.4)
Horseshoe kidney	1 (0.4)
Single kidney	1 (0.4)
AKI	1 (0.4)
RTA Type 1	1 (0.4)
Solitary renal cyst	1 (0.4)
Congenital bladder cyst	1 (0.4)
Family History, n (%)	
Parental consanguinity	
None	242 (94.5)
2°	9 (3.5)
3°	3 (1.2)
4°	2 (0.8)
Family history of USD	
None	99 (38.7)
1°	53 (20.7)
2°	96 (37.5)
3°	8 (3.1)
Reason for Admission, n (%)	
Follow-up for known USD	55 (21.5)
Incidental US for non-nephrology reasons	37 (14.5)
US for other nephrological conditions	34 (13.3)
Abdominal pain	27 (10.5)
Restlessness	22 (8.6)
Hematuria	14 (5.5)
UTI	10 (3.9)
Vomiting	9 (3.5)
Red color or visible stones in the diaper	9 (3.5)
Urinary incontinence	7 (2.7)
Fever	6 (2.3)
Dysuria	5 (2)
Constipation	3 (1.2)
Foul-smelling urine	3 (1.2)
Flank pain	3 (1.2)

IQR: Interquartile range, NICU: Neonatal intensive care unit, MTHFR: Methylene tetrahydrofolate reductase, UPJ: Ureteropelvic junction, CKD: Chronic Kidney Disease, RTA: Renal Tubular Acidosis, AME: Apparent Mineralocorticoid Excess, AKI: Acute Kidney Injury, USD: Urinary Stone Disease, US: Ultrasonography, UTI: Urinary Tract Infection.

Table 2. Radiological findings of pediatric patients with urinary stone disease

Ultrasonography	
Renal stone, n (%)	
Right	57 (22.3)
Left	105 (41.0)
Bilateral	68 (26.6)
Renal stone maximum size, median [IQR]	
Right	3.00 [2.50-4.22]
Left	3.00 [2.37-4.07]
Medullary Nephrocalcinosis, n (%)	11 (4.3)
Ureteral stone, n (%)	11 (4.3)
Pelvicaliectasis, n (%)	25 (9.9)
Calycectasis, n (%)	23 (9.1)
Ureterectasis, n (%)	15 (5.9)
Direct urinary system radiography, n (%)	1 (0.4)

IQR: Interquartile range

Table 3. Age group–based distribution of renal stone size

n (%)	Macrocalculi	Microcalculi	Medullary	p
Total count	162 (63.3)	60 (23.4)	34 (13.3)	<0.012
<2 age	55 (34)	41 (68.4)	4 (11.8)	
2 to 5 age	39 (24)	8 (13.3)	5 (14.7)	
>5 age	68 (42)	11 (18.3)	25 (73.5)	

Table 4. Metabolic abnormalities identified in urinary stone disease according to age

n (%)	Total	<2 age	2 to 5 age	<5 age	p
Hypocitraturia	88 (34,4)	30 (34)	18 (20.5)	40 (45.5)	>0.1
Hypercalciuria	38 (14.8)	14 (36.8)	12 (31.6)	12 (31.6)	>0.1
Hyperoxaluria	16 (6.3)	6 (37.5)	6 (37.5)	4 (25)	>0.1
Cystinuria	2 (0.8)	1 (50)	0 (0)	1 (50)	>0.1
Cystinosis	2 (0.8)	1 (50)	1 (50)	0 (0)	>0.1

Table 5. Treatment modalities applied to pediatric urinary stone disease patients

n (%)	
Medical	181 (70.7)
Potassium citrate	177 (69.1)
Hydrochlorothiazide	2 (0.8)
Tiopronin	1 (0.4)
Cysteamine bitartrate	1 (0.4)
Surgery	45 (17.6)
Extracorporeal shock wave lithotripsy	32 (12.6)
Percutaneous nephrolithotomy	5 (1.9)
Open surgery	8 (3.1)

DISCUSSION

Our study gives pediatric USD by providing a detailed, age-specific analysis of clinical presentation, metabolic risk factors, stone characteristics, and treatment outcomes in a well-defined pediatric population from Türkiye, a known endemic region.

The existing literature shows that USD is more prevalent in males (3,13), while concurrent studies demonstrate a higher incidence of the condition in females.[5,8,9] In our study, the male-to-female ratio was 1.09, and USD was more prevalent in male subjects, consistent with the existing literature. As reported worldwide, urinary tract stones can occur at any age, with the mean age at diagnosis in children ranging from 7.3 to 9.4 years (spanning from 0.2 to 15 years).[7,10,11] Our study comprised 46.09% of subjects aged 0-2 years, 17.19% of subjects aged 2-5 years, and 36.72% of subjects aged over 5 years. The mean age of girls was 4.51±4.24 years, and the mean age of boys was 4.05±4.09.

A key distinguishing feature of our study is the age-related variability in symptomatology. We found that infants under two years old most commonly presented with restlessness or were asymptomatic, while in older children often reported abdominal or flank pain. The statistically significant age-related differences in presenting symptoms ($p<0.0001$) highlight the need for age-specific diagnostic awareness. Additionally, this pattern emphasizes the importance of being vigilant for urinary system disorders in young children who present with vague or behavioral symptoms.[12] Moreover, in 27.8% of patients, USD was diagnosed incidentally through imaging conducted for unrelated reasons. This finding aligns with literature emphasizing the role of ultrasonography in detecting asymptomatic stones due to its accessibility and safety.[13] Routine imaging in high-risk pediatric populations may facilitate early detection and timely intervention.

Metabolic risk factors were identified in 57% of our patients, supporting the idea that pediatric USD is often linked to underlying metabolic issues. Hypocitraturia was the most common abnormality in our cohort, surpassing hypercalciuria, which was traditionally considered the main metabolic etiology cause. This trend matches recent studies indicating a shift toward hypocitraturia as the leading risk factor in pediatric populations.[12] Hypercalciuria ranked second overall but was more common among infants, although this was not statistically significant, whereas hypocitraturia and hyperoxaluria were more common in older children. This age-related variation has also been seen in a national multicenter study by Başţuğ et al.,[3] which reported similar patterns. Additional findings included cases of hyperoxaluria, hyperuricosuria, and cystinuria. These findings highlight the need for comprehensive metabolic screening in all pediatric stone formers to enable timely diagnosis, targeted treatment, and prevention of recurrence.

Our study found that regarding stone size, 75.3% of patients had macrocalculi, while 24.7% had microcalculi. We observed that microcalculi were significantly more common in the 0–2-year age group (p=0.002), likely due to the increased use of high-resolution ultrasonography in young patients. This finding contrasts with the results of Melek et al.,[14] who reported that microcalculi were present in 35.8% of their patients. The lower rate of microcalculi in our cohort may be explained by differences in the definition threshold for stone size, operator dependency of ultrasonographic evaluation, or referral bias toward symptomatic patients with larger calculi. The higher frequency of microcalculi in younger children underscores the importance of early imaging. Therefore, early detection through routine ultrasonography in high-risk infants may allow for timely intervention or close monitoring, potentially avoiding the progression to clinically significant macrocalculi.

A positive family history, present in 61.3% of our patients, and parental consanguinity (5.5%) were notable risk factors. First-degree relatives accounted for 37.5% of familial cases. These findings parallel those of Amancio et al.,[15] who found familial clustering in 85% of cases, with 20.7% involving first-degree relatives. The concordance supports the theory that genetic predisposition, particularly when combined with metabolic abnormalities, plays a crucial role in pediatric USD.

Renal stones were observed in 89.8% of our patients, ureteral stones in 4.3%, and medullary nephrocalcinosis in 4.3%. No bladder or urethral stones were found. These findings differ from those of Ece et al.[5] and Amancio et al.,[15] who reported a higher frequency of lower urinary tract involvement. The predominance of renal localization in our cohort may be attributed to earlier detection through routine ultrasonography.

Our findings also reinforce the importance of metabolic evaluation, particularly in patients with a positive family history or consanguinity. Identification of correctable metabolic abnormalities allows for effective intervention, prevention of recurrence, and preservation of renal function. Regular follow-up and personalized management are essential components of care in pediatric USD.

Medical therapy was started in 70.7% of cases, mainly using potassium citrate (97.8%), reflecting its effectiveness in hypocitraturia, hyperuricosuria, and cystinuria. This is consistent with existing literature recommending potassium citrate for hypocitraturia and its benefits in other metabolic disorders, including hyperuricosuria and cystinuria.[3,16,17] Rare metabolic conditions such as cystinosis and cystinuria were managed with targeted agents like cysteamine and tiopronin. Our individualized treatment strategy-incorporating pharmacologic therapy, dietary counseling, and metabolic monitoring-may have contributed to reducing the need for invasive procedures.

This study has several limitations. First, its retrospective design restricts the ability to establish causality and is subject to potential biases related to data recording and completeness. Second, since it is a single-center study, the findings may not be generalizable to broader pediatric populations. Third, there was no availability of long-term follow-up data regarding stone recurrence, renal function outcomes, and treatment adherence, which prevents a thorough assessment of the effectiveness over time. Future prospective multicenter studies with longer observation periods are needed to address these limitations.

Conclusion

Our study contributes to the understanding of the multifactorial nature of pediatric USD in an endemic setting, with a focus on age-specific clinical features, metabolic risk factors, and family history. The prevalence of hypocitraturia, especially in older children, along with hypercalciuria in infants, may indicate a shifting metabolic profile that requires age-specific evaluation methods. Early imaging, particularly in high-risk or asymptomatic children, can detect microcalculi and help prevent disease progression. While further research is needed, our findings may support the utility of comprehensive metabolic screening and individualized treatment approaches in select patient populations. Although it is a retrospective, single-center study, it may offer valuable insights into the current landscape of pediatric USD and underscores the importance of early diagnosis and customized management to improve long-term kidney health.

Ethics Committee Approval

The study was approved by the Health Sciences University, Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (Date: 28.03.2017, Decision No: 2017/514/104/4).

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: İ.Ü., N.K., N.H.Z., Y.A.; Design: İ.Ü., N.K., N.H.Z., Y.A.; Supervision: İ.Ü., N.K., N.H.Z., Y.A.; Data collection &/or processing: İ.Ü.; Analysis and/or interpretation: İ.Ü., N.K.; Literature search: İ.Ü., N.K.; Writing: İ.Ü., N.K., N.H.Z., Y.A.; Critical review: İ.Ü., N.K., N.H.Z., Y.A.

Conflict of Interest

None declared.

REFERENCES

1. Zhang ZG, Lin QC, Zhou QY, Xu NF, Zheng DQ, Pan QZ, et al. Trend analysis of pediatric urolithiasis prevalence from 1990 to 2021 in the BRICS. Front Pediatr 2025;13:1551046. [CrossRef]
2. Tasian GE, Ross ME, Song L, Sas DJ, Keren R, Denburg MR, et al. Annual incidence of nephrolithiasis among children and adults in South Carolina from 1997 to 2012. Clin J Am Soc Nephrol 2016;11:488–96. [CrossRef]
3. Baştuğ F, Ağbaş A, Tülpar S, Yıldırım ZNY, Çiçek N, Günay N, et al. Comparison of infants and children with urolithiasis: A large case

series. Urolithiasis 2022;50:411–21. [CrossRef]
4. Bush NC, Xu L, Brown BJ, Holzer MS, Gingrich A, Schuler B, et al. Hospitalizations for pediatric stone disease in United States, 2002-2007. J Urol 2010;183:1151–6. [CrossRef]
5. Ece A, Ozdemir E, Gürkan F, Dokucu AI, Akdeniz O. Characteristics of pediatric urolithiasis in south-east Anatolia. Int J Urol 2000;7:330–4. [CrossRef]
6. Sarica K. Pediatric urolithiasis: Etiology, specific pathogenesis and medical treatment. Urol Res 2006;34:96–101. [CrossRef]
7. Edvardsson VO, Goldfarb DS, Lieske JC, Beara-Lasic L, Anglani F, Milliner DS, et al. Hereditary causes of kidney stones and chronic kidney disease. Pediatr Nephrol 2013;28:1923–42. [CrossRef]
8. Sas DJ, Becton LJ, Tutman J, Lindsay LA, Wahlquist AH. Clinical, demographic, and laboratory characteristics of children with nephrolithiasis. Urolithiasis 2016;44:241–6. [CrossRef]
9. Walton RF, Yeh C, Shannon R, Rosoklija I, Rague JT, Johnson EK, et al. Variation in care between pediatric and adult patients presenting with nephrolithiasis to tertiary care pediatric emergency departments in the United States (2009-2020). J Pediatr Urol 2022;18:742.e1–e11. [CrossRef]
10. Ozokutan BH, Küçükaydin M, Gündüz Z, Kabaklioğlu M, Okur H, Turan C. Urolithiasis in childhood. Pediatr Surg Int 2000;16:60–3. [CrossRef]
11. Erbagci A, Erbagci AB, Yilmaz M, Yagci F, Tarakcioglu M, Yurtseven C, et al. Pediatric urolithiasis--evaluation of risk factors in 95 children. Scand J Urol Nephrol 2003;37:129–33. [CrossRef]
12. Dönger U, İncekaş C, Gülleroğlu KS, Baskın E. Pediatric urinary stone disease: A 10-year single-center experience from Türkiye. Turk Arch Pediatr 2025;60:29–33. Erratum in: Turk Arch Pediatr 2025;60:247. [CrossRef]
13. Göktaş C, Horuz R, Akça O, Cetinel CA, Cangüven O, Kafkaslı A, et al. The effect of citrate replacement in hypocitraturic cases on the results of SWL: A preliminary prospective randomized study. Int Urol Nephrol 2012;44:1357–62. [CrossRef]
14. Melek E, Gülleroğlu KS, Bayrakçı US, Aygün C, Baskın E. Clinical and metabolic features of kidney stones in children. Turk J Pediatr Dis 2015;10:40–5. [CrossRef]
15. Amancio L, Fedrizzi M, Bresolin NL, Penido MG. Pediatric urolithiasis: Experience at a tertiary care pediatric hospital. J Bras Nefrol 2016;38:90–8. [CrossRef]
16. Lee ST, Cho H. Metabolic features and renal outcomes of urolithiasis in children. Ren Fail 2016;38:927–32. [CrossRef]
17. Spivacow FR, Negri AL, Polonsky A, Del Valle EE. Long-term treatment of renal lithiasis with potassium citrate. Urology 2010;76:1346–9. [CrossRef]

Pediatrik Nefroloji Polikliniğinde Üriner Sistem Taş Hastalığı Tanısı Alan Hastaların Değerlendirilmesi

Amaç: Bu çalışmada, pediatrik nefroloji polikliniğinde üriner sistem taş hastalığı tanısı alan çocuk hastaların demografik özelliklerinin, klinik başvuru şekillerinin, metabolik bozukluklarının, radyolojik bulgularının ve tedavi sonuçlarının değerlendirilmesi amaçlandı.

Gereç ve Yöntem: Bu retrospektif, tanımlayıcı çalışmaya, Ocak 2016 ve Aralık 2016 tarihleri arasında üriner sistem taş hastalığı tanısı alan 0–18 yaş arası 256 çocuk hasta dahil edildi. Hastaların klinik verileri, laboratuvar sonuçları, radyolojik bulguları ve uygulanan tedavi yöntemleri hasta dosyalarından elde edilerek istatistiksel olarak analiz edildi.

Bulgular: Hastaların %52.3'ü erkekti ve ortanca yaş 39.5 [15.0–87.0] ay olarak belirlendi. En sık başvuru nedeni bilinen taş hastalığı takibi (%21.5) olup bunu abdominal ağrı ve huzursuzluk izledi. Hastaların %61.3'ünde aile öyküsü pozitifti, %5.5'inde ise ebeveynler arasında akraba evliliği mevcuttu. Metabolik anormallikler olguların %57'sinde tespit edildi; en sık saptananlar hipositraturi (%34.4), hiperkalsiüri (%20.7) ve hiperoksalüri (%17.9) idi. Hipositraturi daha çok büyük çocuklarda, hiperkalsiüri ise bebeklerde daha yaygın olarak gözlendi. Hastaların %70.7'sine medikal tedavi başlandı ve bunların %69.1'inde potasyum sitrat kullanıldı. Cerrahi girişimler arasında ekstrakorporeal şok dalga litotripsi (%12.6), perkütan nefrolitotomi (%2) ve açık cerrahi (%3.1) yer aldı.

Sonuç: Pediatrik üriner sistem taş hastalığı sıklıkla metabolik bozukluklarla, özellikle hipositraturi ile ilişkili olup ailevi yatkınlık gösterebilir. Uygun görüntüleme ve metabolik tarama ile erken tanı konulması, ardından hedefe yönelik medikal tedavinin başlanması, renal komplikasyonların önlenmesi ve cerrahi girişim gereksiniminin azaltılması açısından önemlidir.

Anahtar Sözcükler: Metabolik bozukluk; pediatrik nefroloji; üriner sistem taş hastalığı.

