

e-ISSN: 3023-655X

Volume: 4

Issue: 4

Year: 2025

Ankyra

Medical Journal



Pharmacist
Nurse
Dentist
Physiotherapist
Emergency

MEDICAL

MEDICAL

Health Care
Doctor
Hospital
Pharmacist
Nurse
Physiotherapist
Surgeon
Emergency



EDITOR-IN-CHIEF

Assoc. Prof. Yasemin KORKUT KURTOĞLU

Department of Family Medicine, Faculty of Medicine, Kütahya Health Sciences University, Kütahya, Türkiye

ASSOCIATE EDITORS-IN-CHIEF

Spec. Mesut KARATAŞ, MD

Department of Cardiology, Koşuyolu Yüksek İhtisas Training and Research Hospital, İstanbul, Türkiye

EDITORIAL BOARD

Assoc. Prof. Adnan ÖZDEMİR

Department of Radiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Alpaslan TANOĞLU

Department of Gastroenterology, Medical Park Göztepe Hospital Complex, Faculty of Medicine, Bahçeşehir University, İstanbul, Türkiye

Assoc. Prof. Alper ÖZCAN

Division of Pediatric Hematology-Oncology, Department of Pediatrics, Faculty of Medicine, Erciyes University, Kayseri, Türkiye

Prof. Ayça TÖREL ERGÜR

Division of Pediatric Endocrinology and Metabolism, Department of Pediatrics, Faculty of Medicine, Ufuk University, Ankara, Türkiye

Prof. Aydın ÇİFCİ

Department of Internal Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Assoc. Prof. Ayşe Gülşen DOĞAN

Department of Physical Medicine and Rehabilitation, Hitit University Erol Olçok Training and Research Hospital, Çorum, Türkiye

Prof. Ayşegül ALTUNKESER

Department of Radiology, Konya Training and Research Hospital, University of Health Sciences, Konya, Türkiye

Prof. Berna AKINCI ÖZYÜREK

Department of Chest Diseases, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Prof. Bülent Cavit YÜKSEL

Department of General Surgery, Güven Hospital, Ankara, Türkiye

Spec. Bulut DEMİREL, MD

Department of Emergency Medicine, Royal Alexandra Hospital, Paisley, Glasgow, United Kingdom

Prof. Ekrem ÜNAL

Department of Pediatric Hematology-Oncology, Medical Point Gaziantep Hospital, Gaziantep, Türkiye

Prof. Ela CÖMERT

Department of Ear Nose Throat, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Engin TUTKUN

Public Health Specialist, HLC-LAB Medical Director, Ankara, Türkiye

Prof. Ercan YUVANÇ

Department of Urology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Assoc. Prof. Esra Güzel TANOĞLU

Department of Molecular Biology and Genetics, Hamidiye Health Sciences Institute, University of Health Sciences, İstanbul, Türkiye

Assoc. Prof. Faruk PEHLİVANLI

Department of General Surgery, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Fevzi ALTUNTAŞ

Department of Hematology, Dr. Abdurrahman Yurtaslan Ankara Oncology Training and Research Hospital, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye

Prof. Harun DÜĞEROĞLU

Department of Internal Medicine, Faculty of Medicine, Ordu University, Ordu, Türkiye

Assist. Prof. Hatice TOPAL

Department of Pediatrics, Sincan Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Assoc. Prof. Hidayet MEMMEDZADE

Department of Endocrinology and Metabolism, Bakü Medical Plaza Hospital, Baku, Azerbaijan

Prof. İbrahim Celalettin HAZNEDAROĞLU

Division of Hematology, Department of Internal Medicine, Faculty of Medicine, Hacettepe University, Ankara, Türkiye

Assist. Prof. Kadri YILDIZ

Department of Orthopedics and Traumatology, Medicana Bursa Hospital, Bursa, Türkiye

Assoc. Prof. Kenan ÇADIRCI

Department of Internal Medicine, Erzurum Region Training and Research Hospital, Erzurum Faculty of Medicine, University of Health Sciences, Erzurum, Türkiye

Prof. Michele CASSANO

Department of Ear Nose Throat, University of Foggia, Foggia, Italy

Assoc. Prof. Muhammed KARADENİZ

Department of Cardiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Murat KEKİLLİ

Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, Gazi University, Ankara, Türkiye

Assoc. Prof. Murat DOĞAN

Department of Internal Medicine, Hitit University Erol Olçok Training and Research Hospital, Çorum, Türkiye

Assoc. Prof. Mustafa ÇAPRAZ

Department of Internal Medicine, Faculty of Medicine, Amasya University, Amasya, Türkiye

Prof. Mustafa ÖĞDEN

Department of Neurosurgery, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Nilgün ALTUNTAŞ

Division of Neonatology, Department of Pediatrics, Ankara Bilkent City Hospital, Faculty of Medicine, Yıldırım Beyazıt University, Ankara, Türkiye

Assoc. Prof. Özge VERGİLİ

Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Kırıkkale University, Kırıkkale, Türkiye

Assoc. Prof. Ramazan BALDEMİR

Department of Anesthesiology and Reanimation, Ankara Atatürk Sanatorium Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Prof. Salih CESUR

Department of Infectious Diseases and Clinical Microbiology, Ankara Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Assoc. Prof. Selim YALÇIN

Division of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Prof. Serdar GÜL

Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Assoc. Prof. Süleyman GÖKMEN

Department of Food Processing, Technical Sciences Vocational High School, Faculty of Engineering, Karamanoğlu Mehmetbey University, Karaman, Türkiye

Assoc. Prof. Yaşar TOPAL

Department of Pediatrics, Sincan Training and Research Hospital, University of Health Sciences, Ankara, Türkiye

Assoc. Prof. Yücel YILMAZ

Department of Cardiology, Kayseri City Hospital, Kayseri, Türkiye

Assoc. Prof. Ziya ŞENCAN

Department of Ear Nose Throat, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

ENGLISH LANGUAGE EDITOR

Mohammad Bilal ALSAVAF, MD

Department of Otorhinolaryngology, Faculty of Medicine, Ohio State University, OH, USA

STATISTICS EDITOR

Assist. Prof. Maruf GÖĞEBAKAN

Department of Maritime Business and Administration, Maritime Faculty, Onyedi Eylül University, Balıkesir, Türkiye

LAYOUT EDITOR

Hatice AKYIL

Biologist, MediHealth Academy Publishing, Ankara, Türkiye

Volume: 4 Issue: 4 Year: 2025

ORIGINAL ARTICLES

Evaluation of the management of the Huzur Köy Project for substance use disorder 69-73

Kaplan Kasar K, Derhem B.

The burden of pressure ulcers among inpatients in a tertiary physical medicine and rehabilitation center: a retrospective analysis74-79

Tezen Ö, Ulusoy S.

Association between red cell distribution width coefficient of variation and coronary slow flow.....80-84

Astan R.

The relationship between zinc status and inflammatory marker levels in FMF..... 85-87

Uysal A, Kandur Y, Gürkan M, Pek ME, Şanlı C, Alpcan A.

CALLY index in patients admitted in the intensive care unit with a diagnosis of decompensated heart failure 88-92

Eygi E, Sakallı S, Durucu B, Dondurmacı E, Akyüz İnanç F, Polat E.

LETTER TO THE EDITOR

Complex spinal case associated with Angelman syndrome..... 93-94

Baloğlu M.

Evaluation of the management of the Huzur Köy Project for substance use disorder

 Kübra Kaplan Kasar¹,  Baki Derhem²

¹Department of Family Medicine, Kırıkkale Provincial Health Directorate, Kırıkkale, Türkiye

²Department of Family Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale University, Kırıkkale, Türkiye

Cite this article: Kaplan Kasar K, Derhem B. Evaluation of the management of the Huzur Köy Project for substance use disorder. *Ank Med J.* 2025;4(4):69-73.

Received: 16/08/2025

Accepted: 17/09/2025

Published: 19/10/2025

ABSTRACT

Aims: This study aims to retrospectively evaluate the treatment outcomes of individuals at the Huzur Köy Addiction Treatment and Social Reintegration Center in Türkiye and to identify sociodemographic and treatment-related factors associated with post-discharge abstinence.

Methods: In this retrospective descriptive study, the medical records of 152 individuals treated at the center between 2022 and 2024 were analyzed. Sociodemographic characteristics, substance use history, treatment process details, and post-discharge follow-up data were examined. Staying clean was defined as the complete absence of psychoactive substance use following discharge.

Results: The mean age of participants was 28.6 years, and the post-discharge abstinence rate was 30.9%. Statistically significant associations with abstinence were found for marital status (higher rates in married individuals, $p=0.037$) and positive family relationships ($p=0.035$). Crucially, the length of stay was a significant predictor of success ($p<0.001$). The staying clean rate for individuals who stayed 3–6 months was 45.3%, compared to 20.5% for those who stayed 0–3 months ($p=0.001$).

Conclusion: The findings of this retrospective analysis indicate that a longer duration of inpatient rehabilitation is strongly associated with higher rates of staying clean. Furthermore, social support systems, specifically being married and having good family relationships, appear to be significant protective factors. These results highlight the importance of long-term, structured rehabilitation programs and suggest that interventions aimed at strengthening social support may improve treatment outcomes in Türkiye.

Keywords: Substance use disorder, rehabilitation, treatment outcome, retrospective study, length of stay

INTRODUCTION

Substance use disorder is a highly prevalent public health problem worldwide and a leading cause of significant disability.¹ Substances involved in this disorder include alcohol, caffeine, cannabis, hallucinogens, inhalants, opioids, sedatives, hypnotics, anxiolytics, stimulants (such as amphetamine derivatives, cocaine, and other stimulants), and tobacco.² These substances are addictive psychoactive agents that possess both stimulant and euphoric effects as well as depressant properties on the central nervous system.³

Substance use disorder is recognized as a major health issue on a global scale. According to the 2023 World Drug Report published by the United Nations Office on Drugs and Crime (UNODC), an estimated 284 million people aged 15–64 worldwide used drugs at least once between 2021 and 2022.⁴ A nationwide survey conducted in the United States reported that approximately 14.5% of individuals aged 12 years or

older were diagnosed with substance use disorder, with 10.2% meeting criteria for alcohol use disorder and 6.6% for illicit drug use disorder.⁵ Furthermore, data from the National Center for Health Statistics of the U.S. Centers for Disease Control and Prevention (CDC) indicate that during the twelve months ending in December 2023, 107,543 individuals died from drug overdose.⁶

Similarly, substance use disorder represents a serious health concern in Türkiye. A study conducted by the Turkish Statistical Institute (TÜİK) estimated that, as of 2022, approximately 2.7 million people (4% of the population) in the country had used drugs at least once in their lifetime.⁷ The increasing number of individuals receiving treatment services is also noteworthy. In 2013, 218,574 outpatients and 7,897 inpatients were treated, whereas in 2018 these numbers rose to 251,593 and 13,841, respectively.^{8,9} In 2022, the number

of outpatients receiving treatment reached 302.911, and the number of inpatients was 18.187.¹⁰ In 2023, outpatient visits numbered 349.393, while admissions to inpatient treatment centers totaled 16.291.¹¹

The harms caused by alcohol and substance use disorders extend beyond the individual's health, producing multidimensional legal, social, and economic consequences that affect the family, social environment, and society at large.¹ These disorders represent one of the most costly health problems for healthcare systems, creating a significant burden both at the individual and societal levels. Treatment expenses, loss of workforce, decreased functionality, increased substance-related crime rates, and traffic accidents constitute the main components of these costs.¹² The increasing prevalence of substance addiction, both globally and in Türkiye, threatens not only the individual's social functioning but also public health.