SCIE DOI: 10.14744/scie.2025.60963
South. Clin. Ist. Euras. 2025;36(3):273-278

Original Article

The Newborn Outcomes Following HFNCO in Term Parturients Undergoing Caesarean Section: A Prospective Randomized Study

Hatice Durmuş,[1] Mehmet Yılmaz,[2] Emine Yurt,[2] Ayse Zeynep Turan Cıvraz,[2] Ayten Saracoglu,[3] Bedirhan Günel,[2] Kemal Tolga Saracoglu[3]

[1]Department of Anesthesiology and Reanimation, Pursaklar State Hospital, Ankara, Türkiye
[2]Department of Anesthesiology and Reanimation, University of Health Sciences Kocaeli City Hospital, Kocaeli, Türkiye
[3]Department of Anesthesiology, University of Florida UF Health College of Medicine, Jacksonville, USA

Submitted: 13.06.2025
Revised: 10.07.2025
Accepted: 07.08.2025

Correspondence: Bedirhan Günel, Department of Anesthesiology and Reanimation, University of Health Sciences Kocaeli City Hospital, Kocaeli, Türkiye
E-mail: bedirhangunel71@gmail.com

Keywords: Apgar score; cesarean section; high-flow nasal oxygenation; preoxygenation.

ABSTRACT

Objective: High-flow nasal oxygenation (HFNO) is a well-established preoxygenation technique in non-pregnant patients. However, its efficacy in term parturients remains uncertain, with some studies reporting suboptimal results. Moreover, data on neonatal outcomes in this population are limited. To evaluate the effects of HFNO on neonatal outcomes in parturients undergoing cesarean section under general anesthesia, focusing on Apgar scores as the primary outcome and umbilical cord venous blood gas parameters as the secondary outcome.

Methods: Following Ethics Committee approval and clinical trial registration (NCT03903003), 102 term parturients were randomized into two groups: HFNO (n=50) and conventional face mask preoxygenation (n=52). The HFNO group received oxygen at 60 L/min, while the conventional group received 100% oxygen at 10 L/min. Induction was initiated once end-tidal oxygen (etO_2) reached 90%, and oxygenation continued during intubation. Neonatal Apgar scores at 1 and 5 minutes, umbilical cord venous blood gas values, and maternal hemodynamic parameters were recorded.

Results: The HFNO group showed significantly higher Apgar scores at both 1 minute (9 (3-10) vs. 8 (3-10); p<0.001) and 5 minutes (10 (7-10) vs. 10 (4-10); p<0.001) compared to the conventional group. Cord venous blood gas parameters were comparable between the groups.

Conclusion: HFNO use for preoxygenation before and during induction in parturients undergoing cesarean section improved neonatal Apgar scores compared to conventional face mask oxygenation. These findings support HFNO as a safe and effective preoxygenation method in obstetric anesthesia.

INTRODUCTION

Pregnancy is characterized by respiratory and cardiovascular system changes. Functional residual capacity is decreased, and minute ventilation is increased in pregnant women. On the other hand, oxygen consumption is increased.[1] Therefore, airway management can become complicated.[2] The incidence of hypoxemia occurring during general anesthesia in pregnant women is common and can lead to serious fatal outcomes in both maternal and fetal terms. In a prospective multicenter study, preoxygenation was performed by giving oxygen with a flow of at least 12 L/min, and although induction was started after at least 90% FeO2 was reached, hypoxia during tracheal intubation was reported in 19% of the patients.[3] Besides, severe hypoxia was reported in 9.4% of the patients. In another study on parturients, it was reported that the incidence of severe hypoxia resulting in SpO_2 below 85% in induction was 2%.[4] Re-oxygenation after hypoxia brings the risk of aspiration pneumonia. The failure rate of preoxygenation with conventional methods has been reported as 30% in the non-pregnant population, and similarly 29% in the pregnant population.[5,6] The technique of applying preoxygenation with conventional methods in pregnant women is also controversial. It has been argued that four vital capacity breaths are effective.[7] On the other hand, it has been re-

ported that this is ineffective and requires eight vital capacity breaths.[8] The effectiveness of High-Flow Nasal Oxygenation (HFNO) for pre-oxygenation has been proven in non-parturient patients.[9] Its use is recommended during preoxygenation in the DAS difficult airway management guideline.[10] However, HFNO outcome in pregnant women are also controversial. In a study conducted in term parturients, a worse outcome was reported.[11] In another study, it was concluded that preoxygenation with HFNO is inadequate in term pregnant women and further studies are needed.[12] Au et al.[6] reported that the time period required for effective preoxygenation in parturients could not be determined. Our primary outcome measurement was the 1st and 5th min. Apgar scores in the newborn. Secondary outcome measurement was the intergroup comparison of cord blood gas analysis.

MATERIALS AND METHODS

This study protocol was reviewed and approved by Kocaeli University Clinical Research Ethics Committee (No: 2018/506, Date: 27/11/2018) Written informed consent was obtained from all participants prior to study enrollment. The study was conducted in accordance with the Declaration of Helsinki. This clinical trial was registered before patient enrollment.

This research is a prospective randomized study. Following the University Ethics Committee approval, the study was registered at clinical trials.gov (NCT03903003). The study was carried out on 106 term parturients undergoing elective caesarean section between January 1, 2019 and December 31, 2019. All patients provided written informed consent prior to enrollment, and the study was conducted in accordance with the principles of the Declaration of Helsinki. Inclusion criteria were the age between 18 and 40 years old, no known respiratory disorder, patients who refuse neuraxial block and are scheduled for elective surgery, American Society of Anesthesiologists risk score 2 and a gestational age between 37 and 41 weeks. Patients were randomized into two groups: Group 1 (HFNO, n=50) and group 2 (conventional, n= 52). Randomization was performed using Random Integer Generator software (https: www.random.org). While patients and anesthesiologists administering anesthesia were not blinded due to the nature of the intervention, the anesthesiologist responsible for evaluating the 1- and 5-minute Apgar scores and performing umbilical cord venous blood gas analysis remained blinded to group allocation to minimize assessment bias. Premedication was not administered. Patients' heads were elevated by 25° in the supine position. Preoxygenation was performed until the end-tidal oxygen (etO_2) level reached 90% in both groups. In Group 1 (HFNO), preoxygenation was initiated with the patients' mouths closed, using a fraction of inspired oxygen (FiO_2) of 1.0, a humidifier temperature of 37°C, and a flow rate of 20 L/min. The flow rate was gradually increased up to 60 L/min based on patient tolerance.

In Group 2 (conventional face mask), preoxygenation was performed with a tight-fitting oxygen face mask delivering 100% FiO_2 at a flow rate of 10 L/min, allowing spontaneous tidal volume breathing. Oxygenation continued until etO_2 reached 90% in both groups.

General anesthesia induction was performed with iv propofol 2.5 mg/kg, 1 mcg/kg fentanyl, 1,2 mg/kg rocuronium. Modified rapid sequence induction was performed.[13] Train of Four (TOF Watch) monitoring was performed at 1 Hz intervals, followed by tracheal intubation. Tracheal tube no. 6.5 or 7 mm were used by direct laryngoscopy. The time elapsed from the start of holding the laryngoscope until the end-tidal CO2 trace observation was recorded as the tracheal intubation duration. The patients were ventilated with a tidal volume of 6-8 mL/kg, a respiratory rate of 12/min, 6 cmH_2O PEEP and inspiration: Expiration ratio of 2. Maintenance was performed with sevoflurane 2% in a 50% mixture of oxygen and air. The demographic data and hemodynamic parameters were measured. Systolic blood pressure, diastolic blood pressure, heart rate, peripheral oxygen saturation values were recorded in preoxygenation phase, in preoperative period before induction and during the intraoperative period. Desaturation was defined as <95% according to the World Health Organization definition.[14] The 1- and 5-minute Apgar scores of the newborn were recorded. Umbilical cord venous blood gas analysis was recorded as pH, $PaCO_2$, PaO_2, HCO_3, lactate, base deficit and anion gap values.

Statistical Analysis

Mean, standard deviation, median, minimum, maximum, frequency and percentage values were used in the descriptive statistics of the data. The normality assumption of the continuous numerical variables was checked separately in the groups through Kolmogorov–Smirnov test. Independent sample t-test was used for the variables that were normally distributed while Mann-Whitney-U test was used for those that were not. Statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) package program. The significance level was determined as <0.05 for all analyses.

Sample size calculation

Power analysis of the study was performed through G Power 3.1.9.2 package program. In a confidence interval of 95%, the standard effect size of the study, which was conducted with 102 patients, was found to be 0.50 (effect size, medium level), the degree of freedom to be 1, and the power of the study to be 0.80.

RESULTS

A total of 5 patients were excluded from the study. One patient had a BMI>35, two patients had history of diabetes mellitus type 2 and two patients refused to participate. In total, data from 102 patients were analyzed.

The demographic data of groups were similar (p>0.05). The gestational age values of the groups were not found similar (p=0.001, Table 1). The tracheal intubation duration and newborn weights of the groups were found to be statistically similar (p=0.575 and p=0.397, respectively). Both 1st and 5th min Apgar scores were found significantly higher in HFNO group (p<0.001; p=0.001, respectively, Table 2). In cord venous blood gas analysis comparison, pH, PaO_2, $PaCO_2$, lactate and base deficit values were found statistically similar (Table 3).

Desaturation was not observed in any patients during laryngoscopy. The basal SPO_2 values and the SPO_2 values at the end of preoxygenation period were similar in both groups. The basal heart rates of parturients were statistically similar. The heart rates and maternal systolic blood pressure values of groups were similar before and after preoxygenation period. Before and after preoxygenation maternal diastolic blood pressure was found significantly higher in the HFNO group (Table 4).

DISCUSSION

In this prospective randomized study, we compared the effectiveness of preoxygenation through HFNO with conventional oxygen face mask in patients undergoing elective caesarean section. Maternal hemodynamic variables and cord blood venous gas analysis did not change, however both 1st and 5th min Apgar scores were found to be significantly higher in high-flow oxygenation group.

Extending the apneic period with high-flow oxygenation is successfully applied in pregnant women.[15] To the best of our knowledge, this study is the first to investigate the effects of high-flow oxygenation on fetus. Both high-flow oxygenation prevented the development of maternal desaturation, and provided better outcome in newborns. Siriussawakul et al.[16] administered oxygen to parturients using a nasal cannula with 3 L/min flow, and umbilical cord venous blood gases and Apgar scores in newborns did not show a significant difference when compared to pregnant women breathing room air. However, this study was performed in

Table 1. Demographic data of groups

	HFNO Group (n:50)	Conventional Group (n:52)	p*-value
Age (year)	29.50 (18-40)	30 (20-43)	0.976^{m}
BMI (kg/m^2)	30 (25-33)	31 (26-38)	0.146^{m}
Gestational age (week)	39 (28-40)	38 (38-40)	**0.001**^{m*}

BMI: Body Mass Index. Data are presented as median (minimum–maximum). ^{m}: Mann-Whitney U test *p<0.05 was considered statistically significant.

Table 2. Comparison of newborn related data between groups

	HFNO Group (n:50)	Conventional Group (n:52)	p*-value
Tracheal Intubation duration (min)	1 (1-1.5)	1 (1-2)	0.575^{m}
1-minute Apgar score	9 (3-10)	8 (3-10)	<0.001^{m*}
5-minute Apgar score	10 (7-10)	10 (4-10)	0.001^{m*}
Weight (kg)	3 (2.7-3.5)	3 (2.8-3.5)	0.397^{m}

Data are presented as median (minimum–maximum). m: Mann-Whitney U test. *p<0.05 was considered statistically significant.

Table 3. The comparison of umbilical cord venous blood gas analysis

	HFNO Group (n:50)	Conventional Group (n:52)	p-value
pH	7.32 (7.27-7.37)	7.33 (7.27-7.37)	0.661^{m}
PO_2 (mmHg)	34 (16-67)	29 (16-49)	0.078^{m}
PCO_2 (mmHg)	46.22±5.30	47.25±4.79	0.308^{t}
Lactate	1.49 (0.80-2.90)	1.50 (1.10-2.32)	0.114^{m}
BE	-1 (-8-2)	-1 (-4-2)	0.642^{m}

Data are presented as mean±standard deviation and median (minimum–maximum). m Mann-Whitney U test, tStudent's t-test.

Table 4. Comparison of maternal vital signs between groups

	HFNO Group (n:50)	Conventional Group (n:52)	p*-value
SpO_2 (%)			
Before Preoxygenation	99 (97-100)	99 (97-100)	0.751[m]
After Preoxygenation	100 (100-100)	100 (100-100)	1.000[m]
Heart rate (beat/min)			
Before Preoxygenation	85 (75-95)	84.50 (70-95)	0.345[m]
After Preoxygenation	98 (67-109)	97 (84-106)	0.051[m]
Systolic blood pressure (mmHg)			
Before Preoxygenation	124 (110-132)	120 (106-134)	0.345[m]
After Preoxygenation	126 (118-131)	124 (115-131)	0.134[m]
Diastolic blood pressure (mmHg)			
Before Preoxygenation	76.50 (70-85)	72.50 (70-85)	<0.001[m*]
After Preoxygenation	80 (75-85)	78 (75-83)	0.045[m*]

Data are presented as median (minimum–maximum). m Mann-Whitney U test. *p<0.05 was considered statistically significant.

spontaneously ventilating patients under spinal anesthesia. Therefore, the respiratory pattern of all patients could not be standardized. In our study, high-flow oxygen was given to patients undergoing general anesthesia and the mechanical ventilator parameters were standardized. As a result, blood gas parameters did not change, but Apgar scores improved. Although its results have been controversial in recent years, the effects of high-flow oxygenation in pregnant women have begun to be investigated frequently. In a study comparing the efficacy of preoxygenation methods performed with HFNO and conventional face masks on obstetric patients, the authors concluded that preoxygenation with HFNO delivered worse performance than that with face masks in maintaining etO_2 concentration above 90%.[17] The researchers declared that this could be because of the problem experienced by the patients in the HFNO group in keeping their mouths closed and the dilutional effect of the air intake. Opening the mouth while applying high-flow oxygenation reduces the effectiveness of the method as the amount of leakage increases. Pillai et al.[17] compared the effectivity of high-flow in patients with open and closed mouths. The authors stated that high-flow oxygenation was worse with open mouths than closed ones during the first 3 min of preoxygenation. The effectivity of closed-mouth high-flow oxygenation was found equivalent to conventional technique. In our study, reaching the end tidal oxygen concentration to 90% was our main goal during preoxygenation. However, a period exceeding 3 min was not observed in any of the patients. In order to ensure this, all patients were informed before obtaining their written consent preoperatively. A dedicated researcher was assigned to observe and keep their mouths closed during preoxygenation.

Conducted on healthy volunteers, a study compared preoxygenation applications with HFNO and conventional oxygen face masks. It was stated that the end-tidal O_2 concentration in the HFNO group was lower than that in the face mask group. They concluded that preoxygenation with HFNO was not a reliable method. However, in this study, it is noteworthy that the etO_2 value in the HFNO group showed a great deal of individual variation when compared to the face mask group.[18] Patient results may vary depending on body mass index, age, gender or diseases such as preeclampsia or eclampsia.

The Apgar score is a scoring method used worldwide to assess the condition of the newborn and their response to resuscitative interventions. Several factors may affect the Apgar score, including gestational age, maternal diabetes, BMI, smoking, medications, trauma, infection, hypovolemia, hypoxemia and low birth weight. In our study these parameters were found to be statistically similar. The lower limit value for a low Apgar score was determined as '<7'.[19,20] Umbilical cord blood gas analysis is an objective method that shows the oxygenation and metabolic status of the newborn at birth.[21,22] In our study, a similarity was observed between groups in terms of pH, pCO_2 and base deficit values. In addition, although there was no statistically significant difference, the pO_2 value was higher, lactate level was lower in the HFNO group. We are in the opinion that these better results might have been the reason for higher Apgar scores in this study. Obviously further studies with larger number of patients are needed on this subject.

As the hemodynamic variables were comparable, we concluded that preoxygenation with HFNO is a method that can easily be tolerated by patients.

Limitations

The major limitation of our study is that the amount of reactive oxygen species in umbilical cord or maternal blood samples has not been compared. Supplemental oxygen supplementation is known to increase these species. Therefore, there is a need for future research on this subject. The other limitation is the single-centered nature of our study. Prospective multicenter studies with more patients are needed.

Conclusion

In conclusion, preoxygenation with HFNO before general anesthesia induction in obstetric patients has positive effects on the newborn's 1st and 5th min Apgar scores. Although further studies are needed, we are in the opinion that the HFNO preoxygenation method should be more preferable compared to the preoxygenation method with conventional oxygen face mask technique in term parturients.

Ethics Committee Approval

The study was approved by the Kocaeli University Clinical Research Hospital Ethics Committee (Date: 27.11.2018, Decision No: 2018/506).

Informed Consent

Written informed consent was obtained from all participants. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: H.D. M.Y., E.O.Y.; Design: H.D. M.Y., E.O.Y., A.Z.T.C.; Supervision: K.T.S.; Data collection &/or processing: H.D., A.Z.T.C.; Analysis and/or interpretation: B.G., H.D., M.Y.; Literature search: B.G., H.D., K.T.S., A.S.; Writing: H.D. M.Y., E.O.Y., A.Z.T.C., K.T.S.; Critical review: M.Y., K.T.S., A.S.

Conflict of Interest

None declared.

REFERENCES

1. Azam Danish M. Preoxygenation and anesthesia: A detailed review. Cureus 2021;13(2):e13240. [CrossRef]
2. Tolga Saracoglu K, Cakmak G, Saracoglu A. Airway management during pregnancy and labor. In Shallik NA ed. Special Considerations in Human Airway Management. London: IntechOpen; 2021. [CrossRef]
3. Bonnet MP, Mercier FJ, Vicaut E, Galand A, Keita H, Baillard C; CAESAR working group. Incidence and risk factors for maternal hypoxaemia during induction of general anaesthesia for non-elective Caesarean section: A prospective multicentre study. Br J Anaesth 2020;125:e81–7. [CrossRef]
4. McDonnell NJ, Paech MJ, Clavisi OM, Scott KL. Difficult and failed intubation in obstetric anaesthesia: An observational study of airway management and complications associated with general anaesthesia for caesarean section. Int J Obstet Anesth 2008;17:292–7. [CrossRef]
5. Baillard C, Boubaya M, Statescu E, Collet M, Solis A, Guezennec J, et al. Incidence and risk factors of hypoxaemia after preoxygenation at induction of anaesthesia. Br J Anaesth 2019;122:388–94. [CrossRef]
6. Au K, Shippam W, Taylor J, Albert A, Chau A. Determining the effective pre-oxygenation interval in obstetric patients using high-flow nasal oxygen and standard flow rate facemask: A biased-coin up–down sequential allocation trial. Anaesthesia 2020;75:609–16. [CrossRef]
7. Bernard F, Louvard V, Cressy ML, Tanguy M, Mallédant Y. Préoxygénation avant induction pour césarienne. Ann Fr Anesth Reanim 1994;13:2–5. [CrossRef]
8. Chiron B, Laffon M, Ferrandiere M, Pittet JF, Marret H, Mercier C. Standard preoxygenation technique versus two rapid techniques in pregnant patients. Int J Obstet Anesth 2004;13:11–4. [CrossRef]
9. Ayten S, Halime Hanim P, Mehmet Y, Kemal Tolga S. Apneic oxygenation and high-flow. Int J Anesth Anesth 2018;5:081. [CrossRef]
10. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. Br J Anaesth 2015;115:827–48. [CrossRef]
11. Shippam W, Preston R, Douglas J, Taylor J, Albert A, Chau A. High-flow nasal oxygen vs. standard flow-rate facemask pre-oxygenation in pregnant patients: A randomised physiological study. Anaesthesia 2019;74:450–6. [CrossRef]
12. Tan PCF, Millay OJ, Leeton L, Dennis AT. High-flow humidified nasal preoxygenation in pregnant women: A prospective observational study. Br J Anaesth 2019;122:86–91. [CrossRef]
13. Ehrenfeld JM, Cassedy EA, Forbes VE, Mercaldo ND, Sandberg WS. Modified rapid sequence induction and intubation. Anesth Analg 2012;115:95–101. [CrossRef]
14. WHO. Using Pulse Oximeters. Tutorial 1: The basics. Geneva: World Health Organization; 2011.
15. Sjöblom A, Hedberg M, Johansson S, Henningsson R, Soumpasis I, Lafrenz H, et al. Pre-oxygenation using high-flow nasal oxygen in parturients undergoing caesarean section in general anaesthesia: A prospective, multi-centre, pilot study. Acta Anaesthesiol Scand 2023;67:1028–36. [CrossRef]
16. Siriussawakul A, Triyasunant N, Nimmannit A, Ngerncham S, Hirunkanokpan P, Luang-Aram S, et al. Effects of supplemental oxygen on maternal and neonatal oxygenation in elective cesarean section under spinal anesthesia: A randomized controlled trial. Biomed Res Int 2014;2014:1–6. [CrossRef]
17. Pillai A, Daga V, Lewis J, Mahmoud M, Mushambi M, Bogod D. High-flow humidified nasal oxygenation vs. standard face mask oxygenation. Anaesthesia 2016;71:1280–3. [CrossRef]
18. Hanouz JL, Lhermitte D, Gérard JL, Fischer MO. Comparison of pre-oxygenation using spontaneous breathing through face mask and high-flow nasal oxygen. Eur J Anaesthesiol 2019;36:335–41. [CrossRef]
19. Rogers JF, Graves WL. Risk factors associated with low Apgar scores in a low-income population. Paediatr Perinat Epidemiol 1993;7:205–16. [CrossRef]
20. Lai S, Flatley C, Kumar S. Perinatal risk factors for low and moderate five-minute Apgar scores at term. Eur J Obstet Gynecol Reprod Biol 2017;210:251–6. [CrossRef]
21. Knutzen L, Svirko E, Impey L. The significance of base deficit in acidemic term neonates. Am J Obstet Gynecol 2015;213:373.e1–7. [CrossRef]
22. Georgieva A, Moulden M, Redman CWG. Umbilical cord gases in relation to the neonatal condition: The EveREst plot. Eur J Obstet Gynecol Reprod Biol 2013;168:155–60. [CrossRef]

Sezaryenle Doğum Yapan Term Gebelerde Yüksek Akım Nazal Kanül Oksijen Uygulamasının Yenidoğan Sonuçlarına Etkisi: Prospektif Randomize Bir Çalışma

Amaç: Yüksek akım nazal oksijenasyon (YANO), gebe olmayan hastalarda iyi bilinen bir preoksijenasyon tekniğidir. Ancak, term gebelerdeki etkinliği belirsizliğini korumakta olup bazı çalışmalar yetersiz sonuçlar bildirmiştir. Ayrıca, bu hasta grubunda yenidoğan sonuçlarına ilişkin veriler sınırlıdır. Bu çalışma, genel anestezi altında sezaryen uygulanacak gebelerde YANO'nun yenidoğan sonuçlarına etkisini değerlendirmeyi amaçlamaktadır. Birincil sonuç olarak Apgar skorları, ikincil sonuç olarak ise umbilikal venöz kan gazı parametreleri incelenmiştir.

Gereç ve Yöntem: Etik Kurul onayı ve klinik çalışma kaydı (NCT03903003) sonrasında 102 term gebe rastgele iki gruba ayrıldı: YANO grubu (n=50) ve konvansiyonel yüz maskesi ile preoksijenasyon grubu (n=52). YANO grubuna 60 L/dk hızında oksijen, konvansiyonel gruba ise %100 oksijen 10 L/dk hızında uygulandı. End-tidal oksijen (etO_2) düzeyi %90'a ulaştığında indüksiyon başlatıldı ve entübasyon sırasında oksijenasyon sürdürüldü. Yenidoğanların 1. ve 5. dakikadaki Apgar skorları, umbilikal venöz kan gazı değerleri ve maternal hemodinamik parametreler kaydedildi.

Bulgular: YANO grubunda Apgar skorları hem 1. dakikada (9 (3-10) vs. 8 (3-10); $p<0.001$) hem de 5. dakikada (10 (7-10) vs. 10 (4-10); $p<0.001$) anlamlı olarak daha yüksekti. Kordon venöz kan gazı parametreleri gruplar arasında benzerdi.

Sonuç: Sezaryen uygulanacak gebelerde preoksijenasyon amacıyla YANO'nun indüksiyon öncesi ve sırasında kullanımı, konvansiyonel yüz maskesi oksijenasyonuna kıyasla yenidoğan Apgar skorlarını iyileştirmiştir. Bu bulgular, obstetrik anestezide YANO'nun güvenli ve etkili bir preoksijenasyon yöntemi olduğunu desteklemektedir.

Anahtar Sözcükler: Apgar skoru; sezaryen; preoksijenasyon; yüksek akım nazal oksijenasyon.

SCIE DOI: 10.14744/scie.2025.05579
South. Clin. Ist. Euras. 2025;36(3):279-285

Original Article

Comparison of Vaginal Estrogen, Hyaluronic Acid, and Oral Probiotics for the Treatment of Genitourinary Syndrome of Menopause

Emre Mat,[1] İsmail Bağlar,[2] Esra Keles[1]

[1]Department of Gynecologic Oncology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye
[2]Department of Obstetrics and Gynecology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye

Submitted: 06.07.2025
Revised: 31.07.2025
Accepted: 05.08.2025

Correspondence: İsmail Bağlar, Department of Gynecologic Oncology, Kartal Lütfi Kırdar City Hospital, Istanbul, Türkiye
E-mail: ismailbg@gmail.com

Keywords: Hyaluronic acid; estrogens; menopause; probiotics; vaginal atrophy.

ABSTRACT

Objective: The objective of this study was to compare the efficacy of a non-hormonal alternatives, vaginal hyaluronic acid, oral probiotics, to a standard of care therapy, vaginal estrodiol, for the treatment of genitourinary syndrome of menopause (GSM).

Methods: This prospective study was conducted in the Obstetrics and Gynecology Clinic of the Education and Research Hospital between June and September 2024. Women with GSM were assigned to hyaluronic acid vaginal ovules, estradiol vaginal tablets or oral probiotics for 8 wk. The primary outcome was the change in the Vaginal Health Index (VHI) score. Secondary outcomes included changes in the Female Sexual Distress Scale-Revised (FSDS-R) and the Menopause Rating Scale (MRS).

Results: Sixty participants (vaginal estrogen=20, vaginal HA=20, oral probiotic=20) provided data at week 8. All three treatment groups showed statistically significant improvements in VHI scores and significant reductions in FSDS-R and MRS scores from baseline to week 8 ($p<0.001$) for within-group comparisons). Changes in FSDS-R scores were similar across all three groups ($p=0.176$). No treatment-related serious adverse events occurred.

Conclusion: This study found that vaginal estradiol, vaginal hyaluronic acid, and oral probiotics led to significant improvements in vaginal health, reductions in sexual distress, and alleviation of menopausal symptoms in women with GSM. In addition, oral probiotics and vaginal hyaluronic acid may represent promising non-hormonal alternatives for the management of GSM, particularly for women who prefer to avoid hormone therapy.

INTRODUCTION

Genitourinary syndrome of menopause (GSM), is a prevalent condition affecting a substantial proportion of postmenopausal women due to the decline in estrogen levels.[1] This estrogen deficiency leads to a cascade of changes in the vulvovaginal tissues, resulting in thinning of the vaginal epithelium, decreased vascularity, and reduced lubrication. Consequently, women experience a wide range of symptoms, such as vaginal dryness, pruritus, dyspareunia, and urinary discomfort, all of which can significantly impair their quality of life and sexual function.[2] Despite its high prevalence and substantial impact, GSM remains underdiagnosed and undertreated in many women, highlighting the need for effective and acceptable treatment options.

Vaginal estrogen therapy is considered a well-established and highly effective first-line treatment for GSM.[3] By directly addressing the estrogen deficiency in the vaginal tissue, topical estrogens, available in various formulations such as creams, tablets, and rings,[4] can effectively alleviate symptoms and improve vaginal health. However, some women may have concerns about potential systemic absorption and the long-term safety associated with hormone therapy, leading to a desire for non-hormonal alternatives.

Hyaluronic acid has emerged as a non-hormonal option for managing GSM symptoms.[5] As a natural polysaccharide with significant water-binding capacity, hyaluronic acid can provide lubrication and hydration to the vaginal mucosa, potentially alleviating dryness and other vulvavaginal athropy-related discomforts.[6] While some systematic reviews suggest that hyaluronic acid has comparable efficacy to vaginal estrogens in improving certain aspects of GSM,[7-9] others indicate that estrogen may be superior in relieving vaginal symptoms and improving objective markers of vaginal health.[10,11] These inconsistencies highlight the need for further comparative research.

Another less conventional approach under investigation for managing GSM symptoms is the use of oral probiotics. The rationale behind this approach lies in the gut-vagina axis, suggesting that the composition of the gut microbiome can influence the vaginal microbiome.[12] Specific strains of probiotics, particularly Lactobacillus species, are known to play an important role in sustaining a healthy vaginal microenvironment by producing lactic acid, which aids to lower vaginal pH and inhibit the growth of pathogenic microorganisms.[13] While research on the efficacy of oral probiotics for GSM is still emerging, and many studies focus on vaginal probiotics for conditions like bacterial vaginosis,[14,15] the potential for oral probiotics to positively impact the vaginal microbiome and alleviate GSM symptoms warrants further investigation.

Given the need for more comparative evidence to guide treatment decisions for postmenopausal women with GSM, this study aimed to compare the efficacy of vaginal estradiol, hyaluronic acid, and oral probiotics on vaginal health, sexual distress, and menopausal symptoms. The primary objective was to assess and compare the changes in the Vaginal Health Index (VHI) among the three treatment groups. Secondary objectives included comparing the effects on sexual distress, as measured by the Female Sexual Distress Scale-Revised (FSDS-R), and overall menopausal symptoms, as assessed by the Menopause Rating Scale (MRS).

MATERIALS AND METHODS

Study Design, Setting, and Ethical Approval

This prospective study was conducted in the Obstetrics and Gynecology Clinic of the Education and Research Hospital. Before starting the research, ethical permission was obtained from the Ethics Committee of the hospital (Approval No: 2023/514/256/23, Date: 28 August 2023). The study adheres to the tenets of Declaration of Helsinki. Patient recruitment and data collection took place between June 1 and September 1, 2024.

Participant Recruitment and Informed Consent

Postmenopausal women who visited the gynecology outpatient clinic reporting symptoms of vaginal dryness, itching, burning, or dyspareunia were invited to participate in the study. A female healthcare provider thoroughly explained the study's purpose, methodology, potential risks, and benefits in a private consultation room. Each participant had ample opportunity to ask questions and discuss any concerns before providing written informed consent. We emphasized that participation was entirely voluntary and assured confidentiality, clarifying that all collected data would be anonymized and used exclusively for research purposes.

Inclusion and Exclusion Criteria

Inclusion criteria for participation were: Being sexually active, having serum estradiol levels <20 pg/mL, follicle-stimulating hormone levels >40 IU/L, a negative Pap smear result within the past year, no pathological findings suggestive of malignancy on bilateral mammography, no family history of breast or endometrial cancer, absence of neurological disorders requiring treatment, no contraindications to hormone therapy (such as acute thromboembolism or a history of myocardial infarction), age between 45 and 65 years, at least 12 months of amenorrhea, and the presence of bothersome vaginal symptoms including dryness, itching, burning, and/or dyspareunia.

Exclusion criteria were: A history of breast cancer or any other type of cancer, unexplained genital bleeding, active thrombophlebitis or a history of estrogen-dependent thromboembolism, use of any form of hormone therapy within the 12 months prior to study enrollment, and the presence of an active vaginal infection.

Interventions

Eligible participants were non-randomly assigned to one of three treatment groups based on clinical assessment and patient preference. The three intervention groups were: (1) Vaginal estradiol group (n=20) received estradiol vaginal tablets (Vagifem 25 mg, Novo Nordisk). The treatment regimen consisted of one vaginal tablet administered daily for the first two weeks, followed by a maintenance dose of one tablet administered twice weekly for the remaining six weeks. (2) Hyaluronic acid group (n=20) received hyaluronic acid vaginal ovules (Cicatridina, Farma-Derma). Participants were instructed to insert one vaginal ovule daily for the entire duration of the 8-week treatment period. (3) Oral probiotic group (n=20) received one oral probiotic capsule daily (Evo probiyotik kapsül, Evopharm). Each capsule contained a blend of Lactobacillus acidophilus (1x109 CFU), Bifidobacterium longum (1x109 CFU), Streptococcus thermophilus (1x109 CFU), Lactobacillus bulgaricus (1x109 CFU), Lactobacillus rhamnosus (1x109 CFU), and 50 mg of inulin. This specific combination of probiotic strains was chosen based on evidence suggesting their potential to positively influence the vaginal microbiome by promoting the growth of beneficial Lactobacillus species and contributing to a lower vaginal pH, which inhibits the proliferation of pathogens.[12] Inulin was included as a prebiotic to further support the growth and activity of the probiotic bacteria.

Participants were provided with detailed instructions on how to use their assigned treatment and were encouraged to adhere to the prescribed regimen for the entire 8-week study period. They were also instructed not to use any other vaginal treatments or hormone therapies during the study.

Outcomes

The primary endpoint of this study was the difference in VHI scores between baseline and the 8-week follow-up assessment after treatment initiation. The VHI is a clinical assessment tool used to evaluate vaginal wellness based

on five parameters: Mucosal thickness, moisture, pH level, elasticity, and epithelial integrity. Each parameter is graded on a scale from 1 (worst condition) to 5 (best condition), resulting in a total score ranging from 5 to 25. A total VHI score of 15 or less is generally considered indicative of vaginal atrophy.[15] The VHI was assessed through clinical inspection by the same experienced gynecologist at both baseline and week 8.

Secondary endpoints included changes in sexual distress and menopausal symptoms, evaluated using two validated instruments: We assessed sexual distress using the Turkish version of the FSDS-R, a 13-item questionnaire measuring distress related to sexual dysfunction. Participants rated each item on a 5-point Likert scale (0="never" to 4="always"), with total scores ranging from 0-52. A cut-off score of ≥11 indicated clinically significant sexual distress.[16] Participants completed the FSDS-R at baseline and week 8. Menopausal symptom severity was evaluated using the MRS questionnaire, which comprises 11 items across three domains: Somatic (hot flushes, heart discomfort, sleep problems), psychological (depressive mood, irritability, anxiety), and urogenital (sexual problems, bladder problems, vaginal dryness). Each item is scored from 0 (asymptomatic) to 4 (extremely severe), yielding a total score range of 0-44, where higher scores reflect greater symptom burden.[17] Participants completed the MRS at baseline and week 8.

Endometrial thickness was assessed using transvaginal ultrasonography with a 6.5 MHz vaginal endoprobe (Voluson PRO 730, General Electrics®, USA) at baseline and week 8.