Various studies conducted in Türkiye on addiction reveal that the current health service provision is mainly focused on crisis intervention and treatment centres are inadequate in number and limited in terms of capacity. In addition, it is reported that treatment periods are short and the methods applied are inadequate in terms of effectiveness.¹³

The Huzur Köy Addiction Treatment and Social Reintegration Center is a full-time rehabilitation facility operating under the auspices of the Governorship of Kırıkkale and managed by the Kırıkkale Provincial Health Directorate. It provides inpatient care for individuals with substance addiction. Eligible participants are male, aged 18 years or older, able to communicate in Turkish, free of any physical health conditions that would prevent participation in communal living, and have voluntarily completed at least three weeks of detoxification treatment at an Alcohol and Substance Addiction Treatment Center (AMATEM).

The Huzur Köy Model adopts a holistic case management approach that focuses not only on the treatment process but also on the long-term social reintegration of individuals. This approach aims to facilitate access to necessary services, encourage active participation in the process, and promote sustainable recovery. Rehabilitation programs are structured into 3-and 6-month modules, with the 6-month program being recommended. Participation is voluntary, and individuals may choose to withdraw from the program at any time.

The center provides regular psychotherapy sessions and family meetings, with monitoring by a multidisciplinary team of psychologists, social workers, and physicians. With the support of the Provincial Mufti's Office, values-based education is offered to address spiritual needs. Operating under the governorship, the center collaborates with public institutions to provide comprehensive support to participants.

To facilitate social reintegration, vocational courses, entrepreneurship training, sports activities, and planned social events are organized throughout the rehabilitation process.

The aim of this study is to evaluate the effectiveness of the Huzur Köy Project, a strengths-based, case management-oriented intervention model for individuals undergoing treatment for substance use disorder.

METHODS

This study is a file-based, retrospective descriptive study in which the records of individuals receiving treatment at the Huzur Köy Addiction Treatment and Social Reintegration Center. All individuals who had received treatment services at the center since its establishment and whose medical records were accessible were included in the study. A total of 152 clients' data were evaluated. No specific inclusion restrictions were applied, and only individuals whose records could not be retrieved were excluded.

The study was conducted after obtaining approval from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 12.05.2025, Decision No: 2025.01.06) and official permission from the Kırıkkale Provincial Health Directorate. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Data were manually collected from the institution's patient record archives by the researcher. A data collection form developed by the researcher was used, which included headings on sociodemographic characteristics, substance use history, treatment process, participation in vocational courses, disciplinary status, and post-discharge follow-up. In this study, "staying clean" was defined as the complete absence of psychoactive substance use during the follow-up period after discharge from the center. Remission was considered as a period entirely free from substance use.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics, version 25.0. Descriptive statistics included frequency, percentage, mean, and standard deviation values. Independent samples t-test was used for comparisons of continuous variables between groups. Pearson's Chi-square test was applied to evaluate relationships between categorical variables; in cases where expected cell counts were insufficient, Fisher's Exact test and Yates' corrected Chi-square test were employed. A significance level of $p < 0.05$ was considered statistically significant for all analyses.

RESULTS

In this study, the medical records of a total of 152 individuals treated at the Huzur Köy Addiction Treatment and Social Reintegration Center between 2022 and 2024 were retrospectively reviewed. The mean age of participants was 28.6 ± 5.6 years, and the mean age of initiation of substance use was 17.3 ± 5.5 years. Of the participants, 80.3% were single and 19.7% were married.

Family relationships were self-rated as "good" by 55.3% of participants, "moderate" by 28.9%, and "poor" by 15.8%. A family history of substance use was present in 15.1% of participants. Among them, 87.5% reported having previously attempted to quit, with a mean prior staying clean duration of only 10.3 ± 14.5 weeks. Before admission, 17.1% had received subcutaneous implant treatment, and 25.7% had benefited from psychosocial support services. Suicidal ideation prior to admission was reported by 24.3% of individuals.

The mean length of stay at the Huzur Köy facility was 67.6 ± 49.5 days. The most frequently attended vocational

courses were greenhouse cultivation (34.2%), pastry and culinary arts (21.7%), and ceramic tile painting (21.7%). While 59.2% of participants did not receive any disciplinary penalties, 36.2% accumulated penalty points, and 4.6% were expelled from the center due to disciplinary action.

Post-discharge, 40.1% of individuals completed the treatment program, 50% left voluntarily, and 9.9% were discharged due to disciplinary measures. During follow-up, the employment rate was 46.7%, and the staying clean rate was 30.9%.

Statistically significant relationships were determined with some variables affecting the cleanliness of individuals after discharge. A significant relationship was found between marital status and staying clean ($p=0.037$); the rate of staying clean was found to be higher in married individuals. Similarly, family relationships were significantly associated with staying clean ($p=0.035$); the rate of staying clean was significantly higher in individuals who rated their family relationships as good.

No significant associations were found between staying clean status and other variables such as educational level, psychosocial support, family history of substance use, previous quit attempts, subcutaneous implant therapy, or suicidal ideation. The relationship between staying clean status and participants' sociodemographic characteristics is presented in [Table](#).

The relationship between the length of stay in Huzur Köy and their ability to stay clean after discharge was found to be statistically significant ($p<0.001$). While the average rehabilitation period of the individuals who managed to stay clean was 93.38 ± 51.31 days, this period was calculated as 56.05 ± 44.29 days in individuals who could not stay clean. In addition, when the individuals were divided into two groups according to the time they spent in rehabilitation (0-3 months and 3-6 months), it was observed that 45.3% of those who stayed between 3-6 months remained clean after

discharge, whereas this rate remained at 20.5% in individuals who stayed 0-3 months ($p=0.001$). These findings suggest that individuals who received treatment in Huzur Köy for a longer period of time were significantly more likely to remain clean after discharge and that the duration of treatment may be a determining factor in rehabilitation success.

DISCUSSION

Substance use disorder is a multidimensional public health issue that adversely affects not only an individual's physical and mental health but also social functioning, family structure, and community relationships.¹ In recent years, models focusing solely on medical interventions in addiction treatment have proven insufficient; instead, comprehensive rehabilitation approaches that address the psychosocial aspects of the individual have gained increasing importance. In this context, recovery-oriented therapeutic community models in Europe such as San Patrignano (Italy), Parceval (Germany), and the United Kingdom stand out for their long-term, inpatient, individualized, multidisciplinary, and vocational skill-building approaches.^{14,15} In Türkiye, institutions such as AMATEM, BAHAR, and YEDAM are developing both outpatient and inpatient service models for addiction treatment.¹⁶ The Huzur Köy Addiction Treatment and Social Integration Center examined in this study represents a unique application in Türkiye. This center offers long-term inpatient treatment combined with psychosocial support, vocational training, and social integration simultaneously, showing structural similarities to therapeutic communities in Europe.

In this study, the sociodemographic characteristics, treatment processes, and post-discharge cleanliness outcomes of individuals treated at Huzur Köy were evaluated, and the findings show parallels with both national and international literature. The predominance of young adults (mean age 28.6 years) and single individuals (80.3%) among the participants indicates that substance use is more common in younger

Table. Relationship between sociodemographic variables and staying clean

Variable		Not clean (n=105)	Clean (n=47)	Total (n=152)	p
Marital status	Single	89 (73.0%)	33 (27.0%)	122 (80.3%)	0.037
	Married	16 (53.3%)	14 (46.7%)	30 (19.7%)	
Family relationships	Poor	16 (66.7%)	8 (33.3%)	24 (15.8%)	0.035
	Modarete	37 (84.1%)	7 (15.9%)	44 (28.9%)	
Education level	Good	52 (61.9%)	32 (38.1%)	84 (55.3%)	0.092
	Primary school	4 (40.0%)	6 (60.0%)	10 (6.6%)	
	Secondary school	40 (67.8%)	19 (32.2%)	59 (38.8%)	
History of receiving psychosocial support	High school and above	61 (73.5%)	22 (26.5%)	83 (54.6%)	0.67
	Yes	28 (71.8%)	11 (28.2%)	39 (25.7%)	
Family history of substance use	No	77 (68.1%)	36 (31.9%)	113 (74.3%)	0.301
	Yes	18 (78.3%)	5 (21.7%)	23 (15.1%)	
History of quit attempts	No	87 (67.4%)	42 (32.6%)	129 (84.9%)	0.551
	Yes	93 (69.9%)	40 (30.1%)	133 (87.5%)	
Subcutaneous implant application	No	12 (63.2%)	7 (36.8%)	19 (12.5%)	0.654
	Yes	17 (65.4%)	9 (34.6%)	26 (17.1%)	
Suicidal ideation	No	88 (69.8%)	38 (30.2%)	126 (82.9%)	0.556
	Yes	27 (73.0%)	10 (27.0%)	37 (24.3%)	
	No	78 (67.8%)	37 (32.2%)	115 (75.7%)	

age groups. Although 87.5% of individuals had previously attempted to quit, the average duration of cleanliness remained short (10.3 weeks), highlighting the chronic and relapsing nature of addiction. The National Institute on Drug Abuse (NIDA) defines addiction as a brain disease that requires long-term monitoring and multicomponent intervention.¹⁷

Within the treatment model applied at Huzur Köy, individuals receive structured cognitive behavioral therapy (CBT) throughout their stay. CBT aims to identify biased thoughts and cognitions related to substance use and replace them with functional alternatives, as well as recognize and restructure behavior patterns that trigger substance use.¹⁸ Literature has shown that CBT produces small but significant effects in the treatment of substance use disorders compared to other psychosocial interventions.^{19,20} Long-term inpatient programs, such as those at Huzur Köy, provide individuals not only with short-term psychoeducation but also prolonged, systematic, and repetitive exposure to CBT. This therapeutic continuity facilitates the internalization of behavioral change and reduces relapse risk.

One of the most striking findings of this study is the positive and statistically significant relationship between the length of stay at the center and cleanliness outcomes ($p < 0.001$). This finding shows that the rehabilitation process, i.e. its duration, is of critical importance in terms of the individual's integration into treatment, the development of coping skills, and the ability to break away from old habits. In the Iowa Case Management Project conducted by Hall and colleagues,²¹ it was emphasised that clients' active participation in the treatment process was decisive for the outcomes; the concept of 'participation' was highlighted. The fact that individuals who stayed longer at Huzur Village were able to remain clean at a higher rate suggests that they were exposed to the treatment content more extensively and were able to reinforce the skills they learned. Similarly, the literature indicates that long-term inpatient rehabilitation increases sustainability and that the duration of treatment is associated with behavioural change.^{22,23}

Studies evaluating the effects of long-term rehabilitation services for substance dependence in Türkiye are quite limited. The only comprehensive follow-up study in this field in the literature is the study evaluating the 2-year data of the BAHAR Centre affiliated with the Erenköy Mental and Nervous Diseases Training and Research Hospital. In this study, 52% of the 179 individuals who applied to the centre were enrolled in a part-time rehabilitation programme, while 48% were enrolled in a full-time programme. Of these, 75 individuals completed the first three-month programme and 54 individuals completed the six-month programme in remission and in a compliant manner. However, only 19 individuals were reported to have completed the one-year programme in remission. These findings indicate that participation rates in rehabilitation programmes remain limited and that success rates decrease with long-term follow-up.¹⁶ Compared to Huzur Köy data, a total of 152 individuals have been admitted to the program since its inception; only 10 completed the six-month program, and 51 completed the three-month program. Approximately 50% of participants withdrew voluntarily, while 9.9% left due to disciplinary reasons. Although the continuation rates were

low, individuals who completed the program demonstrated significantly higher post-discharge cleanliness rates.

While the Huzur Köy model shares structural similarities with the BAHAR model, the fact that a significant portion of participants left before three months indicates the need for strategies to improve retention in rehabilitation. Enhancing motivational interviewing, actively involving family support, and establishing individualized treatment goals early could be effective interventions to increase program success and continuity.