Demographic and clinical characteristics, including age, gravidity, parity, body mass index (BMI), age at menopause, duration of menopause, history of surgical menopause, comorbidities, were recorded at the baseline visit through patient interviews and review of medical records.

Data Collection Procedures

Data were collected at two time points: At the initial visit (baseline) before the start of the treatment and after eight weeks of treatment. At both visits, a thorough gynecological examination and the assessment of the endometrial thickness via transvaginal ultrasound were performed. Then, participants were asked to complete the VHI, FSDS-R and MRS questionnaires.

Sample size

Sample size of the study was determined using the G Power 3.1 based on established literature.[18] A 90% statistical power (1-β) was considered at the 0.05 (α) significance level, and the two-way ANOVA was used for medium effect size. The required sample size was computed to be 45 subjects, with 15 patients per group. However, to account for potential attrition during the follow-up period, 20 patients were recruited for each group, yielding a total of 60 participants.

Table 1. Baseline characteristics

Characteristic	Hyaluronic Acid (n=20)	Probiotic (n=20)	Estradiol (n=20)	p-value
Age (years), Mean±SD	54.8±6.6	54.6±6.5	53.4±4.4	0.724
BMI (kg/m^2), Mean±SD	27.7±5.1	28.7±4.4	31.8±4.3	0.019
Parity (median, IQR)	3 (1-6)	3 (1-5)	3 (1-6)	0.658
Mode of Delivery (CS delivery, n (%))	2 (10.0)	2 (10.0)	1 (5.0)	0.804
Married, n (%)	19 (95.0)	19 (95.0)	20 (100.0)	0.596
Education Level (n (%))			0.857	
Primary	6 (30.0)	4 (20.0)	3 (15.0)	
Secondary	5 (25.0)	6 (30.0)	6 (30.0)	
High School	1 (5.0)	1 (5.0)	9 (45.0)	
University	6 (30.0)	9 (45.0)	2 (10.0)	
Place of Residence, n (%)			0.733	
Village	3 (15.0)	4 (20.0)	4 (20.0)	
Town	2 (10.0)	1 (5.0)	2 (10.0)	
District	6 (30.0)	2 (10.0)	6 (30.0)	
City	9 (45.0)	12 (60.0)	7 (35.0)	
Abroad	0 (0.0)	1 (5.0)	1 (5.0)	
Menopause Age (years), Mean±SD	48.1±2.9	48.8±3.0	47.6±3.4	0.465
Menopause Duration (years), Mean±SD	6.7±5.1	5.9±5.1	5.8±3.5	0.789
Surgical Menopause (n (%))	1 (5.0)	1 (5.0)	1 (5.0)	0.596
Endometrial Thickness (mm), Mean±SD	4.8±0.9	4.8±0.8	5.0±0.7	0.813

* $p<0.05$ considered statistically significant.

Table 1. Demographic and characteristic features of the patients

Scale	Time	Hyaluronic Acid (n=20) Mean±SD	Probiotic (n=20) Mean±SD	Estradiol (n=20) Mean±SD	p-value¥
VHI	Baseline	11.40±3.45	12.10±3.06	12.10±2.44	0.700
	Week 8	15.20±3.62	18.25±2.82	19.80±1.12	0.001
	Change	3.80±1.11	6.15±1.56	7.70±1.38	0.001
p-valueΩ		0.001	0.001	0.001	
FSDS-R	Baseline	54.45±9.54	56.30±8.46	52.95±9.18	0.508
	Week 8	44.45±7.92	43.70±7.12	41.70±7.40	0.491
	Change	-10.00±4.03	-12.60±4.83	-11.25±4.40	0.176
p-valueΩ		0.001	0.001	0.001	
MRS	Baseline	34.60±6.32	39.45±4.67	40.15±4.25	0.002
	Week 8	25.15±5.63	24.85±4.67	26.55±4.50	0.516
	Change	-9.45±1.82	-14.60±2.60	-13.60±2.39	0.001
p-valueΩ		0.001	0.001	0.001	

VHI: Vaginal Health Index; FSDS-R: Female Sexual Distress Scale-R; MRS: Menopause Rating Scale. ¥: comparison between groups, Ω: comparison within groups. *p<0.05 considered statistically significant.

Statistical Analysis

Analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables are reported as mean±SD; categorical variables as n (%). Normality was assessed via Shapiro-Wilk tests with Q-Q plot verification. Baseline characteristics were compared using ANOVA (continuous) or χ^2 tests (categorical). Within-group changes (baseline to week 8) were evaluated with paired t-tests (normal) or Wilcoxon signed-rank tests (non-normal). Between-group differences at week 8 were analyzed using ANOVA or Kruskal-Wallis tests, with Bonferroni-corrected post hoc tests for significant findings. The level of statistical significance was set at p<0.05.

RESULTS

Demographic Characteristics

Table 1 shows the sociodemographic and baseline clinical characteristics of the participants in the three treatment groups. No statistically significant differences were found between the groups regarding age, parity, mode of delivery, marital status, education level, place of residence, age at menopause, duration of menopause, history of surgical menopause, or baseline endometrial thickness. However, a significant difference was found in baseline body mass index (p=0.019), with the vaginal estradiol group having a significantly higher mean weight and BMI compared to the vaginal hyaluronic acid and oral probiotic.

Comparison of Scale Scores

As presented in Table 2, all three treatment groups showed clinically and statistically significant improvements in vaginal health, as measured by VHI scores, from baseline to the 8-week follow-up (p<0.001 for each within-group comparison). The complete descriptive statistics and comparative results for VHI, FSDS-R, and MRS scores at both assessment points are detailed for each treatment arm. The magnitude of this increase was significantly different between the groups (p<0.001 for between-group comparison of change scores). Post-hoc analysis revealed that the improvement in VHI was significantly lower in the hyaluronic acid group (mean change=3.80±1.11) compared to both the probiotic group (mean change=6.15±1.56, p=0.001) and the estradiol group (mean change=7.70±1.38, p<0.001).

All three groups showed a statistically significant decrease in FSDS-R scores from baseline to week 8 (p<0.001 for all within-group comparisons), indicating a reduction in sexual distress. No statistically significant difference was observed in the magnitude of this reduction between the three groups (p=0.176 for between-group comparison of change scores).

All three groups also exhibited a statistically significant decrease in MRS scores from baseline to week 8 (p<0.001 for all within-group comparisons), indicating an improvement in overall menopausal symptoms. The magnitude of this reduction significantly differed between the groups (p<0.001 for between-group comparison of change scores). Post-hoc analysis showed that the reduction in MRS scores was significantly smaller in the hyaluronic acid group (mean change=-9.45±1.82) compared to both the probiotic group (mean change=-14.60±2.60, p<0.001) and the estradiol group (mean change=-13.60±2.39, p<0.001).

DISCUSSION

This prospective study investigated the comparative effectiveness of vaginal estradiol, hyaluronic acid vaginal ovules,

and oral probiotics in treating postmenopausal women with symptoms of GSM. The findings of this study indicate that all three interventions resulted in significant improvements in vaginal health, as measured by the VHI, and significant reductions in both sexual distress, assessed by the FSDS-R, and overall menopausal symptoms, evaluated by the MRS.

A key finding of this study was the significantly lower improvement in VHI scores observed in the hyaluronic acid group compared to the vaginal estradiol group. This suggests that while hyaluronic acid provided some benefit in improving objective markers of vaginal health, its efficacy in this regard may be less pronounced than that of topical estrogen used in this study. This finding contrasts with some systematic reviews that have reported comparable efficacy between hyaluronic acid and vaginal estrogens for treating GSM.[19-21] However, other reviews have indicated the superiority of estrogen in relieving vaginal symptoms and improving objective measures.[22,23] The discrepancy in findings might be attributed to variations in the specific formulations and dosages of hyaluronic acid used across different studies, as well as the characteristics of the study populations.

Interestingly, the oral probiotic group demonstrated comparable efficacy to the topical estradiol group in improving VHI scores and reducing FSDS-R and MRS scores. This is a novel and potentially significant finding, as the use of oral probiotics for managing GSM symptoms is a less established approach compared to topical hormone therapy. While much of the research on probiotics in vaginal health has focused on the use of vaginal probiotics for conditions like bacterial vaginosis,[24] the comparable efficacy observed in this study suggests that specific strains of oral probiotics may exert a positive influence on the vaginal environment, possibly through the gut-vagina axis.[25] The Lactobacillus species included in the probiotic formulation are known to contribute to a healthy vaginal microbiome by producing lactic acid, which lowers vaginal pH and inhibits the growth of pathogens.[26] Further research is needed to elucidate the specific mechanisms by which oral probiotics may alleviate GSM symptoms and to identify the most effective strains and dosages.

The clinical implications of these findings are noteworthy. Vaginal estradiol, as standard-of-care therapy, effectively improved VHI scores and reduced menopausal symptoms and sexual distress, which is consistent with the well-established efficacy of topical estrogen therapy for GSM.[27] The comparable efficacy of oral probiotics to topical estradiol in improving VHI and reducing menopausal symptoms suggests that oral probiotics may represent a viable non-hormonal alternative for managing GSM, particularly for women who prefer to avoid hormone therapy or have contraindications to its use.[20] As hyaluronic acid has shown benefit in improving VHI, it may also be an effective option to improve the objective signs of vaginal atrophy in this specific population.[28]

This study has several strengths, including its prospective design, the use of validated outcome measures to assess multiple relevant domains (vaginal health, sexual distress, and menopausal symptoms), the direct comparison of three relevant treatment modalities, and the comprehensive data collection at baseline and after the intervention period. However, the study also has some limitations that should be considered when interpreting the findings. The relatively small sample size may limit the generalizability of the results. The short duration of the intervention (8 weeks) may not be sufficient to fully capture the long-term effects of these treatments. The single-center design also restricts the generalizability of the findings to other populations and settings. The baseline difference in BMI between the estradiol group and the other two groups could potentially have influenced the results, although correlation analysis did not reveal a significant relationship between BMI and treatment response. The lack of randomization and blinding of participants and investigators to the treatment assignments could also introduce bias in the subjective outcome measures. Furthermore, the specific strains and dosage of the oral probiotic used in this study may not be representative of all available probiotic formulations, and the findings may not be generalizable to other probiotic products.

This study highlights several important avenues for subsequent investigation. First, methodological enhancements should include larger-scale randomized controlled trials with adequate statistical power, extended follow-up periods to evaluate treatment durability, and multi-center designs to enhance generalizability.

Conclusion

In conclusion, this study found that vaginal estradiol, vaginal hyaluronic acid, and oral probiotics led to significant improvements in vaginal health, reductions in sexual distress, and alleviation of menopausal symptoms in postmenopausal women experiencing GSM. These findings suggest that oral probiotics and vaginal hyaluronic acid may represent promising non-hormonal alternatives for the management of GSM, particularly for women who prefer to avoid hormone therapy.

Ethics Committee Approval

The study was approved by the Kartal City Hospital Ethics Committee (Date: 28.08.2023, Decision No: 2023/514/256/23).

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: E.M., İ.B., E.K.; Design: E.M., İ.B.; Supervision: E.M., E.K.; Fundings: E.M., İ.B., E.K.; Materials: E.M., İ.B., E.K.; Data collection &/or processing: İ.B., E.K.; Analysis and/or interpretation: E.M., İ.B., E.K.; Literature search: E.M., E.K.; Writing: E.M., İ.B., E.K.; Critical review: İ.B., E.K.

Conflict of Interest

None declared.

REFERENCES

1. Naumova I, Castelo-Branco C. Current treatment options for postmenopausal vaginal atrophy. Int J Womens Health 2018;10:387–95. [CrossRef]
2. Krychman M, Graham S, Bernick B, Mirkin S, Kingsberg SA. The Women's EMPOWER Survey: Women's knowledge and awareness of treatment options for vulvar and vaginal atrophy remains ınadequate. J Sex Med 2017;14:425–33. [CrossRef]
3. Biehl C, Plotsker O, Mirkin S. A systematic review of the efficacy and safety of vaginal estrogen products for the treatment of genitourinary syndrome of menopause. Menopause 2019;26:431–53. [CrossRef]
4. Lethaby A, Ayeleke RO, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev 2016;2016:CD001500. [CrossRef]
5. Donders GGG, Ruban K, Bellen G, Grinceviciene S. Pharmacotherapy for the treatment of vaginal atrophy. Expert Opin Pharmacother. 2019;20:821–35. [CrossRef]
6. Nappi RE, Martella S, Albani F, Cassani C, Martini E, Landoni F. Hyaluronic acid: A valid therapeutic option for early management of genitourinary syndrome of menopause in cancer survivors? Healthcare (Basel) 2022;10:1528. [CrossRef]
7. Dos Santos CCM, Uggioni MLR, Colonetti T, Colonetti L, Grande AJ, Da Rosa MI. Hyaluronic acid in postmenopause vaginal atrophy: A systematic review. J Sex Med 2021;18:156–66. [CrossRef]
8. Jafarzade A, Mungan T, Aghayeva S, Yıldırım BB, Ekiz OU, Biri A. A comparison of hyaluronic acid and estradiol treatment in vulvovaginal atrophy. Eur Rev Med Pharmacol Sci 2024;28:571–6.
9. Albalawi NS, Almohammadi MA, Albalawi AR. Comparison of the efficacy of vaginal hyaluronic acid to estrogen for the treatment of vaginal atrophy in postmenopausal women: a systematic review. Cureus 2023;15:e44191. [CrossRef]
10. Rahn DD, Carberry C, Sanses TV, Mamik MM, Ward RM, Meriwether KV, et al. Vaginal estrogen for genitourinary syndrome of menopause: A systematic review. Obstet Gynecol 2014;124:1147–56. [CrossRef]
11. Constantine G, Millheiser LS, Kaunitz AM, Parish SJ, Graham S, Bernick B, et al. Early onset of action with a 17β-estradiol, softgel, vaginal insert for treating vulvar and vaginal atrophy and moderate to severe dyspareunia. Menopause 2019;26:1259–64. [CrossRef]
12. Mei Z, Li D. The role of probiotics in vaginal health. Front Cell Infect Microbiol 2022;12:963868. [CrossRef]
13. Romeo M, D'Urso F, Ciccarese G, Di Gaudio F, Broccolo F. Exploring oral and vaginal probiotic solutions for women's health from puberty to menopause: A narrative review. Microorganisms 2024;12:1614. [CrossRef]
14. Rezazadeh MB, Zanganeh M, Jarahi L, Fatehi Z. Comparative efficacy of oral and vaginal probiotics in reducing the recurrence of bacterial vaginosis: A double-blind clinical trial. BMC Womens Health 2024;24:575. [CrossRef]
15. Lee D, Kim TH, Lee HH, Kim JM, Jeon DS, Kim YS. A pilot study of the impacts of menopause on the anogenital distance. J Menopausal Med 2015;21:41–6. [CrossRef]
16. Kitiş Y, Şentürk EA, Gurcuoglu EA. Turkish adaptation of Female Sexual Distress Scale-R: A validity and reliability study. Sex Cult 2019;23:927–42. [CrossRef]
17. Gürkan CÖ. The validity and reliabitity of Turkish version of menopouase rating scale. Available at: https://toad.halileksi.net/wp-content/uploads/2022/07/menopoz-semptomlari-degerlendirme-olcegi-toad.pdf. Accessed Sep 9, 2025.
18. Agrawal S, LaPier Z, Nagpal S, Oot A, Friedman S, Hade EM, et al. A randomized, pilot trial comparing vaginal hyaluronic acid to vaginal estrogen for the treatment of genitourinary syndrome of menopause. Menopause 2024;31:750–5. [CrossRef]
19. Jokar A, Davari T, Asadi N, Ahmadi F, Foruhari S. Comparison of the hyaluronic acid vaginal cream and conjugated estrogen used in treatment of vaginal atrophy of menopause women: A randomized controlled clinical trial. Int J Community Based Nurs Midwifery 2016;4:69–78.
20. Chen J, Geng L, Song X, Li H, Giordan N, Liao Q. Evaluation of the efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: A multicenter, randomized, controlled, open-label, parallel-group, clinical trial. J Sex Med 2013;10:1575–84. [CrossRef]
21. Duque-Estrada Edo, Rosa VP, Mosca MM, Nascimento HLd. Perceived efficacy of vaginal dryness relief: A comparative clinical study between sodium hyaluronate vaginal gel vs. promestriene cream. Adv Sex Med 2017;7:34–43. [CrossRef]
22. Ekin M, Yaşar L, Savan K, Temur M, Uhri M, Gencer I, et al. The comparison of hyaluronic acid vaginal tablets with estradiol vaginal tablets in the treatment of atrophic vaginitis: A randomized controlled trial. Arch Gynecol Obstet 2011;283:539–43. [CrossRef]
23. Le Donne M, Caruso C, Mancuso A, Costa G, Iemmo R, Pizzimenti G, et al. The effect of vaginally administered genistein in comparison with hyaluronic acid on atrophic epithelium in postmenopause. Arch Gynecol Obstet 2011;283:1319–23. [CrossRef]
24. Vujic G, Jajac Knez A, Despot Stefanovic V, Kuzmic Vrbanovic V. Efficacy of orally applied probiotic capsules for bacterial vaginosis and other vaginal infections: A double-blind, randomized, placebo-controlled study. Eur J Obstet Gynecol Reprod Biol 2013;168:75–9. [CrossRef]
25. Silva VF, Refinetti P, Vicariotto F, Baracat EC, Soares Junior JM. Oral probiotics and vaginal microbiome in post-menopause women: An opinion for the improvement of natural therapies in gynecology. Rev Assoc Med Bras 2024;70:e702EDIT. [CrossRef]
26. Chee WJY, Chew SY, Than LTL. Vaginal microbiota and the potential of Lactobacillus derivatives in maintaining vaginal health. Microb Cell Fact 2020;19:203. [CrossRef]
27. Wasnik VB, Acharya N, Mohammad S. Genitourinary syndrome of menopause: A narrative review focusing on ıts effects on the sexual health and quality of life of women. Cureus 2023;15:e48143. [CrossRef]
28. Origoni M, Cimmino C, Carminati G, Iachini E, Stefani C, Girardelli S, et al. Postmenopausal vulvovaginal atrophy (VVA) is positively improved by topical hyaluronic acid application: A prospective, observational study. Eur Rev Med Pharmacol Sci 2016;20:4190–5.

Menopozal Genitoüriner Sendrom Tedavisinde Vajinal Östrojen, Hiyalüronik Asit ve Oral Probiyotiklerin Karşılaştırılması

Amaç: Bu çalışmanın amacı, menopozal genitoüriner sendromun (GÜSM) tedavisinde standart tedavi yöntemi olan vajinal östradiol ile hormonal olmayan alternatifler olan vajinal hiyalüronik asit ve oral probiyotiklerin etkinliğini karşılaştırmaktır.

Gereç ve Yöntem: Bu prospektif çalışma, Haziran-Eylül 2024 tarihleri arasında Kartal Dr. Lütfi Kırdar Şehir Hastanesi'nde yürütüldü. GÜSM tanısı konulan kadınlar, sekiz hafta süreyle vajinal hiyalüronik asit ovülleri, vajinal östradiol tabletleri veya oral probiyotik tedavisine randomize edildi. Birincil sonuç ölçütü, Vajinal Sağlık İndeksi (Vaginal Health Index, VHI) skorundaki değişimdi. İkincil sonuç ölçütleri arasında Kadın Cinsel Sıkıntı Ölçeği-Gözden Geçirilmiş (Female Sexual Distress Scale-Revised, FSDS-R) ve Menopoz Değerlendirme Ölçeği (Menopause Rating Scale, MRS) skorlarındaki değişiklikler yer aldı.

Bulgular: Çalışmaya toplam 60 katılımcı (vajinal östrojen=20, vajinal hiyalüronik asit=20, oral probiyotik=20) sekizinci haftada veri sağladı. Üç tedavi grubunun tamamında VHI skorlarında anlamlı iyileşmeler ve FSDS-R ile MRS skorlarında başlangıca kıyasla anlamlı azalmalar gözlendi (grup içi karşılaştırmalarda $p<0.001$). FSDS-R skorlarındaki değişim açısından gruplar arasında anlamlı fark saptanmadı ($p=0.176$). Tedaviye bağlı ciddi advers olay bildirilmedi.

Sonuç: Bu çalışma, vajinal östradiol, vajinal hiyalüronik asit ve oral probiyotiklerin GÜSM'li kadınlarda vajinal sağlıkta belirgin iyileşme, cinsel sıkıntıda azalma ve menopozal semptomların hafiflemesinde etkili olduğunu göstermiştir. Ayrıca, oral probiyotikler ve vajinal hiyalüronik asit, özellikle hormon tedavisinden kaçınmak isteyen kadınlar için umut vaat eden hormonal olmayan tedavi seçenekleri olabilir.

Anahtar Sözcükler: Hiyalüronik asit; menopoz; östrojenler; probiyotikler; vajinal atrofi.

SCIE DOI: 10.14744/scie.2025.22230
South. Clin. Ist. Euras. 2025;36(3):286-288

Case Report

Wide Resection of a Giant Sternal Chondrosarcoma and Reconstruction with a Custom-Made 3D Titanium Plate in a Patient with Kartagener Syndrome

Recep Demirhan, Berk Cimenoglu

Department of Thoracic Surgery, Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Türkiye

Submitted: 21.08.2025
Revised: 21.08.2025
Accepted: 30.08.2025

Correspondence: Berk Cimenoglu, Department of Thoracic Surgery, Kartal Dr. Lutfi Kirdar City Hospital, Istanbul, Türkiye
E-mail: berkcimenoglu@hotmail.com

Keywords: 3D reconstruction; chest wall; chondosarcoma.

ABSTRACT

Sternal tumors are rare, but the majority of these tumors are chondrosarcomas. Chondrosarcomas are generally resistant to chemotherapy, and the first-line treatment is surgical resection. For malignancies located in the anterior chest wall, wide resection should be performed to prevent recurrence. After a wide resection, the defective area should be reconstructed in a way that preserves chest wall rigidity. This is crucial both to protect intrathoracic organs from trauma and to maintain effective respiratory mechanics. In this report, we aimed to present a case of a patient with Kartagener syndrome and sternal chondrosarcoma, in whom we performed a custom-made three-dimentional (3D) reconstruction.

INTRODUCTION

Sternal tumors are very rare, and sternal chondrosarcomas account for 2% of all chondrosarcomas.[1] To prevent recurrence in chondrosarcoma resection, a surgical margin of at least 4 cm should be preserved.[2] To achieve a 4 cm surgical margin, especially in cases of giant chondrosarcomas, it is necessary to perform an en bloc resection of the sternum along with the neighboring ribs.After resection, the large anterior chest wall defect must be reconstructed in a way that preserves chest wall rigidity.In clinical practice, conventional approaches such as titanium bars or meshes and methyl methacrylate have sometimes been found to provide insufficient chest wall rigidity, resulting in paradoxical breathing. This has highlighted the need for methods that allow for more effective reconstruction of anterior chest wall defects. To meet this need, custom made three-dimentional (3D) titanium prostheses have been introduced in recent years. In this article, we present a case in which we applied a custom-made 3D titanium prosthesis, a reconstruction method recently introduced into thoracic surgery practice.

CASE REPORT

A 68-year-old female patient presented to our outpatient clinic with a swelling and pain in the anterior chest wall. Physical examination reveals a mass measuring approximately 6×10 at the lower end of the sternum. Chest computed tomography (CT) of the patient revealed dextrocardia, bronchiectasis in the right lower lobe, and a 6 cm exophytic mass lesion at the lower end of the sternum. An incisional biopsy performed on the patient was reported as chondrosarcoma. A positron emission tomography/computed tomography (PET-CT) scan performed for staging revealed no distant organ metastases. A preoperative 3D thoracic CT scan was obtained, and a custom-made titanium implant was prepared using a 3D printer. Following a

full-thickness chest wall resection, the patient underwent partial resection of the sternum and the 2nd to 5th ribs, extending 4 cm laterally. A composite mesh was placed between the lung and the titanium plate and secured with prolene sutures.The titanium plate was fixed to the manubrium and the ribs. The plastic surgery team reconstructed the tissue defect by transposing a latissimus dorsi muscle flap (Fig. 1) Intraoperative frozen section work-up confirmed that the tumor surgical margins were negative. The patient was transferred to the intensive care unit postoperatively under mechanical ventilation. The patient had difficulty weaning from mechanical ventilation due to dextrocardia and secretion stasis from bronchiectasis, so a tracheostomy was performed in the intensive care unit. The patient was monitored for a period on home ventilation in the ward and was subsequently discharged in good condition. No recurrence was detected in the patient at the 2-year follow-up.

DISCUSSION

Chondrosarcoma is a chemo-resistant tumor, and wide surgical resection remains the first-line treatment. The large chest wall defect resulting from surgical resection of the sternum and adjacent ribs should be properly reconstructed to protect intrathoracic organs from external trauma and preserve the chest wall's impact on respiratory mechanics. Therefore, when performing chest wall reconstruction, the use of rigid materials that can substitute for the resected bone tissue is especially critical, particularly after sternum resection. The muscle and skin covering these rigid materials should also be reconstructed using fasciocutaneous muscle flaps, regional flaps, or free muscle flaps.[3]

Conventionally, rigid reconstruction is performed using materials such as titanium bars or meshes, or methyl methacrylate–Prolene mesh.However, the effectiveness of these materials is limited, as they do not provide strong chest wall stabilization and may cause paradoxical respiration, thereby failing to preserve respiratory mechanics.[4] To address these issues, custom-made 3D titanium prostheses have been introduced in recent years for chest wall resection.

To prepare a 3D titanium prosthesis, the patient's CT data is first imported into the Materialise Interactive Medical Image Control System (MIMICS) Research 20.0 (Materialise, Belgium) to create a digital model. The designed prosthesis model is then transferred to a 3D printer to produce a plastic prototype. This prototype model is used as a guide on a computer numerical control (CNC) machine to produce the final pure titanium prosthesis.

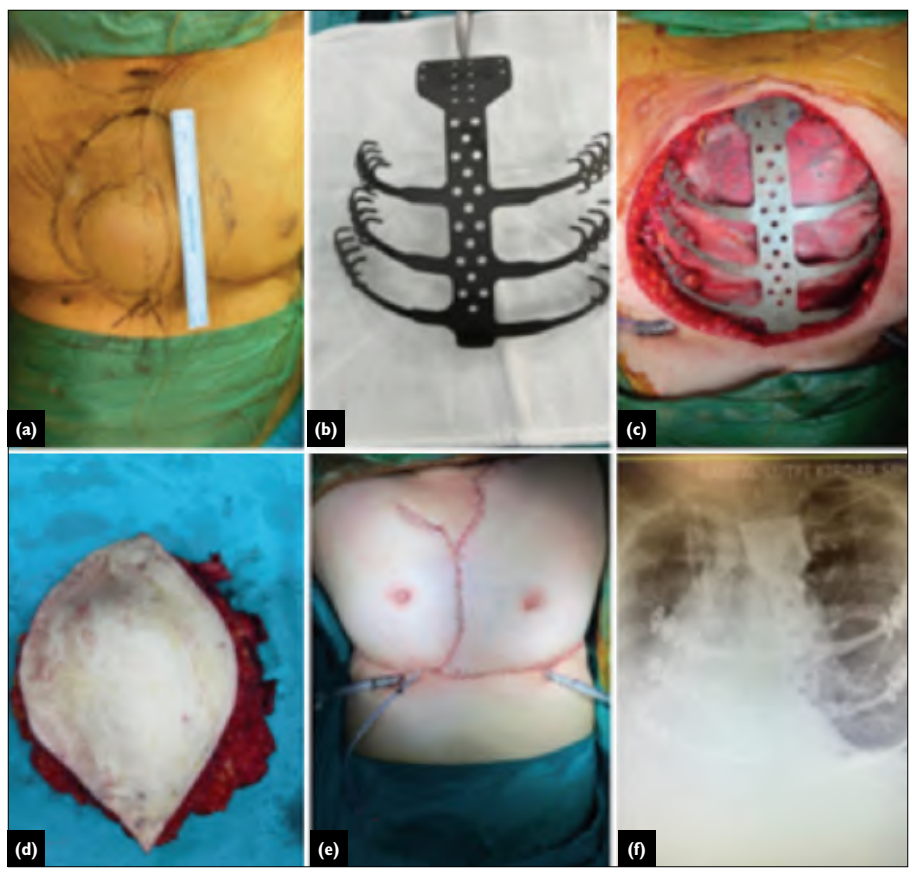


Figure 1. (a) Preoperative appearance of sternum with tumor, **(b)** Custom-made 3D material, **(c)**Peroperativen view, **(d)** Resected material, **(e)** Postoperative view, **(f)** Postoperative X-ray.

Anterior chest wall reconstructions using 3D titanium prostheses have yielded encouraging results.[5] Although no studies have yet compared this new technique with conventional methods, it appears to be more robust due to its single-piece implantation. Additionally, it is effective in covering larger defects and helps reduce operative time.

In conclusion, the patient-specific 3D titanium prosthesis method used to reconstruct defects following chest wall resection for sternal tumors preserves chest wall rigidity and respiratory mechanics. By perfectly matching the patient's anatomy, it provides stronger mechanical stabilization as well as a more aesthetic and functional chest wall reconstruction. Moreover, it is effective in facilitating the closure of large defects with at least a 4 cm surgical margin, reducing complications, and shortening operative time.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: R.D.; Design: R.D.; Supervision: R.D.; Materials: R.D., B.Ç.; Data:R.D., B.Ç.; Analysis: R.D., B.Ç.; Literature search: R.Ç.; Writing: B.Ç.; Critical revision: R.D.

Conflict of Interest

None declared.

REFERENCES

1. Jadhav SS, Dhok AP, Mitra KR, Onkar PM, Phatak SV. Chondrosarcoma of sternal origin: A rare case. Cureus 2023;15:e40393. [CrossRef]
2. Nicastri DG, Swati GN, Williams EE, Flores RM. Chest wall tumors. In: Cicero J 3rd, Feins RH, Colson YL, Rocco G, Eds. Shields' General Thoracic Surgery, 8th Ed, Philadelphia: Wolters Kluwer.
3. Koole D, Bemelman M, Schijen J, de Fijter M, van der Niet J. Reconstruction of chest wall defects using a technique ınvolving mesh, titanium plates, and a pedunculated muscle flap. Korean J Thorac Cardiovasc Surg 2018;51:308–11. [CrossRef]
4. Wang W, Yang S, Han M, Liu H, Feng Q, Su Y, et al. Three-dimensional printed titanium chest wall reconstruction for tumor removal in the sternal region. J Cardiothorac Surg 2024;19:579. [CrossRef]
5. Goldsmith I, Dovgalski L, Evans PL. 3D printing technology for chest wall reconstruction with a sternum-ribs-cartilage titanium ımplant: From ideation to creation. Innovations 2023;18:67–72. [CrossRef]

Kartagener Sendromu Olan Hastada Dev Sternal Kondrosarkomun Geniş Rezeksiyonu ve 3D Titanyum Plak ile Rekonstrüksiyonu

Sternum tümörleri nadir görülmekle beraber bu tümörlerin büyük çoğunluğunu kondrosarkomlar oluşturur. Kondrosarkomlar kemoterapiye genellikle duyarsızdır ve birinci seçenek tedavi cerrahi rezeksiyondur. Göğüs ön duvarında yerleşmiş malignitelerde nüksü engellemek için geniş rezeksiyon yapılmalıdır. Geniş rezeksiyondan sonra oluşan defektif alanın göğüs duvarı rijiditesini bozmayacak şekilde rekonstükte edilmesi hem intratorasik organların travmalara duyarlılığını azaltmada hem de solunum mekaniğini devam ettirme açısından önemlidir. Bu raporda sternal kondrosarkomu olan Kartagener sendromlu hastada kişiye özgü 3D rekonstrüksiyonu uyguladığımız olguyu sunmayı amaçladık.

Anahtar Sözcükler: 3D rekonstrüksiyon; göğüs duvarı; kondrosarkom.

SCIE DOI: 10.14744/scie.2025.40336
South. Clin. Ist. Euras. 2025;36(3):289-293

Case Report

Efficacy of Amniotic Membrane Use in Chronic Wound Treatment

Samed Oğuzhan Akın,[1] Emrah Aras,[1] Çağla Çiçek,[2] Gaye Filinte[1]

[1]Department of Plastic, Reconstructive and Aesthetic Surgery, Kartal Dr. Lutfi Kirdar City Hospital Health Sciences University, Istanbul, Türkiye
[2]Department of Plastic, Reconstructive and Aesthetic Surgery, Kartal Dr. Lutfi Kirdar City Hospital, Istabul, Türkiye

Submitted: 05.06.2025
Revised: 19.08.2025
Accepted: 21.08.2025

Correspondence: Samed Oğuzhan Akın, Department of Plastic, Reconstructive and Aesthetic Surgery, Kartal Dr. Lutfi Kirdar City Hospital Health Sciences University, Istanbul, Türkiye
E-mail: samedoguzhan.akin@sbu.edu.tr

Keywords: Chronic wound; human amniotic membrane; wound treatment.

ABSTRACT

This study investigates the application of human amniotic membrane in chronic wound care, focusing on its efficacy in promoting tissue regeneration and reducing the need for surgical interventions. Chronic wounds, often associated with comorbidities such as diabetes and vascular diseases, present significant treatment challenges. Human amniotic membrane, an avascular structure rich in extracellular matrix components and growth factors, offers a promising solution due to its immunomodulatory and regenerative properties. The study includes seven patients treated with human amniotic membrane for chronic wounds at a specialized wound care unit. Treatments were conducted over one to two-week intervals, emphasizing the importance of sterile application and consistent follow-up. Outcomes demonstrated significant wound size reduction, accelerated granulation and epithelialization, and minimized need for complex surgeries. Patients with comorbidities particularly benefited, showing improved wound bed preparation for simpler reconstructive procedures. Despite the promising results, limitations such as small sample size and lack of a control group were noted. The findings align with existing literature but emphasize the need for standardized protocols and further large-scale, controlled studies. Overall, human amniotic membrane demonstrates potential as a cost-effective, innovative therapy in chronic wound management, bridging gaps between conservative and surgical approaches.