Social support systems emerged as a significant determinant in this study. Marital status (being married) and good family relationships significantly increased staying clean rates ($p = 0.037$ and $p = 0.035$). Family support is known to enhance motivation, act as a buffer against relapse, and help individuals develop a sense of belonging and responsibility.²² Hall et al.²¹ reported that case management positively influenced family functioning and parenting attitudes. The critical role of family in post-inpatient reintegration into society has also been highlighted in the study by Çölgeçen et al.²⁴

In this study, variables such as educational level, receipt of psychosocial support, subcutaneous implant use, family history of substance use, and suicidal ideation were not significantly associated with staying clean outcomes. This suggests that comprehensive and structured inpatient rehabilitation models, such as Huzur Köy, can have a strong impact on behavioral change regardless of individuals' initial risk profiles. Hall et al.²¹ similarly observed significant reductions in substance use during the first three months of treatment across all clients, indicating that treatment content may be more influential than individual differences.

Additionally, the Huzur Köy model not only provides external support (counseling, referrals, etc.) but also offers hands-on vocational training (greenhouse work, cooking, pastry making, etc.), which enhances self-efficacy and social integration. These structured, skill-oriented interventions can foster hope, productivity, and identity in individuals, thereby reducing relapse risk. Even the Iowa study reported limited but positive effects of case management on employment, supporting the notion that employment and productivity can serve as strong protective factors in addiction rehabilitation.^{14,21}

Limitations

This study has several limitations. In particular, the retrospective design, the absence of a control group, and the reliance of variables solely on recorded documents should be considered as constraints. Nevertheless, despite these limitations, the study provides important findings suggesting that various aspects of the Huzur Köy model may be effective in addiction treatment based on real-world data.

CONCLUSION

This study highlights that treatment duration, social support systems, and structured interventions aimed at developing vocational skills are critical factors in addiction management. Holistic models such as Huzur Köy offer a recovery-oriented approach that targets not only substance use but also all areas of an individual's life, enabling long-term success. The

wider implementation of such models across the country, as well as future controlled, prospective, and long-term studies to systematically evaluate their effects, is of significant importance.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted after obtaining approval from the Non-interventional Clinical Researches Ethics Committee of Kırıkkale University (Date: 12.05.2025, Decision No: 2025.01.06).

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement:

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

- Degenhardt L, Whiteford HA, Ferrari AJ, et al. Global burden of disease attributable to illicit drug use and dependence: findings from the Global Burden of Disease Study 2010. *Lancet*. 2013;382(9904):1564-1574. doi:10.1016/S0140-6736(13)61530-5
- Erath TG, LaCroix R, O'Keefe E, Higgins ST, Rawson RA. Substance use patterns, sociodemographics, and health profiles of harm reduction service recipients in Burlington, Vermont. *Harm Reduct J*. 2024;21(1):76. doi:10.1186/s12954-024-00995-y
- Er F. Askerlerde başlıca ruhsal-davranışsal sorunlar ve sosyal hizmet uygulamaları. Sakarya H, Çetinkaya AB, Tunaç ÇA. (Ed.). Askeri sosyal hizmet. Nika Yayınevi. 2021.
- United Nations Office on Drugs and Crime. World drug report 2023. Vienna: UNODC; 2023 (cited 2025 March 5). Available from: <https://www.unodc.org/unodc/en/data-and-analysis/world-drug-report-2023.html>
- Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2020 National Survey on Drug Use and Health. HHS Publication No. PEP21-07-0. Rockville, MD: Center for Behavioral Health Statistics and Quality; 2021.
- Ahmad FB, Cisewski JA, Rossen LM, Sutton P. National Center for Health Statistics: provisional drug overdose death counts. Centers for Disease Control and Prevention; Department of Health and Human Services. 2024.
- Türkiye İstatistik Kurumu. Türkiye sağlık araştırması 2022 (cited 2025 March 5). Available from: <https://data.tuik.gov.tr/Bulten/Index?p=Türkiye-Saglik-Arastirmasi-2022-49747>
- T.C. Narkotik Suçlarla Mücadele Daire Başkanlığı. Türkiye uyuşturucu raporu 2014 (cited 2025 March 8). Available from: <https://www.narkotik.pol.tr/kurumlar/narkotik.pol.tr/Arsiv/TUBIM/Documents/TURKIYE%20UYUSTURUCU%20RAPORU%202014.pdf>
- T.C. Narkotik Suçlarla Mücadele Daire Başkanlığı. Türkiye uyuşturucu raporu 2019 (cited 2025 March 8). Available from: <https://www.narkotik.pol.tr/kurumlar/narkotik.pol.tr/TUB%C4%B0M/Ülusal%20Yay%C4%B1nlar/2019-TURKIYE-UYUSTURUCU-RAPORU.pdf>
- T.C. Narkotik Suçlarla Mücadele Daire Başkanlığı. Türkiye uyuşturucu raporu 2023 (cited 2025 March 8). Available from: <https://www.narkotik.pol.tr/kurumlar/narkotik.pol.tr/TUB%C4%B0M/Ülusal%20Yay%C4%B1nlar/2023-TURKIYE-UYUSTURUCU-RAPORU.pdf>
- T.C. Narkotik Suçlarla Mücadele Daire Başkanlığı. Uyuşturucu raporu Eylül 2024 (cited 2025 March 8). Available from: https://www.narkotik.pol.tr/kurumlar/narkotik.pol.tr/Duyurular/2024/Eylul/2024_uyus_raporu.pdf
- Kosten TR, George TP. The neurobiology of substance dependence: implications for treatment. In: Clinical textbook of addictive disorders. 3rd ed. 2005.
- Gündüz Türkes S, Buz S. Alkol/madde kullanım bozukluğu olan bireylerin tedavi süreci ve taburculuk sonrası gereksinimleri üzerine bir araştırma: Ankara AMATEM örneği. *Toplum Ve Sosyal Hizmet*. 2022;33(2):437-462. doi:10.33417/tsh.956642
- Molina-Fernandez AJ. Manual on drug rehabilitation and recovery of drug users. Madrid: Triple R. 2017.
- Çiftçi GE, Uluocak PG. Almanya'da madde bağımlısı çocuk ve gençlere yönelik bir rehabilitasyon modeli. *Kriz Dergisi*. 2010;18(2):11-18. doi:10.1501/Kriz_0000000314
- Ünüböl B, Çinka E, Mayi M, et al. Bağımlı hastalar için rehabilitasyon: Erenköy Bahar modeli. *Psikiyatriye Güncel Yaklaşımlar*. 2021;13(3):412-427. doi:10.18863/pgy.796479
- National Institute on Drug Abuse (NIDA). Treatment approaches for drug addiction. Bethesda, MD: NIDA. 2019.
- Carroll KM. A cognitive-behavioral approach: treating cocaine addiction. Rockville: National Institute on Drug Abuse. 1998.
- Agosti V, Nunes EV, O'Shea D. Do manualized psychosocial interventions help reduce relapse among alcohol-dependent adults treated with naltrexone or placebo? A meta-analysis. *Am J Addict*. 2012; 21(6):501-507. doi:10.1111/j.1521-0391.2012.00270.x
- Hobbs JD, Kushner MG, Lee SS, Reardon SM, Maurer EW. Meta-analysis of supplemental treatment for depressive and anxiety disorders in patients being treated for alcohol dependence. *Am J Addict*. 2011; 20(4):319-329. doi:10.1111/j.1521-0391.2011.00140.x
- Hall JA, Sarrazin MS, Huber DL, et al. Iowa case management for rural drug abuse. *Res Soc Work Pract*. 2009;19(4):407-422. doi:10.1177/1049731509331925
- Reif S, Braude L, Lyman DR, et al. Peer recovery support for individuals with substance use disorders: assessing the evidence. *Psychiatr Serv*. 2014;65(7):853-861. doi:10.1176/appi.ps.201400047
- Guydish J, Sorensen JL, Chan M, et al. A randomized trial comparing day and residential drug abuse treatment: 18-month outcomes. *J Consult Clin Psychol*. 1999;67(3):428. doi:10.1037//0022-006x.67.3.428
- Çölgeçen Y, Abay AR. Psikiyatrik sosyal hizmet-koruyucu, tedavi edici ve rehabilite edici ruh sağlığı alanında sosyal çalışmacıların rolü. *OPUS Int J Soc Res*. 2018;9(16):2147-2185. doi:10.26466/opus.484950

The burden of pressure ulcers among inpatients in a tertiary physical medicine and rehabilitation center: a retrospective analysis

 Özge Tezen¹,  Serap Ulusoy²

¹Department of Physical Therapy and Rehabilitation, Ankara Bilkent City Hospital, Ankara, Türkiye

²Department of General Surgery, Ankara Bilkent City Hospital, Ankara, Türkiye

Cite this article: Tezen Ö, Ulusoy S. The burden of pressure ulcers among inpatients in a tertiary physical medicine and rehabilitation center: a retrospective analysis. *Ank Med J.* 2025;4(4):74-79.

Received: 22/09/2025

Accepted: 12/10/2025

Published: 19/10/2025

ABSTRACT

Aims: This study aimed to describe the clinical characteristics, risk factors, and treatment outcomes of pressure ulcers (PUs) among inpatients in a tertiary physical medicine and rehabilitation (PM&R) center. We hypothesized that advanced-stage ulcers would be associated with longer hospitalization, lower healing rates, and adverse laboratory parameters.

Methods: This retrospective cross-sectional study included 240 adult patients with PUs admitted to the PM&R Hospital of Ankara Bilkent City Hospital between June 1, 2022, and June 1, 2023. Demographic, clinical, laboratory, and wound-related data were extracted from medical records and standardized wound care forms. PUs were staged according to the 2019 EPUAP/NPIAP/PPPIA guideline. Treatment modalities and outcomes were analyzed. Linear regression was performed to identify predictors of residual wound size.

Results: The mean age of patients was 52.8±22.1 years; 63.3% were male. Frequent comorbidities included arterial hypertension (34.6%), hyperlipidemia (40.4%), diabetes mellitus (15.4%), and coronary artery disease (10.8%). The most common admission diagnoses were spinal cord injury (45.0%) and stroke (26.7%). Sacral ulcers (56.1%) predominated, with stage 2–3 lesions representing 77.1% of cases. Overall healing rate was 78.5%, but declined sharply in stage 4 ulcers (25.0%). Predictors of larger residual ulcer size included pre-admission ulcer presence ($p=0.028$), baseline ulcer size ($p<0.001$), and lower albumin ($p=0.002$). Debridement significantly reduced ulcer size ($p<0.001$). Functional outcomes improved, with 57.6% of non-ambulatory patients achieving therapeutic ambulation at discharge ($p<0.001$).

Conclusion: PUs remain a persistent challenge in rehabilitation, limiting both medical care and functional progress. Advanced-stage ulcers, malnutrition, and osteomyelitis predict poor outcomes, whereas surgical debridement is pivotal for healing. Integrating preventive strategies, nutritional optimization, and evidence-based therapies into structured rehabilitation programs can enhance recovery and reduce healthcare burden.

Keywords: Pressure ulcer, rehabilitation, spinal cord injuries

INTRODUCTION

Pressure ulcers (PUs) are a common and consequential health problem, particularly in clinical conditions associated with prolonged immobility. Patients admitted to PM&R clinics due to cerebrovascular events (CVE), spinal cord injury (SCI), or other neurological disorders are at heightened risk. Additional predisposing factors include extended intensive care unit (ICU) stays, advanced age, malnutrition, anemia, cognitive impairment, and restricted mobility.

Beyond local tissue damage, PUs increase the risk of infection and sepsis, contribute to mortality, complicate treatment,

prolong hospitalization, escalate healthcare costs, and limit participation in rehabilitation programs, thereby diminishing quality of life. A nationwide cross-sectional study from Finland reported a PU prevalence of 12.7% in acute inpatient care settings, including hospitals and rehabilitation units.¹ In patients with SCI, a systematic review and meta-analysis demonstrated that approximately 32% develop a PU during their lifetime.² Among trauma patients, a retrospective study from a referral trauma center in Northern Iran found a prevalence of 27.6%, with older age and lower hemoglobin levels identified as significant risk factors.³

While international guidelines delineate the definition, classification, prevention, and treatment of PUs,⁴ patient profiles and outcomes vary substantially across clinical settings. Accordingly, characterizing PU features and admission diagnoses (e.g., CVE, SCI, other neurological conditions) in PM&R inpatients is essential to inform effective treatment strategies and preventive interventions.

This study aimed to describe the clinical characteristics, risk factors, and treatment outcomes of PUs in patients hospitalized at a tertiary PM&R center. We hypothesized that, among PM&R inpatients, advanced-stage PUs would be associated with longer hospital stays, lower healing rates, and adverse laboratory parameters.

METHODS

Ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ankara Bilkent City Hospital No. 2 Clinical Researches Ethics Committee (Date: 21.02.2024, Approval No: E2-24-6500).

Study Design and Setting

This investigation was designed as a retrospective cross-sectional study and was conducted at the Physical Medicine and Rehabilitation Hospital (PM&RH) of Ankara Bilkent City Hospital between June 1, 2022, and June 1, 2023.

Patient Selection and Characteristics

A total of 240 patients were included in the study.

Inclusion criteria:

- Patients admitted to the PM&RH with a PU at the time of hospitalization
- Patients without a PU at admission but who developed one during follow-up
- Age ≥ 18 years
- Availability of complete medical records

Exclusion criteria:

- Patients without a PU at admission and who did not develop one during follow-up
- Age < 18 years
- Diagnosis of active malignancy
- Congenital or acquired immunodeficiency
- Incomplete clinical or laboratory data

Data Collection

Medical records and standardized wound care forms completed by wound care nurses were retrospectively reviewed. The following variables were extracted for each patient:

- **Demographic data:** Age, sex, height, weight, body-mass index (BMI)

- **Clinical variables:** Comorbidities, admission diagnosis to the PM&R clinic, history and duration of ICU stay, mobility status
- **Wound-related data:** Time of onset, duration, anatomical location, stage, wound size, treatment modalities applied, and wound outcome
- **Laboratory parameters:** Hemoglobin, albumin, and 25-hydroxy vitamin D levels at admission
- **Discharge data:** Discharge destination (home, nursing facility, death) and wound status at discharge

PUs were classified according to the 2019 International Guideline issued by the European Pressure Ulcer Advisory Panel (EPUAP), the National Pressure Injury Advisory Panel (NPIAP), and the Pan Pacific Pressure Injury Alliance (PPPIA).⁴

Wound assessments were based on retrospective chart review. Wound size was documented in centimeters (cm), recorded as the longest measurable length and width noted in the wound care forms. Staging was determined according to clinical notes, and in cases of uncertainty, classifications were confirmed by senior physicians as documented in the medical files.

Treatment modalities were categorized as conventional wound dressings, advanced wound care products (e.g., silver dressings, foam dressings), and negative pressure wound therapy (NPWT). Surgical debridement was recorded as a separate variable due to its invasive nature and distinct clinical implications. All treatment data applied during hospitalization were obtained retrospectively from medical records and wound care documentation.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 26.0 (Armonk, NY, USA). Continuous variables were summarized as mean, standard deviation, median, minimum, and maximum values, whereas categorical variables were expressed as counts and percentages. Normality of distribution was assessed with the Kolmogorov-Smirnov test. For paired comparisons within the same patients, the paired-Samples-t test was used for normally distributed data, and the Wilcoxon signed-rank test for non-normally distributed data. Changes in categorical variables between admission and discharge were evaluated using the McNemar test. To identify factors associated with wound size, a linear regression analysis was performed. A two-tailed $p < .05$ was considered statistically significant.

RESULTS

Between June 1, 2022, and June 1, 2023, a total of 5103 patients aged ≥ 18 years were admitted to the PM&RH of Ankara Bilkent City Hospital. Among them, 240 patients with PU were included in the study. The mean age was 52.8 ± 22.1 years (range, 18–92), and 63.3% were male. The mean BMI was 25.2 ± 5.2 . Regarding comorbidities, 15.4% of patients had diabetes mellitus, 34.6% had arterial hypertension, 40.4% had hyperlipidemia, and 10.8% had coronary artery disease (Table 1).

Table 1. Demographic characteristics and comorbidities of the patients

Characteristic	Value
Age (mean±SD, min-max)	52.8±22.1 (18-92)
Sex	63.3% male
BMI (mean±SD)	25.2±5.2
Diabetes mellitus	15.4%
Arterial hypertension	34.6%
Hyperlipidemia	40.4%
Coronary artery disease	10.8%

SD: Standard deviation, Min: Minimum, Max: Maximum, BMI: Body-mass index

Among patients admitted to the PM&R clinic with PU, the most frequent underlying condition was SCI (45.0%), followed by stroke (26.7%) and immobility syndrome (12.5%). Less common etiologies included anoxic brain injury (10.8%), polyneuropathy (3.8%), and multiple sclerosis (1.3%) (**Table 2**).

Table 2. Admission diagnoses of patients to the PM&R clinic

Diagnosis	n	%
Spinal cord injury	108	45.0
Stroke	64	26.7
Immobility syndrome	30	12.5
Anoxic brain injury	26	10.8
Polyneuropathy	9	3.8
Multiple sclerosis	3	1.3
Total	240	100

PM&R: Physical medicine and rehabilitation

Of the 240 patients included in the study, 197 (82.1%) presented with a PU at the time of admission to the PM&R clinic. Among these, 38 patients (19.3%) had developed the ulcer during their prior stay in ICUs before referral to rehabilitation. In 30 patients (12.5%), PUs developed during hospitalization in the rehabilitation clinic. In 13 patients (5.4%), the exact onset time of the ulcer could not be determined. The mean duration since diagnosis was 14.8 months (range, 1-360 months). The mean length of hospital stay in the rehabilitation clinic was 53.6 days (range, 6-162 days).

The most frequent site of PUs was the sacral region (56.1%; n=134), followed by the heel (25.1%; n=60) and the ischial tuberosity (13.0%; n=31). The majority of patients (97.5%) received daily dressing care with conventional wound products, whereas only 2.5% underwent NPWT, and 5.0% (n=12) required surgical debridement. Osteomyelitis was identified in 1.7% of cases (n=4). Following treatment, a statistically significant reduction in wound size was observed compared with baseline measurements ($p<.001$) (**Table 3**).

Table 3. Comparison of wound size at admission and discharge

	Admission median (min-max) mean±SD	Discharge median (min-max) mean±SD	P
Wound size	4.5 (0.001-3900)	0.5 (0.001-1500)	<0.001

SD: Standard deviation, Min: Minimum, Max: Maximum

Patients with stage 4 PUs had the longest mean length of hospital stay. A statistically significant difference was observed

among the stages in terms of the duration elapsed since diagnosis ($p=.010$). Furthermore, the length of hospital stay increased significantly with advancing ulcer stage ($p=.042$) (**Table 4**).

Table 4. Distribution of pressure ulcers by stages and healing rates

Stage	n	%	Healing rate (%)	Mean length of stay (days)
Stage 1	25	10.4	96.0	47.3±28.1
Stage 2	112	46.7	89.3	49.7±26.4
Stage 3	73	30.4	66.7	56.8±29.4
Stage 4	8	3.3	25.0	77.5±39.0
Suspected deep tissue injury	3	1.2	0.0	85.0±40.0
Unstageable pressure injury	19	7.9	18.2	61.6±32.4
Total	240	100	-	-

The laboratory findings of the patients are presented in **Table 5**. The mean serum 25-OH vitamin D level was 58.3 ± 34.3 ng/ml, albumin level was 36.4 ± 7.6 g/L, and hemoglobin level was 12.5 ± 7.1 g/dl. These results indicate that, particularly albumin and hemoglobin levels, were close to the lower limit of the normal range, reflecting impaired nutritional and hematological status in this patient population.

Table 5. Mean laboratory values of the patients

Parameter	Mean	Standard deviation
25-OH vitamin D level (ng/ml)	58.33	34.29
Albumin level (g/L)	36.42	7.58
Hemoglobin level (g/dl)	12.46	7.13

There was a statistically significant improvement in functional status between admission and discharge among patients with pressure injuries in the rehabilitation hospital ($p<.001$). A substantial proportion of patients who were non-ambulatory at admission progressed to therapeutic ambulation (57.6%) or indoor ambulation (5.1%) by discharge. Similarly, 31.0% of patients who were initially at the therapeutic ambulation level advanced to indoor ambulation. Although the transition to community ambulation was limited (1% of patients), an overall significant improvement in functional mobility was observed.

A linear regression analysis was performed to identify the factors influencing post-treatment PU size. The model was statistically significant ($F=12.141$, $p<.001$), explaining 51% of the variance in ulcer size. Significant predictors included the presence of hyperlipidemia ($B=-1.764$, $p=.001$), which was associated with smaller ulcer size, whereas coronary artery disease ($B=1.517$, $p=.004$) and arterial hypertension ($B=0.632$, $p=.045$) were associated with larger ulcer dimensions. Pre-admission ulcer presence ($B=0.854$, $p=.028$) and baseline ulcer size ($B=0.904$, $p<.001$) were strong predictors of increased residual wound size. Lower albumin levels ($B=-0.681$, $p=.002$) were independently associated with larger ulcers. Hemoglobin level ($B=0.251$, $p=.013$) was also identified as a significant predictor, although the direction of this association was clinically unexpected. Debridement significantly reduced ulcer size ($B=-3.855$, $p<.001$), whereas the presence of osteomyelitis predicted larger ulcer dimensions ($B=2.657$, $p=.017$). Diabetes mellitus,

25-OH vitamin D level, time since diagnosis, and treatment modalities were not statistically significant predictors (Table 6).

Table 6. Factors influencing pressure ulcer size (linear regression analysis)

Variable	B (coefficient)	t value	p value
Comorbidity: diabetes mellitus	0.096	0.221	0.895
Comorbidity: arterial hypertension	0.632	1.874	0.045
Comorbidity: hyperlipidemia	-1.764	-3.033	0.001
Comorbidity: coronary artery disease	1.517	2.628	0.004
Time since diagnosis (months)	-0.004	-1.054	0.293
Presence of PU before admission	0.854	2.209	0.028
Pressure ulcer size (baseline)	0.904	7.658	<0.001
25-OH vitamin D level	0.003	0.808	0.453
Albumin level	-0.681	-3.207	0.002
Hemoglobin level	0.251	2.513	0.013
Presence of debridement	-3.855	-6.373	<0.001
Presence of osteomyelitis	2.657	2.413	0.017
Treatment modalities	-0.852	-0.976	0.354

PU: Pressure ulcer

DISCUSSION

PU are among the most serious complications in patients requiring prolonged rehabilitation, contributing to increased morbidity, extended hospital stays, and impaired functional recovery. In this study, we evaluated 240 inpatients with PUs admitted to a tertiary PM&R clinic. Lesions were predominantly located in the sacral region and classified as stage 2-3. The overall healing rate was 78.5%; however, this rate declined substantially with advancing ulcer stage, and outcomes were particularly poor in stage 4 and deep tissue injuries. Low serum albumin levels, prolonged ICU stay, osteomyelitis, and larger baseline ulcer size were associated with adverse outcomes, whereas surgical debridement significantly improved healing. Moreover, functional status improved significantly during hospitalization, with more than half of the initially non-ambulatory patients achieving therapeutic ambulation by discharge. Taken together, these findings underscore the critical importance of early identification, risk factor modification, multidisciplinary management, and the integration of functional goals within rehabilitation practice.