INTRODUCTION

A wound is defined as tissue loss caused by skin, mucosa, or subcutaneous tissue damage due to physical, chemical, thermal, mechanical, or biological factors.[1,2] Acute wounds generally heal through a predictable process involving four stages: Hemostasis, inflammation, proliferation, and maturation.[2-4] These wounds differ from chronic wounds, which result from a disruption or prolongation of one or more of these phases, often due to conditions such as diabetes, obesity, vascular diseases, or immune deficiencies. These comorbidities complicate treatment and increase the need for multidisciplinary care.[5,6]

The primary goal of chronic wound management is to address the underlying etiology, since untreated causes can lead to recurrence. In addition to managing the causes, supplementary measures such as infection control, moisture balance, and biofilm removal are crucial for effective treatment. Innovative approaches that have shown promise in this area include advanced dressings and adjunctive therapies like negative pressure wound therapy and hyperbaric oxygen therapy.[1,5-7]

The amniotic membrane, an avascular stem cell source containing collagen and extracellular matrix components, is gaining attention for its wound-healing properties. It supports microbial defense, promotes cell migration, and facilitates tissue regeneration while maintaining a moist environment and reducing inflammation and pain.[1,8] The use of amniotic membrane has shown potential in diverse chronic wound types, including diabetic foot ulcers and trauma-related defects.[1,9]

This study evaluates the efficacy of the amniotic membrane in chronic wound care, focusing on its potential to reduce the need for surgical intervention and the cost of

Table 1. Demographic, clinical characteristics and treatment outcomes of cases

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age	44	65	18	64	47	54	37
Sex	M	M	W	M	M	M	W
Comorbidities	-	DM, PAD and CHF	-	DM	DM and PAD	-	DM
Treatment	Conservative	Surgery	Surgery	Surgery	Surgery	Conservative	Surgery
Recurrence	+	-	-	+	-	+	-
Duration of Hospital stay	3 months	2 months	1 month	6 weeks	5 weeks	7 weeks	2 months

treatment. However, while this use of amniotic membrane is promising, further research is needed to establish its definitive advantages over traditional methods and its role in optimizing outcomes in chronic wound management.

CASE REPORT

The study included seven patients who had chronic wounds and were hospitalized patients. The applications were performed at intervals of one to two weeks in accordance with the literature. The average number of human amniotic allograft applications was determined to be two sessions. Patients were hospitalized for the application of the amniotic allograft, while follow-up was planned on an outpatient basis. Care was taken to ensure that bacterial tissue culture was negative before the application. The acute phase reactants and vital signs of the patients were regularly monitored during the applications. Patients were also periodically evaluated for potential side effects related to their procedures. Under sterile conditions in the operating room, a cryopreserved amniotic membrane (Stembio®) was applied to the defect site. Following minimal debridement, viable granulation tissue was preserved to the greatest extent possible, and the membrane was carefully adapted to conform to the wound bed. A pressure dressing was then applied, and the wound was left undisturbed for the first three days to allow adequate graft adaptation before the initial dressing change. The outcomes were assessed in terms of reduced need for surgery, decreased wound size, shortened hospital stays, and less time elapsed before returning to social life (Table 1).

Case 1

A 44-year-old male patient was found on follow-up to have a tissue defect containing total dermis loss of 5x1 cm extending from the flexor zone 1 to 2 of the second finger of the left hand after trauma. The patient had no known comorbidities, and there was no growth in the bacterial tissue culture obtained from the patient. Before applying human amniotic allograft, necrotic areas in the defect were surgically debrided. After debridement, the human amniotic allograft was applied to the viable tissue under sterile conditions. No allergic reactions were observed during follow-up. Two weeks later, the defective area was found to be epithelialized. No additional surgical procedures were performed (Fig. 1).

Case 2

A 65-year-old male patient was found on follow-up to have a tissue defect measuring 12x5 cm in the posterior left lower leg, including dermis and subcutaneous fat tissue loss. A bacterial tissue culture obtained before the procedure showed Pseudomonas aeruginosa growth, which was treated with piperacillin/tazobactam in accordance with

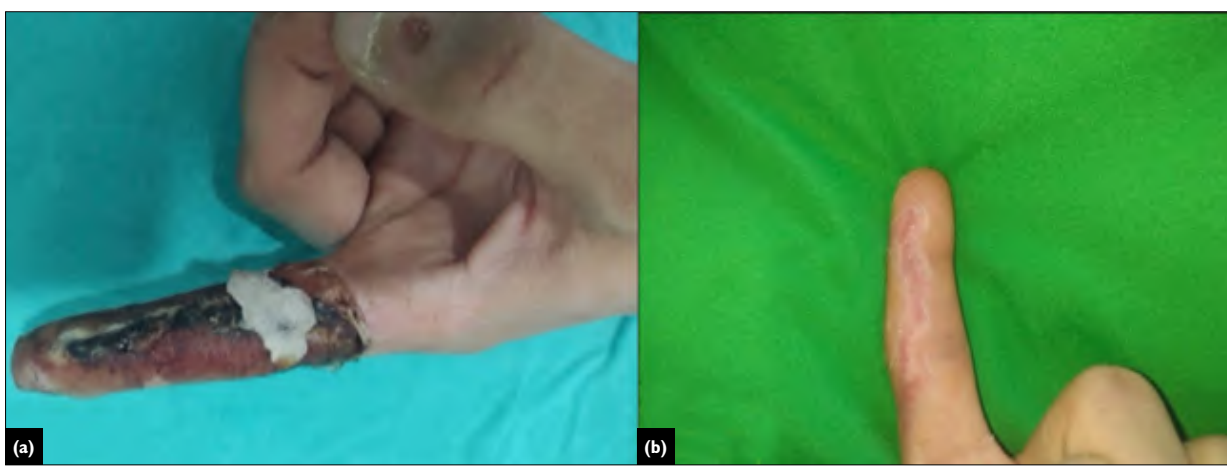


Figure 1. 44 Yo male, post traumatic tissue loss, before amniotic membrane use **(a)**, epithelized tissue after 2 weeks **(b)**.

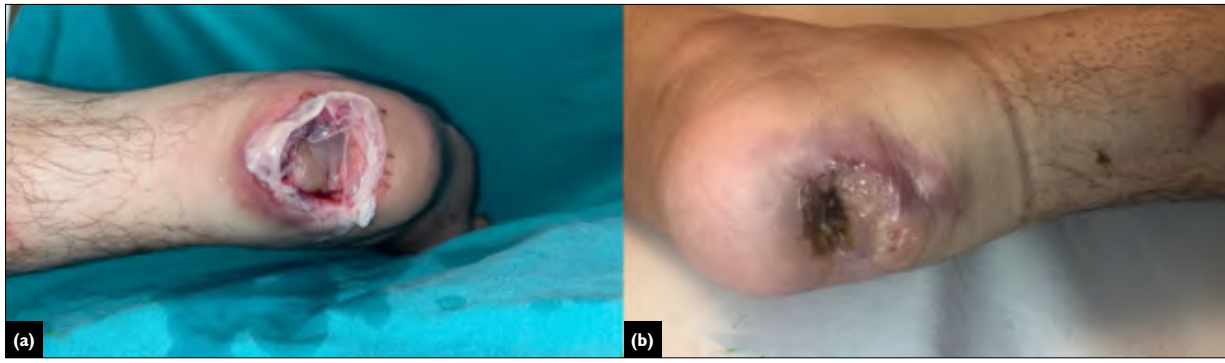


Figure 3. 18 Yo female, application of amniotic membrane to bone-exposed tissue at calcaneal region **(a)**, two weeks after application **(b)**.

the antibiogram. The bacterial tissue cultures revealed no growth. After surgical debridement, a human amniotic allograft was applied under sterile conditions to the viable tissue. A second amniotic allograft application was performed one week after the initial application. Following the procedure, the dressings over the amniotic allograft were changed every other day. No allergic reactions were noted during follow-up. Two weeks later, the area with the defect had reduced to approximately 8x4 cm, and the base appeared granulated. Reconstruction was performed under spinal anesthesia using a split-thickness skin graft harvested from the anterolateral thigh of the same side (Fig. 2).

Case 3

An 18-year-old female patient was followed up with a tissue defect of approximately 4x4 cm in the posterior calcaneal region of the right foot, exposing the calcaneus after trauma. Bacterial tissue culture obtained before the procedure showed no growth. Necrotic tissues in the defect area were surgically debrided, and no additional calcaneus debridement was performed. After debridement, human amniotic allograft was applied under sterile conditions to the viable tissues. Following the procedure, dressings over the amniotic allograft were changed every other day. No allergic reactions were noted during follow-up. Two weeks later, the defect base appeared granulated, and reconstruction was performed under spinal anesthesia using a split-thickness skin graft harvested from the anterolateral thigh of the same side (Fig. 3).

Other Cases

The remaining four cases generally consisted of middle-aged and elderly individuals, most of whom had comorbidities as indicated in Table 1. The procedure applied to these patients was similar to that described for the other cases: After debridement and the exposure of healthy tissue, the treatments were administered and followed up in a similar manner. Clinically, reductions in wound sizes were observed. Among these three cases, two presented with bone-exposed tissue defects; following membrane applications, a granulated wound bed was achieved. Although the patients eventually required surgery, the necessary procedures were less complicated due to the improved wound condition.

DISCUSSION

The application of amniotic membrane therapy in chronic wound management has evolved significantly since its first documented uses in the early 20th century. This technique, originally applied in ocular trauma and infections, has gradually expanded to other fields, including chronic wound care, where its immunomodulatory and regenerative properties have garnered attention.[1,10] Our study contributes to this growing field by examining the efficacy of amniotic membranes in challenging chronic wounds, focusing on the ability of this treatment to promote healing and reduce the need for complex surgical interventions. Numerous studies have highlighted the benefits of amniotic membrane therapy, particularly in diabetic and venous

Figure 2. 65 Yo female with crural tissue loss which complicated with diabetes mellitus **(a)**, after surgical debridment and amniotic membrane use **(b)**, postoperative second week **(c)**.

ulcers. For instance, Zelen et al.[11] demonstrated in a 2013 randomized trial that amniotic membranes achieved a greater reduction in wound size than standard care in diabetic foot ulcers. A 2024 meta-analysis by Alomairi et al.[12] confirmed the efficacy of this approach in chronic venous and diabetic ulcers, underscoring its potential to accelerate wound healing. Our findings align with this literature, particularly regarding cases where the membrane was used before reconstruction to prepare the wound bed, which resulted in reduced surgical complexity. Unlike previous studies that primarily focused on wound closure rates, our research examined the broader implications of using amniotic membrane, including its effect on surgical outcomes. Among our cases, the patients with comorbidities presented significant challenges to traditional treatment modalities. Despite these complexities, the amniotic membrane contributed to granulation and epithelialization, reducing the necessity for advanced reconstructive procedures. Amniotic membranes, with their unique composition of extracellular matrix components, growth factors, and stem cells, provide a robust platform for tissue regeneration. These properties facilitate a moist wound environment, promote epithelialization, and suppress inflammatory responses, which establishes the membrane as a promising tool in chronic wound management. For instance, in trauma cases that do not include additional systemic conditions, using the membrane allows for simpler surgeries, such as skin grafts, which represent a transition from more invasive approaches. This finding highlights the potential for using amniotic membrane to bridge the gap between conservative and surgical management. However, although the outcomes of our study were encouraging, several limitations warrant discussion. First, the small sample size, including seven patients, restricts the ability of our findings to be generalized. Furthermore, the absence of a control group treated with standard care, or other advanced therapies limits direct comparisons. Future studies incorporating larger sample sizes and randomized controlled designs would provide more definitive conclusions. In addition, the variability in the types of amniotic membranes used—lyophilized versus cryopreserved—could influence outcomes, and this warrants further exploration. Also, while amniotic membranes offer significant therapeutic potential, their cost remains a critical factor in clinical decision-making. Effective patient selection is essential to ensure the balance between cost and benefit. Given that chronic wound care often incurs substantial healthcare expenditures, the ability of amniotic membranes to reduce hospital stays and surgical complexity represents a valuable contribution. However, long-term cost-benefit analyses are needed to validate these advantages in diverse healthcare settings.

Our study underscores the versatility of amniotic membrane therapy in managing chronic wounds, particularly in preparing complex wound beds for less invasive surgeries. While the benefits of this therapy are well documented in specific wound types, our findings suggest their potential in broader applications, even in cases with significant comorbidities. Future research should aim to standardize protocols and explore synergistic effects with other advanced therapies to maximize the potential of this innovative approach in wound care.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: G.F., Ç.Ç.; Design: G.F.; Supervision: G.F., Ç.Ç.; Fundings: G.F., Ç.Ç.; Materials: S.O.A., E.A.; Data: S.O.A., E.A.; Analysis: G.F., Ç.Ç.; Literature search: G.F., Ç.Ç.; Writing: S.O.A., E.A.; Critical revision: S.O.A., G.F., Ç.Ç.

Conflict of Interest

None declared.

REFERENCES

1. Ingraldi AL, Audet RG, Tabor AJ. The preparation and clinical efficacy of amnion-derived membranes: A review. J Funct Biomater. 2023;14:531. [CrossRef]
2. Gupta A. Classification of wounds and the physiology of wound healing. In Kumar P, Kothari V, eds. Wound Healing Research. Singapore: Springer; 2021. [CrossRef]
3. Wilkinson HN, Hardman MJ. Wound healing: Cellular mechanisms and pathological outcomes. Open Biol 2020;10:200223. [CrossRef]
4. Summer M, Ali S, Fiaz U, Hussain T, Khan RRM, Fiaz H. Revealing the molecular mechanisms in wound healing and the effects of different physiological factors including diabetes, age, and stress. J Mol Histol 2024;55:637–54. [CrossRef]
5. Han G, Ceilley R. Chronic wound healing: A review of current management and treatments. Adv Ther 2017;34:599–610. [CrossRef]
6. Mahmoudi M, Gould LJ. Opportunities and challenges of the management of chronic wounds: A multidisciplinary viewpoint. Chronic Wound Care Manag Res 2020;7:27–36. [CrossRef]
7. Beyene RT, Derryberry SL Jr, Barbul A. The effect of comorbidities on wound healing. Surg Clin North Am 2020;100:695–705. [CrossRef]
8. Schmiedova I, Dembickaja A, Kiselakova L, Nowakova B, Slama P. Using of amniotic membrane derivatives for the treatment of chronic wounds. Membranes 2021;11:941. [CrossRef]
9. Zelen CM, Serena TE, Denoziere G, Fetterolf DE. A prospective randomised comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. Int Wound J 2013;10:502–7. [CrossRef]
10. Plummer CE, Ollivier F, Kallberg M, Brooks D, Barrie K, Utter M, et al. The use of amniotic membrane transplantation for ocular surface reconstruction: A review and series of 58 equine clinical cases (2002–2008). Vet Ophthalmol 2009;12:17–24. [CrossRef]
11. Zelen CM, Snyder RJ, Serena TE, Li WW. The use of human amnion/chorion membrane in the clinical setting for lower extremity repair: A review. Clin Podiatr Med Surg 2015;32:135–46. [CrossRef]
12. Alomairi AA, Alhatlani RA, Alharbi SM, Alqurain ZJ, Alanazi IZ, Alanazi SA, et al. Assessing the application and effectiveness of human amniotic membrane in the management of venous and diabetic ulcers: A systematic review and meta-analysis of randomized controlled trials. Cureus 2024;16:e56659. [CrossRef]

Kronik Yaralarda Amniyotik Membran Kullanımının Etkinliği

Bu çalışma, insan amniyotik membranının kronik yara bakımındaki etkinliğini incelemekte ve doku rejenerasyonunu destekleyici özellikleri ile cerrahi müdahale gereksinimini azaltmadaki potansiyel rolünü değerlendirmektedir. Diyabet ve vasküler hastalıklar gibi komorbid durumlarla sıklıkla ilişkilendirilen kronik yaralar, klinik yönetim açısından önemli zorluklar teşkil etmektedir. Ekstrasellüler matriks bileşenleri ve büyüme faktörleri bakımından zengin, damarsız bir biyolojik yapı olan insan amniyotik membranı, immünomodülatör ve rejeneratif özellikleri sayesinde umut verici bir tedavi seçeneği sunmaktadır. Çalışmada, bir yara bakım ünitesinde kronik yara nedeniyle insan amniyotik membranı ile tedavi edilen yedi hasta retrospektif olarak değerlendirildi. Tedavi uygulamaları bir ila iki haftalık aralıklarla gerçekleştirilmiş olup, sterilite kurallarına uygun uygulama ve düzenli takip süreçlerine özel önem verilmiştir. Elde edilen bulgular, yara boyutlarında anlamlı küçülme, granülasyon ve epitelizasyon süreçlerinde hızlanma ile karmaşık cerrahi gereksiniminde azalma olduğunu ortaya koymuştur. Özellikle eşlik eden sistemik hastalıkları bulunan hastalarda, daha basit rekonstrüktif cerrahi girişimlere olanak sağlayacak şekilde uygun yara yatağı hazırlığı sağlanmıştır. Olumlu klinik sonuçlara rağmen, çalışmanın sınırlı örneklem büyüklüğü ve kontrol grubunun bulunmaması gibi kısıtlılıkları dikkate değerdir. Bulgular mevcut literatür ile uyum göstermekte olup, insan amniyotik membranının kronik yara yönetiminde standart tedavi protokollerine entegre edilmesine yönelik daha geniş örneklemli ve kontrollü çalışmalara ihtiyaç olduğunu ortaya koymaktadır. Genel olarak, insan amniyotik membranı; konservatif ve cerrahi yaklaşımlar arasında bir köprü işlevi görebilecek, maliyet etkin ve yenilikçi bir tedavi alternatifi olarak öne çıkmaktadır.