In our cohort, PUs were most frequent among patients with SCI and stroke, which is in line with earlier studies. Verschueren et al.⁵ identified SCI patients as the group at highest risk for PU development during inpatient rehabilitation. The predominance of sacral ulcers, followed by heel involvement, also reflects patterns reported in previous investigations. Lee et al.⁶ confirmed that the heel remains the second most frequent anatomical location for PUs in immobilized patients. Similarly, Alito et al.⁷ demonstrated in their seven-year retrospective analysis that the sacrum and heel were consistently the most common sites of ulceration. The predominance of stage 2-3 lesions in our study is also consistent with previous rehabilitation-based cohorts, further underscoring the vulnerability of pressure-bearing areas and highlighting the need for targeted preventive strategies in high-risk populations.

In our study, the most significant factors associated with poor clinical outcomes were low serum albumin levels,

prolonged ICU stay, presence of osteomyelitis, and larger baseline ulcer size. These findings are consistent with the literature emphasizing the negative impact of malnutrition and systemic complications on PU healing. Gheri et al.⁸ reported that high CONUT scores independently predicted PU development in patients with severe acquired brain injury. Similarly, Langer et al.⁹ demonstrated in their systematic review that nutritional interventions, particularly protein supplementation, reduced the incidence of PUs and accelerated healing. Our finding that low albumin levels were strongly associated with worse prognosis aligns with these observations. Osteomyelitis, in particular, was also a significant predictor of adverse outcomes in our cohort. This is consistent with recent evidence showing that PUs complicated by bone infection are especially challenging to manage and are frequently associated with delayed healing and higher recurrence rates, particularly among patients with SCI.¹⁰

Furthermore, rehabilitation intensity and multidisciplinary management also play a critical role in outcomes. Chen et al.¹¹ showed that patients receiving high-intensity rehabilitation after ischemic stroke had a significantly lower risk of PU development.

In addition, Alito et al.,¹² in their seven-year single-center neurorehabilitation experience, reported that patients with traumatic and non-traumatic SCI receiving multidisciplinary care achieved significantly better neurological and functional outcomes. Consistent with these findings, our study highlights that intensive rehabilitation programs, combined with nutritional support and integrated wound care, are essential to improving treatment success in the management of PUs.

The prevention of PUs remains a cornerstone of management, particularly in high-risk rehabilitation populations. Self-management interventions and patient education have been proposed to improve skin care practices and reduce PU incidence in individuals with SCI.¹³ Similarly, a recent umbrella review identified low mobility, low BMI, and a prior history of PU as the strongest risk factors among wheelchair users.¹⁴ Our findings are consistent with these results, as patients with SCI in our cohort disproportionately presented with advanced-stage ulcers. Furthermore, in this group, PUs not only posed medical risks but also restricted functional recovery and social participation, in line with the findings reported by Piatt et al.¹⁵

Support surfaces are also a critical component of prevention. Huang et al.¹⁶ demonstrated in their best-evidence summary that dynamic air mattresses and pressure-redistribution systems significantly reduced PU incidence among immobilized patients. However, the integration of international guidelines (EPUAP/NPIAP/PPPIA) into daily clinical practice remains limited, as highlighted in a recent citation analysis by El Genedy-Kalyoncu and Kottner.¹⁷ In our study, staging and classification were based on these guidelines, demonstrating that local practices are in alignment with international standards.

National data from Türkiye further support our results. Several hospital-based studies have reported PU prevalence rates ranging between 7% and 15%, with hypoalbuminemia

and immobilization consistently identified as the strongest risk factors.¹⁸⁻²⁰ The higher risk profile observed in our cohort can be explained by prolonged ICU stays and neurological morbidity.

With regard to treatment, the use of NPWT was limited in our cohort, being applied in only 2.5% of patients. The main reason was that the device often interfered with mobilization and the performance of active rehabilitation exercises, which are essential in PM&R practice. This finding contrasts with the literature, where NPWT is considered a standard component of advanced wound management, promoting granulation tissue formation, reducing exudate, and accelerating healing when applied appropriately.²¹ Therefore, our results highlight the need to carefully balance wound care technologies with rehabilitation priorities to avoid compromising functional recovery.

In contrast, surgical debridement emerged as one of the most effective therapeutic interventions in our cohort. Regression analysis demonstrated that debridement significantly reduced wound size and improved healing outcomes, confirming its central role in PU management. By effectively removing necrotic tissue and bacterial load, surgical debridement creates an optimal wound bed for granulation and epithelialization. Previous studies have similarly reported that debridement, particularly when combined with appropriate wound care and rehabilitation strategies, accelerates healing and reduces the risk of systemic infection.²¹⁻²⁴ Taken together, these findings suggest that while NPWT remains an evidence-based adjunct for selected cases, surgical debridement is an indispensable modality in the management of advanced-stage PUs.

Another noteworthy finding was that higher hemoglobin levels were associated with larger residual ulcer size. This result contradicts existing literature, which typically associates anemia with impaired healing. Indeed, Jeon et al.²⁵ reported that a hemoglobin level of >11 g/dl was associated with a lower risk of PU worsening. The paradoxical association may be explained by unmeasured confounders (e.g., chronic hypoxia, relative polycythemia in severely immobilized SCI patients) or cohort-specific characteristics. This highlights the complexity of interpreting laboratory markers in heterogeneous rehabilitation populations and underscores the need for prospective studies to clarify the underlying mechanisms.

Wan et al.²⁶ stated that increasing knowledge and awareness regarding the prevention of PUs, as well as addressing the shortage of pressure-relieving beds and materials, should be among the most important strategies. Sen²⁷ also 2025 human wound and its burden update, emphasized a wound management system based on PU prevention, strengthened by education and supported by technology. In our study, since the risk of PU development increased with longer hospital stays, having adequate knowledge and a high level of awareness about preventive measures is of great importance.

Finally, rehabilitation-based interventions extend beyond mobilization and nutritional optimization. Physical modalities such as electrotherapy, laser therapy, and ultrasound have been investigated as adjunctive treatments in wound healing. A recent review concluded that these

modalities may enhance granulation, improve tissue perfusion, and support scar quality, although the overall certainty of evidence remains moderate.²⁴ In this context, incorporating selected physical therapies into comprehensive rehabilitation programs may further optimize PU healing and functional recovery.

Looking ahead, artificial intelligence (AI) based applications hold significant potential in the prevention and management of PUs. Recent advances in machine learning algorithms allow the prediction of ulcer risk by identifying patterns from large patient datasets, thereby enabling the implementation of individualized preventive strategies. Furthermore, AI systems integrated with digital wound imaging technologies can automatically analyze wound size, depth, and necrosis ratio, offering clinicians objective and dynamic monitoring. This approach not only provides more accurate prognostic assessment but also supports rational decision-making regarding the selection of treatment modalities (e.g., support surfaces, biological dressings, adjuvant physical therapy). Therefore, integrating AI-supported decision-making mechanisms into multidisciplinary care in PM&R clinics may represent an innovative step toward improving patient outcomes in the future.

Limitations

This study has several limitations. Its retrospective and single-center design precludes establishing causal relationships and limits the generalizability of the findings. Data were obtained from patient charts and nursing records, which may have resulted in incomplete information, particularly regarding the onset of ulcers and variations in treatment processes. In addition, biochemical parameters were recorded only at certain time points, overlooking potential dynamic changes. The heterogeneity of wound care modalities applied during hospitalization also introduces potential bias. For these reasons, multicenter, prospective studies are needed to provide more robust evidence.

CONCLUSION

PUs remain a persistent clinical challenge in PM&R practice, arising from patient related characteristics and multifactorial clinical determinants. Although they are a common complication, timely and evidence-based management can yield substantial improvements, and their presence should not be considered a contraindication to rehabilitation interventions. On the contrary, rigorously structured and scientifically grounded rehabilitation programs have the potential to promote wound healing and positively influence clinical outcomes.

In our cohort, surgical debridement emerged as a cornerstone in the management of advanced-stage PUs, underscoring its indispensable role alongside preventive and rehabilitative strategies. The findings further emphasize that early identification of high-risk patients, the adoption of individualized preventive measures, and the integration of effective rehabilitation approaches are critical for reducing incidence, enhancing functional recovery, and mitigating the healthcare burden.

Taken together, these results highlight the importance of combining preventive strategies with effective therapeutic

modalities within comprehensive rehabilitation frameworks. To strengthen the generalizability of these findings and to establish more robust evidence for optimizing clinical protocols, well-designed prospective multicenter studies are warranted.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Ankara Bilkent City Hospital No. 2 Clinical Researches Ethics Committee (Date: 21.02.2024, Decision No: E2-24-6500).

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. Tervo-Heikkinen TA, Heikkilä A, Koivunen M, et al. Pressure injury prevalence and incidence in acute inpatient care and related risk factors: a cross-sectional national study. *Int Wound J*. 2022;19(4):919-931. doi:10.1111/iwj.13692
2. Shiferaw WS, Akalu TY, Mulugeta H, Aynalem YA. The global burden of pressure ulcers among patients with spinal cord injury: a systematic review and meta-analysis. *BMC Musculoskelet Disord*. 2020;21(1):334. doi:10.1186/s12891-020-03369-0
3. Mobayen M, Karkhah S, Bagheri P, et al. Hospital-acquired pressure ulcers in trauma patients: a retrospective study of 410 patients at a referral trauma center in the north of Iran. *Open Nurs J*. 2022;16:e187443462209200. doi:10.2174/18744346-v16-e2209200
4. European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel, and Pan Pacific Pressure Injury Alliance. *Prevention and Treatment of Pressure Ulcers/Injuries: Clinical Practice Guideline*. Haesler E, ed. EPUAP/NPIAP/PPPIA; 2019.
5. Verschueren JH, Post MW, de Groot S, van der Woude LH, van Asbeck FW, Rol M. Occurrence and predictors of pressure ulcers during primary in-patient spinal cord injury rehabilitation. *Spinal Cord*. 2011; 49(1):106-112. doi:10.1038/sc.2010.66
6. Lee HJ, Han MY, Hwang JH, et al. Risk factors for heel pressure injury in cardiovascular intensive care unit patients. *Int Wound J*. 2022;19(5): 1158-1164. doi:10.1111/iwj.13711
7. Alito A, Portaro S, Leonardi G, et al. Pressure ulcers—a longstanding problem: a 7-year neurorehabilitation unit experience of management, care, and clinical outcomes. *Diagnostics (Basel)*. 2023;13(20):3213. doi: 10.3390/diagnostics13203213
8. Gheri CF, Scalfi L, Biffi B, et al. Relationship between nutritional risk, clinical and demographic characteristics, and pressure ulcers in patients with severe acquired brain injuries attending a rehabilitative program. *Nutrients*. 2023;15(15):3336. doi:10.3390/nu15153336
9. Langer G, Wan CS, Fink A, Schwingshackl L, Schoberer D. Nutritional interventions for preventing and treating pressure ulcers. *Cochrane Database Syst Rev*. 2024;2(2):CD003216. doi:10.1002/14651858.CD 003216.pub3
10. Le Liepvre H, D'Anglejan E, Chaussard H, et al. Management of pressure injuries with associated osteomyelitis in people with spinal cord injury: a national survey of referral centers in France. *Spinal Cord*. 2025;63(6):319-322. doi:10.1038/s41393-025-01084-y
11. Chen YC, Chen TL, Cheng CC, et al. High-intensity post-stroke rehabilitation is associated with lower risk of pressure ulcer development in patients with stroke: real-world evidence from a nationwide, population-based cohort study. *Medicina (Kaunas)*. 2022; 58(3):402. doi:10.3390/medicina58030402
12. Alito A, Filardi V, Famà F, et al. Traumatic and non-traumatic spinal cord injury: demographic characteristics, neurological and functional outcomes—a 7-year single-centre experience. *J Orthop*. 2021;28:62-66. doi:10.1016/j.jor.2021.11.007
13. Baron J, Swaine J, Presseau J, et al. Self-management interventions to improve skin care for pressure ulcer prevention in people with spinal cord injuries: a systematic review protocol. *Syst Rev*. 2016;5(1):150. doi: 10.1186/s13643-016-0323-4
14. Paquin C, Nindorera F, Gagnon M, Lamontagne MÈ, Routhier F. Personal risk factors for pressure injuries among wheelchair users: an umbrella review of new insights in 2024. *Disabil Rehabil Assist Technol*. 2025;20(5):1219-1234. doi:10.1080/17483107.2024.2448161
15. Piatt JA, Nagata S, Zahl M, Li J, Rosenbluth JP. Problematic secondary health conditions among adults with spinal cord injury and its impact on social participation and daily life. *J Spinal Cord Med*. 2016;39(6):693-698. doi:10.1080/10790268.2015.1123845
16. Huang L, Yan Y, Huang Y, et al. Summary of best evidence for prevention and control of pressure ulcer on support surfaces. *Int Wound J*. 2023;20(6):2276-2285. doi:10.1111/iwj.14109
17. El Genedy-Kalyoncu M, Kottner J. The uptake of the international pressure ulcer/injury prevention and treatment guidelines: an updated systematic citation analysis. *Int Wound J*. 2024;21(9):e70036. doi:10. 1111/iwj.70036
18. Ateşgöz F, Köse G, Seki Z, et al. Bir eğitim ve araştırma hastanesindeki basınç yarısı prevalansı ve risk faktörlerinin belirlenmesi: nokta prevalans çalışması. *Karya J Health Sci*. 2022;3(1):6-12. doi:10.52831/kjhs.1013181
19. Tokgöz OS, Demir O. Nöroloji yoğun bakım ünitesinde bası yarısı insidansı ve risk faktörleri. *Selçuk Med J*. 2019;35(2):103-109.
20. Kartal N, Sayın Y. Yatarak tedavi gören yaşlılarda basınç yarısı prevalansı, nedenleri ve risk faktörleri. *Türk Geriatri Derg*. 2015;18(1):25-31.
21. Atkin L, Buæko Z, Conde Montero E, et al. Implementing TIMERS: the race against hard-to-heal wounds. *J Wound Care*. 2019;28(Suppl 3a):S1-50. doi:10.12968/jowc.2019.28.Sup3a.S1
22. Burke DT, Ho CH, Saucier MA, Stewart G. Effects of hydrotherapy on pressure ulcer healing. *Am J Phys Med Rehabil*. 1998;77(5):394-398. doi: 10.1097/00002060-199809000-00006
23. Kierney PC, Engrav LH, Isik FF, Esselman PC, Cardenas DD, Rand RP. Results of 268 pressure sores in 158 patients managed jointly by plastic surgery and rehabilitation medicine. *Plast Reconstr Surg*. 1998;102(3): 765-772. doi:10.1097/00006534-199809030-00022
24. Fernández-Guarino M, Bacci S, Pérez González LA, Bermejo-Martínez M, Cecilia-Matilla A, Hernández-Bule ML. The role of physical therapies in wound healing and assisted scarring. *Int J Mol Sci*. 2023; 24(8):7487. doi:10.3390/ijms24087487
25. Jeon JH, Chung J, Lim NK. A longitudinal investigation of stage 2 pressure injury outcomes with machine learning technique to identify relevant factors. *Adv Skin Wound Care*. 2025;38(9):E81-E89. doi:10.1097/ ASW.0000000000000347
26. Wan CS, Musgrave-Takeda M, M Gillespie B, Tobiano G, McInnes E. Barriers and facilitators to implementing pressure injury guidelines for nutrition assessment and alternating pressure air mattress allocation: a qualitative study. *J Adv Nurs*. 2025;81(10):6767-6788. doi:10.1111/jan. 16820
27. Sen CK. Human wound and its burden: updated 2025 compendium of estimates. *Adv Wound Care (New Rochelle)*. 2025;14(9):429-438. doi:10. 1177/21621918251359554

Association between red cell distribution width coefficient of variation and coronary slow flow

 **Ramazan Astan**

Department of Cardiology, Batman Training and Research Hospital, Batman, Türkiye

Cite this article: Astan R. Association between red cell distribution width coefficient of variation and coronary slow flow. *Ank Med J.* 2025;4(4):80-84.

Received: 22/09/2025

Accepted: 17/10/2025

Published: 19/10/2025

ABSTRACT

Aims: Coronary slow flow (CSF) is an angiographic phenomenon characterized by delayed distal coronary opacification in the absence of significant epicardial stenosis. Red cell distribution width (RDW), a routinely measured hematologic parameter, has been proposed as a potential marker of inflammation and microvascular dysfunction. However, although several studies have demonstrated an association, its role as an independent predictor of CSF remains to be fully established. This study aimed to evaluate the association between RDW coefficient of variation (RDW-CV) and CSF using multivariate logistic regression and receiver operating characteristic (ROC) analyses.

Methods: We retrospectively analyzed 153 patients with normal or near-normal coronary arteries on angiography, classified into CSF (n=73, 47.7%) and non-CSF (n=80, 52.3%) groups based on corrected TIMI frame counts. Clinical, demographic, and laboratory data were compared between groups. Variables with $p < 0.10$ in univariate analysis were included in multivariate logistic regression. Diagnostic performance was assessed using ROC curve analysis.

Results: RDW-CV values were slightly higher in the CSF group ($13.83 \pm 1.24\%$) compared with the non-CSF group ($13.69 \pm 1.41\%$), but this difference did not reach statistical significance ($p = 0.419$). In multivariate analysis, RDW-CV showed a borderline but non-significant association with CSF (OR=1.338, 95% CI: 0.967-1.852, $p = 0.079$). Hyperlipidemia (OR=5.305, 95% CI: 1.481-18.996, $p = 0.010$) remained independently associated with CSF. RDW-CV alone demonstrated poor discriminative ability (AUC=0.571), whereas the multivariate model achieved good overall predictive performance (AUC=0.833).

Conclusion: RDW-CV is not a strong stand alone predictor of CSF but may contribute to diagnostic accuracy when integrated with other clinical and laboratory variables. Further prospective studies with larger populations are warranted to clarify its prognostic role.

Keywords: Coronary slow flow, red cell distribution width, RDW-CV, TIMI frame count, microvascular dysfunction, logistic regression, ROC analysis

INTRODUCTION

Coronary slow flow (CSF) is an angiographic phenomenon characterized by delayed opacification of the distal coronary vasculature in the absence of significant epicardial stenosis.¹ It is diagnosed most commonly using the thrombolysis in myocardial infarction (TIMI) frame count method, which quantitatively assesses coronary flow velocity.² Although the exact pathophysiology remains incompletely understood, proposed mechanisms include microvascular and endothelial dysfunction, diffuse atherosclerosis, inflammatory activation, and increased small vessel resistance.³⁻⁶ Clinically, CSF has been associated with recurrent chest pain, electrocardiographic changes, and, in some cases, acute coronary syndromes, underscoring its potential prognostic significance.⁷

Red cell distribution width (RDW) is a routinely reported parameter in complete blood counts, reflecting the degree of anisocytosis (heterogeneity in erythrocyte size). While traditionally used in the differential diagnosis of anemia, RDW has emerged as a biomarker linked to inflammation, oxidative stress, and impaired microcirculation.⁸⁻¹⁰ Elevated RDW levels have been reported in various cardiovascular conditions, including heart failure, myocardial infarction, and stable coronary artery disease.¹¹⁻¹³

Several studies have investigated the association between RDW and CSF, with many demonstrating significantly higher RDW values in CSF patients compared with controls.¹⁴⁻¹⁶ For example, Luo et al.¹³ found RDW to be an independent

predictor of CSF in a cohort of 185 patients, while Kalay et al.¹⁴ reported a similar relationship alongside serum uric acid levels. However, not all studies have confirmed RDW as an independent predictor after adjusting for confounders, and differences in study design, population characteristics, and sample sizes have led to inconsistent conclusions. Moreover, most studies have been conducted in specific geographic or ethnic populations, limiting the generalizability of findings.

Given these variations, further investigation is warranted to clarify the independent predictive value of RDW in CSF. In this context, the present study aimed to evaluate the relationship between RDW and CSF in a well-defined patient cohort, using multivariate logistic regression and receiver operating characteristic (ROC) curve analyses to assess its diagnostic performance.

METHODS

Ethics

The study was conducted with the permission of the Non-interventional Clinical Researches Ethics Committee of Batman Training and Research Hospital (Date: 25.06.2025, Decision No: 429). This study was conducted in accordance with the Declaration of Helsinki. This study was conducted under the same ethical approval that covers the investigation of hormonal, metabolic, and inflammatory factors associated with CSF. The present analysis specifically focused on hematologic and inflammatory parameters; patients lacking these laboratory data were excluded. Given the retrospective nature of the study and the use of anonymized patient data, the requirement for informed consent was waived by the ethics committee.

Study Design and Population

This retrospective, observational study was conducted in the Department of Cardiology at Batman Training and Research Hospital between July 1, 2024, and July 1, 2025. A total of 153 patients who underwent coronary angiography for suspected coronary artery disease and were found to have normal or near-normal coronary arteries were included in the analysis. Hyperlipidemia was defined as a previously documented diagnosis or the use of lipid-lowering medication. All participants had complete laboratory data and were deemed eligible for multivariate analysis.

Patients were classified into two groups according to the presence of CSF. CSF was defined as a corrected TIMI frame count (CTFC) greater than the standard reference values for each major coronary artery, as described by Gibson et al.² The control group consisted of patients with normal coronary flow.

Exclusion Criteria

Patients with the following conditions were excluded from the study: Significant epicardial coronary stenosis defined as a diameter reduction greater than 40%, left ventricular systolic dysfunction with an ejection fraction below 50%, and valvular heart disease of moderate or greater severity. Patients with a history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery were also excluded. In addition, individuals with known hematologic disorders, chronic inflammatory or infectious

diseases, malignancy, severe hepatic or renal dysfunction (serum creatinine >2.0 mg/dl or eGFR <30 ml/min/1.73 m²), or acute coronary syndrome at presentation were not eligible. Finally, patients with incomplete demographic, laboratory, or angiographic data were excluded from the analysis.

Coronary Angiography and TIMI Frame Count Analysis

All patients underwent coronary angiography via the femoral or radial approach using a standard protocol and non-ionic contrast medium. Angiographic images were originally recorded at 15 frames per second (fps) and subsequently converted to an equivalent rate of 30 fps to allow standardized TIMI frame count (TFC) assessment. TFCs were determined for the left anterior descending (LAD), left circumflex (LCX), and right coronary arteries (RCA) in accordance with the method described by Gibson et al.² For the LAD, the frame count was divided by 1.7 to obtain the corrected TFC (CTFC). Based on Gibson's reference values, CSF was defined as a CTFC >27 frames for the LAD, >22 frames for the LCX, and >20 frames for the RCA. The mean CTFC was calculated as the average of the three major coronary arteries, and values exceeding these normal limits were considered diagnostic for CSF.

Laboratory Measurements

Venous blood samples were obtained from each patient following an overnight fast, prior to coronary angiography. Complete blood counts were analyzed using an automated hematology analyzer within two hours of sampling. RDW was expressed as the coefficient of variation of red blood cell volume (RDW-CV, %). Serum levels of glucose, creatinine, uric acid, and total cholesterol were measured using enzymatic methods. C-reactive protein (CRP) was determined by the nephelometric method. All biochemical parameters were analyzed in the hospital's central laboratory.

Statistical Analysis

Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median (interquartile range, IQR) according to their distribution, which was assessed using the Kolmogorov-Smirnov test. Differences between groups were compared using the independent samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Categorical variables were presented as counts and percentages, and compared using the Chi-square test or Fisher's exact test, as appropriate.

Variables with a p-value <0.10 in univariate analyses were included in a multivariate logistic regression model to identify independent predictors of CSF. Odds ratios (OR) with corresponding 95% confidence intervals (CI) were reported. The discriminative performance of RDW-CV and the multivariate model was evaluated using ROC curve analysis, with the area under the curve (AUC) calculated.