Anahtar Sözcükler: İnsan amniyotik membran; kronik yara; yara tedavisi.

SCIE DOI: 10.14744/scie.2024.23921
South. Clin. Ist. Euras. 2025;36(3):294-300

Review

The Role of LEF1 Protein in Chronic Lymphocytic Leukemia and Different Treatment Methods

Ayça Nur Demir,[1] Cumali Yalçın,[2] Aycan Acet,[3] Can Özlü[4]

[1]Department of Emergency Medicine, Afyonkarahisar Emirdağ State Hospital, Afyonkarahisar, Türkiye
[2]Department of Hematology, Kütahya City Hospital, Kütahya, Türkiye
[3]Department of Internal Medicine, Kütahya Health Science University Faculty of Medicine, Kütahya, Türkiye
[4]Department of Internal Medicine, Hematology, Kütahya Health Science University Faculty of Medicine, Kütahya, İstanbul, Türkiye

Submitted: 06.06.2024
Revised: 11.03.2025
Accepted: 17.03.2025

Correspondence: Ayça Nur Demir, Department of Emergency Medicine, Afyonkarahisar Emirdağ State Hospital, Afyonkarahisar, Türkiye
E-mail: aycanur15@gmail.com

Keywords: CLL; drugs; LEF-1; treatment.

ABSTRACT

A subtype of white blood cells called lymphocytes is the source of chronic lymphocytic leukemia (CLL), a malignancy of the bone marrow and blood. A single lymphocyte can transform into a cancer cell, proliferate over time, and finally displace normal lymphocytes in the lymph nodes and bone marrow. These cells can no longer fight infection, in contrast to normal lymphocytes. It has been demonstrated that lymphoid enhancer-binding factor-1 (LEF1), a member of the LEF/TCF transcription factor family, plays an essential role in regulating Wnt-pathway target genes. LEF1 plays a crucial role in many cancers. Recent studies have shown that LEF1 is overexpressed in CLL. LEF1 is specifically expressed at early stages of B-cell differentiation and is essential for survival and proliferation. In this review, the general course of the disease in CLL, the applied treatment strategies and the role of the LEF1 protein are analyzed in the light of current studies.

INTRODUCTION

Adult patients with chronic lymphocytic leukemia (CLL) are typically older. CLL is the most prevalent adult leukemia in Western Countries due to its high incidence rate and extended survival rate, which generally starts as a relatively indolent illness. A single CD5+ B cell overgrowth that also expresses low levels of CD79b, CD20, and CD23, as well as surface membrane immunoglobulin (smIg) of a single IG light (L) chain type, causes the disorder. Clinical results for this clonal overgrowth vary greatly; some patients pass just 2-4 years after diagnosis, while others continue to survive for decades. This heterogeneity is caused by both extrinsic (such as inputs provided by different signaling pathways in the tissue microenvironment; TME) and intrinsic (such as genetic and epigenetic changes in coding and noncoding genes) factors in leukemic B cells. [1] Following the introduction of targeted therapies, they have been shown to significantly improve overall survival in CLL patients.[2]

Lymphoid enhancer binding factor (LEF1) functions through the wingless-type mouse mammary tumor virus integration site (Wnt) signaling pathway and is an essential transcription factor for the survival and proliferation of B and T cells.[3] Recent studies have shown that high LEF1 expression is a predictive marker for CLL diagnosis and prognosis. [4-6] This review addresses the role of the LEF1 protein in

the development of CLL, as well as the environmental, genetic, and epidemiologic factors that influence the disease, starting with clinical presentation, diagnosis and prognostic markers. Finally, it concludes with factors that contribute to disease progression or resistance to treatment, identifying both current and novel treatment options.

Chronic Lymphocytic Leukemia Process Distribution by Age, Race and Gender

When we look at it, the average age of diagnosis of the disease is stated as 70. However, it is revealed that the number of cases is highest between the ages of 65-74.[2] In addition, since the incidence of this disease varies according to races or ethnicity, the rates may also vary. When we look at the ratios, the order is as follows: White>Black->Hispanic>Asian>Pacific Islands. The incidence also varies according to gender. It is twice more common in men than in women.[7]

Environmental Factors

When we look at environmental factors, it has been seen that various poisons are associated with the development of CLL.[8] It was revealed that substances used in wars in the past years also triggered the disease. However, it cannot be said that these substances are a serious factor in the disease.[9] More research is needed for this. In addition, some diseases that weaken the immune system (respiratory tract infections, herpes zoster, etc.) may be a precursor to CLL. In addition, hypogammaglobulinemia is common in most CLL patients. This problem is thought to be helpful in the diagnosis of the disease.[10,11]

Genetic Factors

When we look at genetic factors in CLL, it has the highest incidence of familial association. Disease development rates of first-degree relatives increase approximately 8-9 times. But in the Asian region, on the contrary, the incidence of CLL remains low.[7] The nine most probable genes that are transcriptionally active in CLL cells and control human B-cell development, signaling, or immunological function were selected from this group.[12,13] GWASs of myeloma and CLL patients verified this by identifying common risk loci impacted by variants in B-cell regulatory elements that impact genes involved in B-cell development. In accordance with this, mutations in B-cell regulatory elements that impact genes involved in B-cell development found to affect common risk loci in GWASs of CLL and myeloma patients.[13]

Chromosome anomalies in leukemic cells from patients with CLL were observed in another part. Additionally, leukemic clones of normal cells from CLL patients in the early phases of hematopoiesis include mutations. These mutations result in a pre-leukemic condition that is similar to monoclonal B lymphocytosis, but they are insufficient to cause the disease.[14] The somatic abnormalities del13q, tri12, del11q, and del17p are the most frequently observed in mature CLL cells, in that order of frequency. At diagnosis, 13q and tri12 deletions are revealed. Typically, del11q and del17p are identified later in the disease.[15]

Lymphoid Enhancer-binding Factor 1

LEF1/TCF transcription factor family, which includes lymphoid enhancer-binding factor-1 (LEF1), has been demonstrated to be important in controlling Wnt-pathway target genes.[16] The expression of LEF1 is restricted to the initial phases of B-cell differentiation and is essential for the survival and growth of these cells. Studies have shown that LEF1 is overexpressed in CLL. In addition, it has been shown that highly malignant acute leukemias express more LEF1 compared to low-grade chronic leukemias.[17]

Howe et al.[18] found that patients with CLL showed higher expression of LEF1. They discovered that CLL cells showed higher amounts of LEF1, which were almost absent in non-Hodgkin lymphoma cells, when they compared LEF1 expression in the two types of cancer. They concluded that with the exception of CLL, LEF1 is not consistently expressed in all lymphoproliferative malignancies with mature B-cell properties. Further studies into gene expression verified that CLL cells exhibited a substantial overexpression of LEF1 in contrast to typical B lymphocytes.[19,20]

Menter et al.[4] demonstrated the diagnostic utility of LEF1 in CLL. LEF1 was expressed in 77 out of 80 CLL patients. The specificity and sensitivity of LEF1 for the diagnosis of CLL were 0.93 and 0.96, respectively. Walther et al.[21] observed that LEF1 is absent from mantle cell and marginal zone lymphomas but expressed and transcriptionally active in the majority of Burkitt lymphoma patients and 3% of DLBCL. According to Tandon et al.,[22] immunohistochemistry revealed that LEF1 was expressed 100% in CLL; a small subset of high-grade Follicular Lymphoma and several Diffuse Large B Cell Lymphoma (38%) also displayed LEF1 expression, although to a lower extent.

In a study of 197 CLL and 6 Monoclonal B-cell Lymphocytosis patients, the duration of treatment-free survival (TFS) and overall survival (OS) was much longer in CLL patients with low LEF1 expression than in those with high LEF1 levels.[6] Erdfelder et al.[23] showed that high LEF1 expression was associated with poor prognosis and disease progression in patients with CLL. Additionally, the mean LEF1 RER for patients in need of treatment was 85.61, while the mean for patients in the newly diagnosed Binet A stage was just 22.01 ($p<0.001$).

Clinical and Laboratory Parameters

In most Western Countries with developed healthcare systems, CLL is diagnosed by finding a high number of lymphocytes in a complete blood count obtained during standard medical screenings. The diagnosis is established by flow cytometric measurement of the quantity of CD5+CD19+ B cells if the lymphocyte count increases further. Physical examination alone is adequate because most of CLL patients are asymptomatic, since they lack symptoms like fever, sweats at night, weight loss.[24]

Prognostic Markers

Once CLL is diagnosed, a number of prognostic indications identify the disease's stage and indicate the clinical path the disease will take in each individual. This is done by examining the physical examination and whole blood results together. These two conditions are still important in the diagnosis of CLL. Two risk classifications, Modified Rai and Binet, are used in CLL staging.[25,26] Together with these two laboratory-based and clinical categories, a new classification method incorporating genetic data has been introduced. The Chronic Lymphocytic Leukemia-International Prognostic Index (CLL-IPI) is a novel classification method that uses five independent prognostic criteria.[27] Table 1 displays the risk groups and survival percentages assessed in four distinct categories based on this system. Estimates of the clinical progression and result are determined by the analysis of several laboratory data. One of the most reliable methods among these analyzes is IGVH (immunoglobulin variable heavy-chain) mutation status. In other words, the number of somatic mutations in the IGVH gene or the absence of mutations are examined.[28,29]

Therapeutic Methods Applied in CLL

Taking a look back, we are making significant progress on understanding the nature of CLL. There is hope for a cure in the future due to the increased understanding of the disease and the development of new prognostic and treatment alternatives. Comprehensive treatment involves the use of multiple modalities such as immunotherapeutic methods monoclonal antibodies, chemotherapy, and other small molecule therapies.[29]

Treatment of CLL US Food and Drug Administration (FDA) Approved

The frontline settings of CLL include alkylating agents (such as bendamustine, chlorambucil, and cyclophosphamide), purine analogs (such as fludarabine and pentostatin), anti-CD20 monoclonal antibodies (such as obinutuzumab, ofatumumab, and rituximab), and Bruton Tyrosine kinase inhibitors (such as ibrutinib). The US FDA approved cellular therapies (allogenic hematopoetic stem cell transplantation as a relapsed setting of CLL), ibrutinib, phosphatidylinositol-3-kinase inhibitor idelalisib + rituximab, duvelisib, BCL-2 inhibitor (venetoclax) +/− rituximab, and anti-CD20 monoclonal antibodies (Obinutuzumab, Ofatumumab, Rituximab).[30]

Table 1. CLL-International Prognostic Index (CLL-IPI)

Age	≤65: 0 point	
	>65: 1 point	
Clinical stage	Binet A/Rai 0: 0 point	
	Binet B, C/Rai I-IV: 1 point	
B2 mikroglobulin	≤3.5: 0 point	
level (mg/L)	>3.5: 2 point	
IGVH mutation	Yes: 0 point	
	None: 2 point	
Del (17p) and/or p53	None: 0 point	
mutation	Yes: 4 point	
CLL-IPI score	**Risk category**	**5-year OS (%)**
0-1	Low risk	93.2
2-3	Intermediate risk	79.3
4-6	High risk	63.3
7-10	Very high risk	23.3

IGHV: Immunoglobulin variable heavy-chain, OS: Overall survival

Patients with advanced CLL are not cured with conventional therapy. Treatment aims to improve overall quality of life and, particularly, to prolong overall survival by reversing cytopenias and relieving associated symptoms. Predicting overall survival with current treatments including novel agents has proved difficult due of the short follow-up of studies analyzing these combinations. Expected overall survival with new treatments varies from a few years to decades, dependent on the severity of the disease, the patient, and the selected strategy of treatment.[30]

When Del 17p or TP53 mutation positive; there are different options for targetted therapies. Ibrutinib, ibrutinib plus obinituzumab, acalabrutinib, venetoclax plus obinutuzumab, venetoclax are options for del 17p or TP53 positivity. When IGVH unmutated; ibrutinib, ibrutinib plus obinutuzumab, acalabrutinib, venetoclax plus obinutuzumab are treatment options. If IGVH mutated and the patient is fit; ibrutinib, ibrutinib plus obinutuzumab, acalabrutinib with or without obinutuzumab, venetoclax plus obinutuzumab, FCR, BR are treatment options. If IGVH mutated and the patient is unfit; ibrutinib, acalabrutinib with or without obinutuzumab, venetoclax plus obinutuzumab, BR, chlorambucil plus obinutuzumab are treatment options.[30]

Anti-CD 20 Monoclonal Antibodies

For the past ten years, patients with chronic lymphocytic leukemia (CLL), chemoimmunotherapy has been the accepted course of treatment. The development of a new generation of anti-CD20 antibodies with improved therapeutic efficacy is a result of advances in monoclonal antibody technology.[31]

Rituximab, ofatumumab, and obinutuzumab are the three monoclonal antibodies that have been approved for the treatment of CLL Survival rates of patients with CLL have been found to be significantly higher when anti-CD20 monoclonal antibodies (mAbs) and chemotherapy are used together. In patients with CLL who have not received prior treatment, adding rituximab to ibrutinib does not increase PFS because of ibrutinib's antagonistic effect on anti-CD20 antibodies. In patients with CLL who have not received prior treatment, adding rituximab to ibrutinib does not increase PFS because of ibrutinib's antagonistic effect on anti-CD20 antibodies. On the other hand, PFS might be increased by combining a more selective BTKi, acalabrutinib, with a glycoengineered anti-CD20 mAbs, obinutuzumab. For patients with autoimmune cytopenia or rapidly progressive diseases, the combination of an an-

ti-CD20 mAb and a BTKi is recommended. Unlike BTKi, anti-CD20 mAbs combined with fixed-duration venetoclax can result in an elevated rate of undetectable minimal residual disease and profound remission; this combination has been linked to better survival rates for CLL patients in both first line and relapse/resistant.[32]

Purine Analogs

Some of the purine analogs that we're looking at are: Fludarabine, pentostatin, and cladribine. In most reported CLL studies, patient survival was associated with response to chemotherapy and disease onset. Fludarabine can elicit a major cytoreductive response in a proportion of patients with previously untreated CLL.[33] Fludarabine is by far the most extensively studied analogue.[34] It provides complete remission. Specifically, older patients with advanced disease and those who have previously received treatment respond better to single agent fludarabine.

Fludarabine is the most comprehensive and widely evaluated of these nucleoside analogues and is typically the leading and widely used major drug in the FCR (fludarabine, cyclophosphamide, and rituximab) regimen. Because prolonged remissions have been reported in this setting, FCR remains the recommended first-line therapy for eligible young patients (<60 years) with IGVH.[35,36]

Pentostatin has also been shown to have clinical activity in CLL and is less toxic than its fludarabine counterpart, which may provide some important advantages. Pentostatin is used together with cyclophosphamide and rituximab. When administered previously, it did not respond as fully as the more commonly used FCR regimen.[37]

In studies on cladribine, it was noted that it showed remission similar to fludarabine as a single agent or in combination treatments.[38]

Bruton Tyrosine Kinase Inhibitors

There are two types of BTKi. First generation BTKi is İbrutibib. FDA approved ibrutinib who had received at least one previous thereapy or with del 17p, mantle cell lymphoma with ≥ 1 prior therapy Waldenstrom's macroglobulinemia. This indication supported with RESONATE Phase III clinical trial for CLL, Pivotal Phase II trial for mantle cell, Pivotal phase II for Waldenstrom's Macroglobulinemia.[39,40]

Second generation BTK inhibitor is Acalabrutinib FDA approved in year 2019 for treatment of CLL. This indication supported with ELEVATE-TN and ASCEND trials. Obinituzumab plus chlorambucil versus monotherapy acalabrutinib or obinituzumab plus acalabrutinib compared about progression free survival (PFS) therapy of untreated CLL patients in ELEVATE-TN trial PFS was sinificantly longer on the monotherapy acalabrutinib and combination with obinituzumab.[41]

Phosphoinositide 3-kinase (PI3K) inhibitors

There are different types of PI3K inhibitors named İdelalisib, Copanlisib, Alpelisib, Umbralisib, and Duvelisib. İdelalisib approved at 2014 and duvelisib aproved 2018 in FDA. In 2019 umbralisib was approved for fast tract status for CLL. This tree agent was used for relapsed refractory CLL. It is well known that although many CLL patients show disease responsive to treatment with kinase inhibitors, they often discontinue treatment because of side effects.[42]

Chemoimmunotherapy

Immunochemotherapy is another form of treatment. Immunotoxins and monoclonal antibodies are becoming significant agents in this therapeutic modality and are being investigated in clinical studies with patients with CLL. A chimeric human mouse monoclonal antibody that targets the CD20 antigen is called rituximab.[33,34] At every stage of B cell development, with the exception of stem cells and plasma cells, CD20 is expressed.[43] The antileukemia effects of rituximab include lysis that is dependent on complement, cytotoxicity that is mediated by antibodies on cells, and the direct activation of apoptosis. Nevertheless, studies showed that compared to other forms of lymphoma, higher doses of rituximab are successful for CLL.[44,45]

Alemtuzumab is another drug. It is a monoclonal antibody to the CD52 antigen that is recombinant and completely human.[38] Alemtuzumab significantly improves overall response rates and survival rates in individuals with relapsing CLL, according to several studies. Additionally, alemtuzumab has been shown to help CLL as well as other diseases with poor prognosis. Also, the combination of Rituximab with Fludarabine has been found to improve overall response rates in CLL.[46]

Allogeneic Hematopoietic Stem Cell Transplant

Upon reviewing the literature and publications, we find that the European Bone Marrow Transplantation Group has released a study. It is emphasized in this work that the required criteria for allogeneic hematopoietic stem cell transplantation for CLL are given.[47] The scientists who published the study emphasize that this method works well in patients with various abnormalities who are unresponsive to chemotherapy or who relapse after achieving complete remission using a purine analogue. In addition to this study, it is stated that the mortality rate is high in most studies.[48]

Other Treatment Methods

In addition to immunotherapy and other treatments, additional CLL treatment approaches are also reviewed. Oblimersen, an antisense phosphothioate oligonucleotide, is one of them. Oblimersen targets BCL-2, an anti-apoptotic molecule's messenger RNA.[43] This drug has a moderate effect in patients with recurrent CLL in a single use. However, when combined with Fludarabine-Cyclophosphamide, the effect level increases.[45]

How I treat CLL?

As we mentioned, chronic lymphocytic leukemia (CLL) is a type of cancer that is usually seen in middle-aged and

older people and has a slow course in the bone marrow and blood. It occurs when lymphocytes, one of our white blood cells, increase in an uncontrolled and abnormal number in the bone marrow, blood and lymph nodes. The purpose of lymphocytes in the immune system of our body is to create a defense against the diseases that occur. When CLL occurs, lymphocytes become unable to function. As a result, the body's defense system weakens and becomes weak against diseases. When it comes to adult cancer, CLL is often the second most frequent kind. There are several components involved in this disease. One of these is overexpression of the LEF1 protein. Recently studies supported this situation. In addition, various mutations play a role in the emergence of the disease. In addition, the cause of the disease varies in gender, race and different ethnic origins. Looking at the studies, different parameters of the disease were examined and revealed. As a result of these parameters, different treatment methods have emerged.

General chemotherapy applications and specialized biological agents are used in the first and later advanced treatment stages in the treatment of CLL. Generalized non-chemotherapy regimens currently recommended for CLL include monotherapy and combination therapies with BTK inhibitors, monoclonal antibodies, PI3K inhibitors, lenalidomide and B-cell lymphoma inhibitors. Clinical developments focusing on individual CAR T cell monotherapy have been slowed by poor response levels and short periods of remission. Apart from various analogue and drug trials, it was concluded that bone marrow transplantation also gave successful results in some studies, but the mortality rate was high in most studies. It is emphasized that studies on bone marrow transplantation should still be continued. In addition, these treatment variations give the hematologists some great options, to choice the best treatment model.

Conclusion

CLL is still a disease that is challenging to cure and has a significant recurrence rate even with current treatment plans. Consequently, it is still essential to look for new drugs and make a thorough effort to comprehend the molecular processes underlying the disease's pathogenesis. The LEF1 protein, which has a critical role in this disease, needs to be investigated in detail. New drug studies for this protein should be started.

Informed Consent

Retrospective study.

Peer-review

Externally peer-reviewed.

Authorship Contributions

Concept: A.N.D., C.Ö.; Design: A.N.D.; Supervision: C.Y.; Fundings: A.A.; Materials: A.A., C.Y.; Data collection &/or processing: A.N.D., C.Y.; Analysis and/or interpretation: A.A., C.Y.; Literature search: A.N.D., C.Ö.; Writing: A.N.D., C.Ö.; Critical review: C.Ö.

Conflict of Interest

None declared.

REFERENCES

1. Chiorazzi N, Chen SS, Rai KR. Chronic lymphocytic leukemia. Cold Spring Harb Perspect Med 2021;11:a035220. [CrossRef]
2. Alrawashdh N, Sweasy J, Erstad B, McBride A, Persky DO, Abraham I. Survival trends in chronic lymphocytic leukemia across treatment eras: US SEER database analysis (1985-2017). Ann Hematol 2021;100:2501–12. [CrossRef]
3. Staal FJ, Clevers HC. WNT signalling and haematopoiesis: A WNT-WNT situation. Nat Rev Immunol 2005;5:21–30. [CrossRef]
4. Menter T, Trivedi P, Ahmad R, Flora R, Dirnhofer S, Tzankov A, et al. Diagnostic utility of lymphoid enhancer binding factor 1 immunohistochemistry in small b-cell lymphomas. Am J Clin Pathol 2017;147:292–300. [CrossRef]
5. Menter T, Dirnhofer S, Tzankov A. LEF1: A highly specific marker for the diagnosis of chronic lymphocytic B cell leukaemia/small lymphocytic B cell lymphoma. J Clin Pathol 2015;68:473–8. [CrossRef]
6. Wu W, Zhu H, Fu Y, Shen W, Miao K, Hong M, et al. High LEF1 expression predicts adverse prognosis in chronic lymphocytic leukemia and may be targeted by ethacrynic acid. Oncotarget 2016;7:21631–43. [CrossRef]
7. Gale RP, Cozen W, Goodman MT, Wang FF, Bernstein L. Decreased chronic lymphocytic leukemia incidence in Asians in Los Angeles County. Leuk Res 2000;24:665–9. [CrossRef]
8. Leon ME, Schinasi LH, Lebailly P, Beane Freeman LE, Nordby KC, Ferro G, et al. Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA: A pooled analysis from the AGRICOH consortium. Int J Epidemiol 2019;48:1519–35. [CrossRef]
9. Baumann Kreuziger LM, Tarchand G, Morrison VA. The impact of Agent Orange exposure on presentation and prognosis of patients with chronic lymphocytic leukemia. Leuk Lymphoma 2014;55:63–6. [CrossRef]
10. Landgren O, Rapkin JS, Caporaso NE, Mellemkjaer L, Gridley G, Goldin LR, et al. Respiratory tract infections and subsequent risk of chronic lymphocytic leukemia. Blood 2007;109:2198–201. [CrossRef]
11. Landgren O, Gridley G, Check D, Caporaso NE, Morris Brown L. Acquired immune-related and inflammatory conditions and subsequent chronic lymphocytic leukaemia. Br J Haematol 2007;139:791–8. [CrossRef]
12. Di Bernardo MC, Crowther-Swanepoel D, Broderick P, Webb E, Sellick G, Wild R, et al. A genome-wide association study identifies six susceptibility loci for chronic lymphocytic leukemia. Nat Genet 2008;40:1204–10. [CrossRef]
13. Crowther-Swanepoel D, Broderick P, Di Bernardo MC, Dobbins SE, Torres M, Mansouri M, et al. Common variants at 2q37.3, 8q24.21, 15q21.3 and 16q24.1 influence chronic lymphocytic leukemia risk. Nat Genet 2010;42:132–6. [CrossRef]
14. Damm F, Mylonas E, Cosson A, Yoshida K, Della Valle V, Mouly E, et al. Acquired initiating mutations in early hematopoietic cells of CLL patients. Cancer Discov 2014;4:1088–101. [CrossRef]
15. Marsilio S, Khiabanian H, Fabbri G, Vergani S, Scuoppo C, Montserrat E, et al. Somatic CLL mutations occur at multiple distinct hematopoietic maturation stages: Documentation and cautionary note regarding cell fraction purity. Leukemia 2018;32:1041–4. [CrossRef]
16. Travis A, Amsterdam A, Belanger C, Grosschedl R. LEF-1, a gene encoding a lymphoid-specific protein with an HMG domain, regulates T-cell receptor alpha enhancer function [corrected]. Genes Dev 1991;5:880–94. Erratum in: Genes Dev 1991;5:1113. [CrossRef]

17. Reya T, O'Riordan M, Okamura R, Devaney E, Willert K, Nusse R, et al. Wnt signaling regulates B lymphocyte proliferation through a LEF-1 dependent mechanism. Immunity 2000;13:15–24. [CrossRef]
18. Howe D, Bromidge T. Variation of LEF-1 mRNA expression in low-grade B-cell non-Hodgkin's lymphoma. Leuk Res 2006;30:29–32. [CrossRef]
19. Gutiérrez NC, Ocio EM, de Las Rivas J, Maiso P, Delgado M, Fermiñán E, et al. Gene expression profiling of B lymphocytes and plasma cells from Waldenström's macroglobulinemia: Comparison with expression patterns of the same cell counterparts from chronic lymphocytic leukemia, multiple myeloma and normal individuals. Leukemia 2007;21:541–9. [CrossRef]
20. Jelinek DF, Tschumper RC, Stolovitzky GA, Iturria SJ, Tu Y, Lepre J, et al. Identification of a global gene expression signature of B-chronic lymphocytic leukemia. Mol Cancer Res 2003;1:346–61.
21. Walther N, Ulrich A, Vockerodt M, von Bonin F, Klapper W, Meyer K, et al. Aberrant lymphocyte enhancer-binding factor 1 expression is characteristic for sporadic Burkitt's lymphoma. Am J Pathol 2013;182:1092–8. [CrossRef]
22. Tandon B, Peterson L, Gao J, Nelson B, Ma S, Rosen S, et al. Nuclear overexpression of lymphoid-enhancer-binding factor 1 identifies chronic lymphocytic leukemia/small lymphocytic lymphoma in small B-cell lymphomas. Mod Pathol 2011;24:1433–43. [CrossRef]
23. Erdfelder F, Hertweck M, Filipovich A, Uhrmacher S, Kreuzer KA. High lymphoid enhancer-binding factor-1 expression is associated with disease progression and poor prognosis in chronic lymphocytic leukemia. Hematol Rep 2010;2:e3. [CrossRef]
24. Hallek M, Cheson BD, Catovsky D, Caligaris-Cappio F, Dighiero G, Döhner H, et al. IwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood 2018;131:2745–60. [CrossRef]
25. Rai KR, Sawitsky A, Cronkite EP, Chanana AD, Levy RN, Pasternack BS. Clinical staging of chronic lymphocytic leukemia. Blood 1975;46:219–34. [CrossRef]
26. Binet JL, Auquier A, Dighiero G, Chastang C, Piguet H, Goasguen J, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer 1981;48:198–206. [CrossRef]
27. Fidan K. Chronic lymphocytic leukemia. J Curr Hematol Oncol Res 2023;1:59–67. [CrossRef]
28. Schroeder HW Jr, Dighiero G. The pathogenesis of chronic lymphocytic leukemia: Analysis of the antibody repertoire. Immunol Today 1994;15:288–94. [CrossRef]
29. Hashimoto S, Dono M, Wakai M, Allen SL, Lichtman SM, Schulman P, et al. Somatic diversification and selection of immunoglobulin heavy and light chain variable region genes in IgG+ CD5+ chronic lymphocytic leukemia B cells. J Exp Med 1995;181:1507–17. [CrossRef]
30. Ahn IE, Brown JR. Selecting initial therapy in CLL. Hematology Am Soc Hematol Educ Program 2022;2022:323–8. [CrossRef]
31. Yosifov DY, Wolf C, Stilgenbauer S, Mertens D. From biology to therapy: The CLL success story. Hemasphere 2019;3:e175. [CrossRef]
32. Shah HR, Stephens DM. Is there a role for anti-CD20 antibodies in CLL? Hematology Am Soc Hematol Educ Program 2021;2021:68–75. [CrossRef]
33. Del Poeta G, Del Principe MI, Buccisano F, Maurillo L, Capelli G, Luciano F, et al. Consolidation and maintenance immunotherapy with rituximab improve clinical outcome in patients with B-cell chronic lymphocytic leukemia. Cancer 2008;112:119–28. [CrossRef]
34. Robak T, Smolewski P, Cebula B, Szmigielska-Kaplon A, Chojnowski K, Blonski JZ. Rituximab combined with cladribine or with cladribine and cyclophosphamide in heavily pretreated patients with indolent lymphoproliferative disorders and mantle cell lymphoma. Cancer 2006;107:1542–50. [CrossRef]
35. Klepfish A, Gilles L, Ioannis K, Eliezer R, Ami S. Enhancing the action of rituximab in chronic lymphocytic leukemia by adding fresh frozen plasma: Complement/rituximab interactions & clinical results in refractory CLL. Ann N Y Acad Sci 2009;1173:865–73. [CrossRef]
36. Badoux XC, Keating MJ, Wang X, O'Brien SM, Ferrajoli A, Faderl S, et al. Fludarabine, cyclophosphamide, and rituximab chemoimmunotherapy is highly effective treatment for relapsed patients with CLL. Blood 2011;117:3016–24. [CrossRef]
37. Zent CS, Taylor RP, Lindorfer MA, Beum PV, LaPlant B, Wu W, et al. Chemoimmunotherapy for relapsed/refractory and progressive 17p13-deleted chronic lymphocytic leukemia (CLL) combining pentostatin, alemtuzumab, and low-dose rituximab is effective and tolerable and limits loss of CD20 expression by circulating CLL cells. Am J Hematol 2014;89:757–65. [CrossRef]
38. Osterborg A, Mellstedt H, Keating M. Clinical effects of alemtuzumab (Campath-1H) in B-cell chronic lymphocytic leukemia. Med Oncol 2002;19:S21–6. [CrossRef]
39. Smith MR. Ibrutinib in B lymphoid malignancies. Expert Opin Pharmacother 2015;16:1879–87. [CrossRef]
40. Byrd JC, Brown JR, O'Brien S, Barrientos JC, Kay NE, Reddy NM, et al. Ibrutinib versus ofatumumab in previously treated chronic lymphoid leukemia. N Engl J Med 2014;371:213–23. [CrossRef]
41. Sharman JP, Egyed M, Jurczak W, Skarbnik A, Pagel JM, Flinn IW, et al. Efficacy and safety in a 4-year follow-up of the ELEVATE-TN study comparing acalabrutinib with or without obinutuzumab versus obinutuzumab plus chlorambucil in treatment-naïve chronic lymphocytic leukemia. Leukemia 2022;36:1171–5. Erratum in: Leukemia 2025;39:529. [CrossRef]
42. Vanhaesebroeck B, Perry MWD, Brown JR, André F, Okkenhaug K. PI3K inhibitors are finally coming of age. Nat Rev Drug Discov 2021;20:741–69. Erratum in: Nat Rev Drug Discov 2021;20:798. [CrossRef]
43. O'Brien SM, Cunningham CC, Golenkov AK, Turkina AG, Novick SC, Rai KR. Phase I to II multicenter study of oblimersen sodium, a Bcl-2 antisense oligonucleotide, in patients with advanced chronic lymphocytic leukemia. J Clin Oncol 2005;23:7697–702. [CrossRef]
44. O'Connor OA, Czuczman MS, Lacasce AS, Gerecitano J, Leonard JP, Dunleavy K, et al. A phase 1 study evaluating the safety, PK & efficacy of ABT-263 in subjects with refractory or relapsed lymphoid malignancies. Ann Oncol 2008;19:115–6.
45. O'Brien S, Moore JO, Boyd TE, Larratt LM, Skotnicki A, Koziner B, et al. Randomized phase III trial of fludarabine plus cyclophosphamide with or without oblimersen sodium (Bcl-2 antisense) in patients with relapsed or refractory chronic lymphocytic leukemia. J Clin Oncol 2007;25:1114–20. Erratum in: J Clin Oncol 2008;26:820. [CrossRef]
46. Lozanski G, Heerema NA, Flinn IW, Smith L, Harbison J, Webb J, et al. Alemtuzumab is an effective therapy for chronic lymphocytic leukemia with p53 mutations and deletions. Blood 2004;103:3278–81. [CrossRef]
47. Dreger P, Corradini P, Kimby E, Michallet M, Milligan D, Schetelig J, et al. Indications for allogeneic stem cell transplantation in chronic lymphocytic leukemia: The EBMT transplant consensus. Leukemia 2007;21:12–7. [CrossRef]
48. Jabbour E, Keating MJ, Champlin RE, Khouri IF. Stem cell transplantation for chronic lymphocytic leukemia: Should not more patients get a transplant? Bone Marrow Transplant 2004;3:289–97. [CrossRef]

Kronik Lenfositik Lösemide LEF1 Proteininin Rolü ve Farklı Tedavi Yöntemleri

Kemik iliği ve lenf düğümlerinin bir malignitesi olan kronik lenfositik löseminin (KLL) kaynağı, beyaz kan hücrelerinin bir alt türü olan lenfositlerdir. Tek bir lenfosit kanser hücresine dönüşebilir, zamanla çoğalabilir ve sonunda lenf düğümlerinde ve kemik iliğinde normal lenfositlerin yerini alabilir. Bu hücreler artık normal lenfositlerin aksine enfeksiyonla savaşamaz. Lenfoid güçlendirici bağlama faktörü-1 (LEF1), Wnt yolu hedef genlerinin düzenlenmesinde önemli bir rol oynadığı gösterilen LEF/TCF transkripsiyon faktörü ailesinin bir parçasıdır. LEF1 birçok kanserde çok önemli bir rol oynar. Son yıllarda yapılan çalışmalar LEF1'in CLL'de aşırı eksprese edildiğini göstermiştir. LEF1, özellikle B hücresi farklılaşmasının erken aşamalarında eksprese edilir ve hayatta kalma ve çoğalma için gereklidir. Bu derlemede, KLL'de hastalığın genel seyri, uygulanan tedavi stratejileri ve LEF1 proteininin rolü güncel çalışmalar ışığında analiz edilmiştir.

Anahtar Sözcükler: İlaçlar; KLL; LEF-1; tedavi.