All statistical analyses were performed using SPSS software, version [22] (IBM Corp., Armonk, NY, USA). A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

A total of 153 patients were included in the final analysis, of whom 73 (47.7%) had CSF and 80 (52.3%) had normal coronary flow. Patients in the CSF group were significantly

younger than those in the non-CSF group (47.2 ± 10.1 vs. 52.3 ± 10.0 years, $p < 0.05$). The proportion of male patients was also higher in the CSF group (71.7% vs. 47.6%, $p < 0.01$). Likewise, current smoking was more prevalent among patients with CSF compared with those with normal coronary flow (57.5% vs. 31.2%, $p < 0.01$). No significant differences were observed between the two groups regarding the prevalence of hypertension, diabetes mellitus, or hyperlipidemia. Similarly, there were no significant differences in serum creatinine, CRP, or platelet count. Although RDW-CV values were slightly higher in the CSF group compared with the non-CSF group ($13.83 \pm 1.24\%$ vs. $13.69 \pm 1.41\%$), this difference did not reach statistical significance ($p = 0.419$) (Table 1).

Table 1. Demographic and laboratory characteristics of patients with and without coronary slow flow

Variable	No CSF (n:80, 52.3%)	CSF (n:73, 47.7%)
Age (years)	52.33 ± 10.0	47.21 ± 10.1
Male sex (%)	38 (47.6%)	52 (71.7%)
Hypertension (%)	23 (28.7%)	19 (26.0%)
Diabetes mellitus (%)	21 (26.2%)	18 (24.6%)
Hyperlipidemia (%)	27 (33.7%)	26 (35.6%)
Current smoking (%)	25 (31.2%)	42 (57.5%)
Serum creatinine (mg/dl)	0.91 ± 0.16	0.95 ± 0.32
CRP (mg/L)	4.35 ± 8.18	4.76 ± 9.50
WBC ($10^3/\mu\text{L}$)	7.19 ± 1.96	8.29 ± 2.27
Hemoglobin (g/dl)	13.46 ± 1.54	14.38 ± 1.84
Platelets ($10^3/\mu\text{L}$)	234.24 ± 71.85	229.73 ± 54.18
RDW-CV (%)	13.69 ± 1.41	13.83 ± 1.24

CSF: Coronary slow flow, CRP: C-reactive protein, WBC: White blood cell, RDW-CV: Red cell distribution width coefficient of variation. Data are presented as mean $\pm$ standard deviation or n (%). Statistical significance was set at $p < 0.05$.

In univariate analysis, RDW-CV showed a non-significant trend toward higher values in patients with CSF. Variables with $p < 0.10$ in univariate analysis were subsequently entered into a multivariate logistic regression model (Table 2). In this model, RDW-CV demonstrated an OR of 1.338 (95% CI: 0.967-1.852, $p = 0.079$) for the presence of CSF, indicating a borderline but non-significant association. Among the other covariates, hyperlipidemia (OR=5.305, 95% CI: 1.481-18.996, $p = 0.010$) remained independently associated with CSF.

Table 2. Multivariate logistic regression analysis for the presence of coronary slow flow

Variable	OR	95% CI	p-value
RDW-CV	1.338	0.967-1.852	0.079
Age	0.976	0.937-1.017	0.243
Sex-male	1.272	0.416-3.895	0.673
Hypertension	0.478	0.19-1.207	0.118
Diabetes mellitus	0.782	0.276-2.221	0.644
Hyperlipidemia	5.305	1.481-18.996	0.01
Smoking cigarette	1.024	0.33-3.183	0.967
Serum creatinine	1.045	0.832-1.312	0.705

RDW-CV: Red cell distribution width coefficient of variation, OR: Odds ratio, CI: Confidence interval. Statistical significance was set at $p < 0.05$.

ROC curve analysis revealed an AUC of 0.571 for RDW-CV alone, indicating limited discriminatory ability for predicting CSF (Figure 1). By contrast, the multivariate logistic regression model incorporating RDW-CV together with

the other significant covariates yielded an AUC of 0.833, suggesting good overall predictive performance (Figure 2).

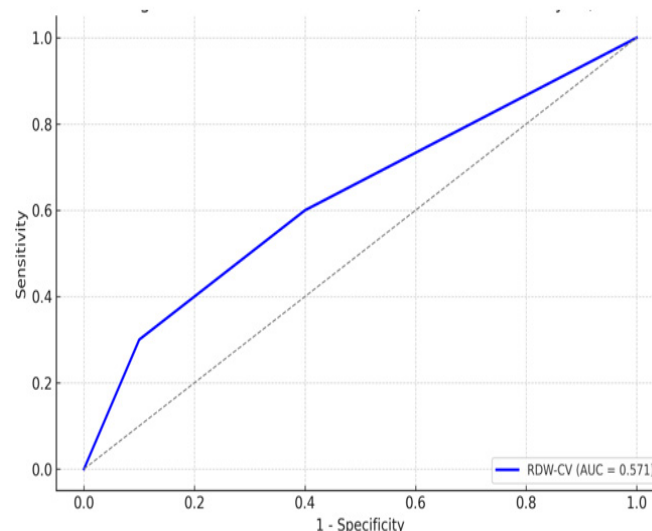


Figure 1. ROC curve of RDW-CV alone for predicting CSF (AUC=0.571)

ROC: Receiver operating characteristic, RDW-CV: Red cell distribution width coefficient of variation, CSF: Coronary slow flow, AUC: Area under the curve

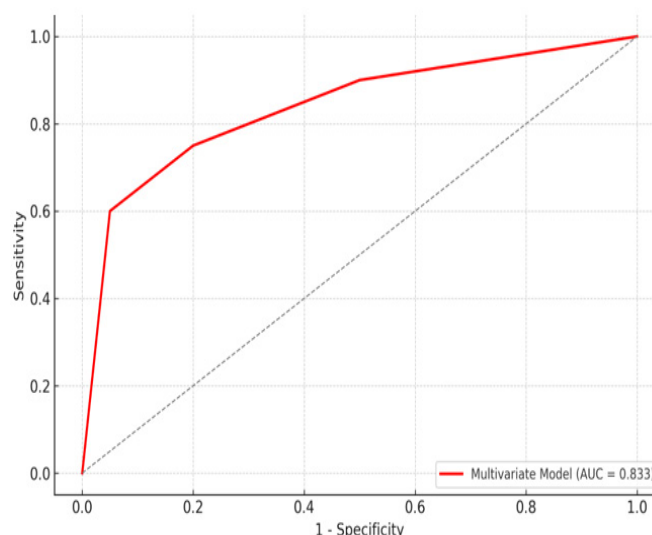


Figure 2. ROC curve of the multivariate logistic regression model including RDW-CV and clinical parameters for predicting coronary slow flow (AUC=0.833).

ROC: Receiver operating characteristic, RDW-CV: Red cell distribution width coefficient of variation, CSF: Coronary slow flow, AUC: Area under the curve

DISCUSSION

In the present study, RDW-CV values were numerically higher in patients with CSF than in those with normal coronary flow; however, the difference did not reach statistical significance in univariate testing, and RDW-CV showed only a borderline but non-significant association in multivariable analysis ($p = 0.079$). These findings suggest that RDW-CV alone is unlikely to serve as a robust standalone predictor of CSF in our cohort, although it may contribute within a multivariable framework.

Our results should be interpreted in the context of prior literature. Several cohorts conducted in different centers and populations reported higher RDW values among CSF patients compared with controls and supported hematologic indices as correlates of the CSF milieu characterized by low-grade inflammation and microvascular dysfunction. Beyond CSF, studies in broader coronary populations have linked RDW

with disease burden and adverse outcomes, reinforcing its biological plausibility as an inflammation and hemorheology related marker.¹⁷⁻²³

Microvascular flow resistance can result from alterations in hemorheological properties of blood. Increased heterogeneity in erythrocyte size, expressed as RDW, may impair blood fluidity and compromise microcirculatory perfusion. In this context, Patel et al.²⁴ demonstrated that elevated RDW was associated with impaired erythrocyte deformability, highlighting a potential mechanism by which anisocytosis adversely affects microvascular flow dynamics. Given that CSF is characterized by increased microvascular resistance and endothelial dysfunction, the relationship between elevated RDW and reduced red cell deformability provides a plausible explanation for the observed association between RDW and CSF. Reduced deformability of erythrocytes may increase blood viscosity, exacerbate microvascular dysfunction, and thereby contribute to the pathophysiology of CSF.

At the same time, heterogeneity across studies complicates direct comparison. Differences in cohort size, ethnicity/geography, timing of blood sampling, analytic platforms for RDW (RDW-CV vs. RDW-SD), and model covariates (e.g., inflammatory and lipid parameters) may substantially influence effect estimates. In our dataset, adjustment for clinical and biochemical covariates attenuated the association of RDW-CV with CSF, which may reflect confounding by inflammation and lipid-related pathways captured more directly by other variables. Notably, although the prevalence of hyperlipidemia was not significantly different between groups in univariate comparisons, it emerged as an independent predictor in our multivariable analysis. This apparent discrepancy may be explained by confounding effects of age, sex, and smoking, which could have masked the association in unadjusted analyses. When these factors were accounted for, the contribution of hyperlipidemia became more evident.

Mechanistically, elevated RDW reflects anisocytosis and impaired red-cell deformability, which can worsen hemorheology and increase flow resistance.²⁵⁻²⁷ Prior work connects higher RDW with endothelial dysfunction and with greater coronary disease burden and severity on angiography.²⁸ These insights are pathophysiologically consistent with microvascular abnormalities described in CSF, even if RDW-CV did not emerge as an independent predictor in our adjusted model.

Limitations

This study has several limitations. First, it was conducted in a single center with a relatively small sample size, which may limit the generalizability of the findings. Second, the observational and cross-sectional design precludes establishing causal relationships between RDW-CV and CSF. Third, RDW-CV measurements were based on a single blood sample obtained at admission; thus, potential temporal variations could not be assessed. Finally, unmeasured confounding factors, including nutritional status, bone marrow function, and other inflammatory markers, may have influenced the results.

CONCLUSION

In this study, RDW-CV levels were slightly higher in patients with CSF compared to those without CSF; however, this difference did not reach statistical significance. RDW-CV alone demonstrated poor discriminative ability for predicting CSF, whereas a multivariate logistic regression model incorporating RDW-CV along with other clinical and laboratory parameters achieved good diagnostic performance. These findings suggest that RDW-CV may not serve as a strong standalone predictor of CSF, but it could contribute meaningfully when integrated into a comprehensive risk assessment model. Reporting such borderline or non-significant results is important for reducing publication bias and providing balanced evidence for future meta-analyses and systematic reviews.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted with the permission of the Non-interventional Clinical Researches Ethics Committee of Batman Training and Research Hospital (Date: 25.06.2025, Decision No: 429).

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. Tambe AA, Demany MA, Zimmerman HA, et al. Angina pectoris and slow flow velocity of dye in coronary arteries: a new angiographic finding. *Am Heart J*. 1972;84(1):66-71. doi:10.1016/0002-8703(72)90307-9
2. Gibson CM, Cannon CP, Daley WL, et al. TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation*. 1996;93(5):879-888. doi:10.1161/01.CIR.93.5.879
3. Sezgin AT, Sigirci A, Barutcu I, et al. Vascular endothelial function in patients with slow coronary flow. *Coron Artery Dis*. 2003;14(2):155-161. doi:10.1097/00019501-200304000-00008
4. Mangieri E, Macchiarelli G, Ciavolella M, et al. Slow coronary flow: clinical and histopathological features in patients with otherwise normal epicardial coronary arteries. *Cathet Cardiovasc Diagn*. 1996;37(4):375-381. doi:10.1002/(SICI)1097-0304(199604)37:4<375::AID-CCD5>3.0.CO;2-D
5. Zhu Q, Wang S, Huang X, et al. Understanding the pathogenesis of coronary slow flow: recent advances. *Trends Cardiovasc Med*. 2024;34:137-144. doi:10.1016/j.tcm.2022.12.001
6. Camsarı A, Pekdemir H, Cicek D, et al. Endothelin-1 and nitric oxide concentrations and their response to exercise in patients with slow coronary flow. *Circ J*. 2003;67:1022-1028. doi:10.1253/circj.67.1022

7. Beltrame JF, Limaye SB, Horowitz JD. The coronary slow flow phenomenon: a new coronary microvascular disorder. *Cardiology*. 2002;97(4):197-202. doi:10.1159/000063121
8. Lippi G, Targher G, Montagnana M, et al. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. *Arch Pathol Lab Med*. 2009;133(4):628-632. doi:10.5858/133.4.628
9. Felker GM, Allen LA, Pocock SJ, et al. Red cell distribution width as a novel prognostic marker in heart failure. *J Am Coll Cardiol*. 2007;50(1):40-47. doi:10.1016/j.jacc.2007.02.067
10. Ani C, Ovbiagele B. Elevated RDW predicts mortality in persons with known stroke. *J Neurol Sci*. 2009;277(1-2):103-108. doi:10.1016/j.jns.2008.10.024
11. Tonelli M, Sacks F, Arnold M, et al. Relation between RDW and cardiovascular event rate in people with coronary disease. *Circulation*. 2008;117(2):163-168. doi:10.1161/CIRCULATIONAHA.107.727545
12. Azab B, Shah N, Akerman M, et al. Value of RDW in predicting long-term mortality after non-ST-elevation myocardial infarction. *Am J Cardiol*. 2011;107(12):1796-1801. doi:10.1016/j.amjcard.2011.02.015
13. Luo SH, Jia YJ, Nie SP, et al. Increased red cell distribution width in patients with slow coronary flow syndrome. *Clinics (Sao Paulo)*. 2013;68(6):732-737. doi:10.6061/clinics/2013(06)02
14. Kalay N, Aytekin M, Kaya MG, et al. The relationship between inflammation and slow coronary flow: increased RDW and serum uric acid levels. *Turk Kardiyol Dern Ars*. 2011;39(6):463-468. doi:10.5543/tkda.2011.01578
15. Akpinar I, Sayin MR, Gursay YC, et al. Plateletcrit and RDW are independent predictors of slow coronary flow. *Cardiol J*. 2015;22(5):517-525. doi:10.1016/j.jcc.2013.07.010
16. Nishizaki Y, Daida H. The relationship between high red blood cell distribution width and low coronary flow reserve in patients with idiopathic dilated cardiomyopathy. *Anadolu Kardiyol Derg*. 2014;14(4):349-350. doi:10.5152/akd.2014.12446120141
17. Ozyurtlu F, Yavuz V, Cetin N, et al. The association between coronary slow flow and platelet distribution width among patients with stable angina pectoris. *Postepy Kardiol Interw*. 2014;10(3):161-165. doi:10.5114/pwki.2014.45142
18. Seyyed Mohammadzad MH, Hosseinsabet A, Zamani B, et al. Echocardiographic and laboratory findings in coronary slow flow: a case-control study. *BMC Cardiovasc Disord*. 2021;21:230. doi:10.1186/s12872-021-02044-z
19. Nagula P, Karumuri S, Otikunta AN, et al. Correlation of red blood cell distribution width with the severity of coronary artery disease: a single-center study. *Indian Heart J*. 2017;69(1):97-99. doi:10.1016/j.ihj.2017.04.007
20. Osadnik T, Strzelczyk J, Hawranek M, et al. Red cell distribution width is associated with long-term prognosis in patients with stable coronary artery disease. *BMC Cardiovasc Disord*. 2013;13:113. doi:10.1186/1471-2261-13-113
21. Zalawadiya SK, Veeranna V, Panaich SS, et al. Red cell distribution width and risk of coronary heart disease events. *Am J Cardiol*. 2010;106(7):988-993. doi:10.1016/j.amjcard.2010.06.006
22. Isik T, Uyarel H, Tanboga IH, et al. Relation of red cell distribution width with the presence, severity, and complexity of coronary artery disease. *Coron Artery Dis*. 2012;23(1):51-56. doi:10.1097/MCA.0b013e32834e4f5c
23. Dabbah S, Hammerman H, Markiewicz W, et al. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. *Am J Cardiol*. 2010;105(3):312-317. doi:10.1016/j.amjcard.2009.09.027
24. Patel KV, Mohanty JG, Kanapuru B, Hesdorffer C, Ershler WB, Rifkind JM. Association of the red cell distribution width with red blood cell deformability. *Adv Exp Med Biol*. 2013;765:211-216. doi:10.1007/978-1-4614-4989-8_29
25. Bujak K, Wasilewski J, Osadnik T, et al. The prognostic role of red blood cell distribution width in coronary artery disease: a review of the pathophysiology. *Dis Markers*. 2015;2015:824624. doi:10.1155/2015/824624
26. Patel KV, Ferrucci L, Ershler WB, et al. Red blood cell distribution width and the risk of death in middle-aged and older adults. *Arch Intern Med*. 2009;169(5):515-523. doi:10.1001/archinternmed.2009.11
27. Ananthaseshan S, Sampath S, Subramanian R, et al. Effect of red blood cell distribution width on blood flow and wall shear stress: a computational study. *Sci Rep*. 2022;12:13764. doi:10.1038/s41598-022-17847-z
28. Solak Y, Yilmaz MI, Saglam M, et al. Red cell distribution width is independently related to endothelial dysfunction in patients with chronic kidney disease. *Am J Med Sci*. 2014;347(2):118-124. doi:10.1097/MAJ.0b013e3182996a96

The relationship between zinc status and inflammatory marker levels in FMF

 Alperen Uysal¹,  Yaşar Kandur²,  Mustafa Gürkan¹,  Muhammed Enes Pek¹,  Cihat Şanlı¹,
 Ayşegül Alpcan¹

¹Department of Pediatrics, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

²Division of Pediatric Nephrology, Department of Pediatrics, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Cite this article: Uysal A, Kandur Y, Gürkan M, Pek ME, Şanlı C, Alpcan A. The relationship between zinc status and inflammatory marker levels in FMF. *Ank Med J.* 2025;4(4):85-87.

Received: 13/07/2025

Accepted: 18/10/2025

Published: 19/10/2025

ABSTRACT

Aims: This study aimed to evaluate serum zinc concentrations in individuals diagnosed with FMF and to determine whether zinc status influences inflammatory activity.

Methods: We retrospectively reviewed the medical records of patients with FMF, who were under the follow-up of our nephrology-rheumatology center between 2018 and 2025.

Results: One hundred twelve FMF patients (M/F=52/60) with a mean age of 11.9 ± 5.1 years were included in this study. 35 (31.3%) of the patients have compound heterozygous mutation and 77 (68.8%) have heterozygous mutation. There was no difference in mean of leucocyte count and zinc level between these mutation groups. The mean pre-treatment sedimentation was significantly higher in patients with frequent attacks ($p=0.021$). However there was no difference between the attack frequency groups in mean of gender age, both of pre and post-treatment CRP, zinc, leucocyte count and post-treatment sedimentation ($p>0.05$). There was a positive correlation between mean zinc and mean leucocyte count, CRP levels ($p=0.019$, $r=0.334$ and $p=0.016$, $r=0.344$ respectively), but not with sedimentation.

Conclusion: Notably, in our current study, serum zinc levels were positively associated with inflammatory markers in FMF patients.

Keywords: Familial Mediterranean fever, zinc, inflammation, C-reactive protein, leukocyte count, pediatric rheumatology

INTRODUCTION

Chronic inflammation is known to contribute to progressive tissue and organ damage and is associated with a greater likelihood of developing chronic diseases. Inflammation is typically characterized by increased levels of acute-phase reactants such as C-reactive protein (CRP), leucocyte count, erythrocyte sedimentation rate (ESR) and other inflammatory mediators (IL-6, TNF- α).¹ Zinc, recognized for its antioxidant and anti-inflammatory functions, has been found to inversely correlate with CRP concentrations in previous studies.^{2,3} Zinc supports the activity of these antioxidant enzymes and serves as a key micronutrient in defending cells against oxidative stress.^{4,5} Familial Mediterranean fever (FMF) is a hereditary inflammatory disorder associated with mutations in the MEFV gene, located on chromosome 16p, which encodes the pyrin (also known as marenostrin) protein.⁶ Pyrin is predominantly expressed in neutrophils and regulates intracellular pathways that drive excessive IL-1 β production.⁷

This study aimed to evaluate serum zinc concentrations in individuals diagnosed with FMF and to determine whether zinc status influences inflammatory activity.

METHODS

The ethics committee approval of the study was obtained from the Kırıkkale University Clinical Researches Ethics Committee (Date: 25.06.2025, Decision No: 2025.25.08). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients diagnosed with FMF during the study period were included in the study. We retrospectively reviewed the medical records of patients with FMF, who were under the follow-up of our nephrology-rheumatology center between 2018 and 2025. At the time of data entry we recorded demographic information, the data on mutation type, and

the levels of zinc, CRP, leucocyte count, and ESR at the pre-treatment stage and also post-treatment. The patients were categorized as patients with compound and heterozygous mutations as well as patients with rare and frequent attacks. To evaluate the frequent attack we used the criteria proposed by Pras et al.⁸ Patients with malnutrition, active infection, or using a zinc supplement were excluded.

Statistical Analysis

The study data underwent analysis using the SPSS (Statistical Package for Social Science) 27.0 software package. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. Differences between the continuous variables in the two groups were evaluated using the Student's t-test. Differences in proportions were evaluated using the Chi-square test. Correlations between parameters were assessed using Pearson/Spearman correlation tests. The level of significance was set at $p < 0.05$.

RESULTS

One hundred twelve FMF patients (M/F=52/60) with a mean age of 11.9 ± 5.1 years who presented to the pediatric nephrology/rheumatology clinic were included in this study. 35 (31.3%) of the patients have compound heterozygous mutation and 77 (68.8%) have heterozygous mutation. There was no difference between the mutation groups in mean of gender and age ($p=0.358$ and $p=0.182$, respectively).

Both pre and post-treatment CRP and sedimentation levels were higher in the compound mutation group than in the heterozygous group ($p < 0.05$). However there was no difference in mean of leucocyte count and zinc level between these mutation groups (Table 1).

Table 1. Comparison of the mutation groups

Variable	Heterozygous n=77	Compound n=35	p-value
Gender (male) n (%)	38 (49.4)	14 (40)	0.358
Mean age at diagnosis* (year)	8.3 ± 4.4	7.0 ± 4.4	0.182
CRP** (mg/dl)			
Pre-treatment	2.1 (0.05-121.6)	39 (0.5-250.4)	<0.001
Post-treatment	0.6 (0.03-139)	3 (0.2-160)	<0.001
Sedimentation (mm/hr)**			
Pre-treatment	17 (3-98)	35 (7-129)	<0.001
Post-treatment	13 (2-114)	21 (4-68)	0.011
Leucocyte count (/10³)**			
Pre-treatment	7930 (4230-23680)	9450 (4480-23820)	0.159
Post-treatment	7820 (4850-20250)	8045 (4220-14560)	0.929
Zinc (µg/dl)*			
Pre-treatment	100.9 ± 22.0	98.3 ± 19.6	0.667
Post-treatment	102.4 ± 16.7	104.1 ± 14.0	0.704

CRP: C-reactive protein, *Mean±Standard deviation, **Median (minimum-maximum)

The mean pre-treatment sedimentation was significantly higher in patients with frequent attacks ($p=0.021$). However there was no difference between the attack frequency groups in mean of gender age, both of pre and post-treatment CRP, zinc, leucocyte count and post-treatment sedimentation ($p > 0.05$) (Table 2).

Leucocyte count, CRP, Zinc, Sedimentation averages were obtained for correlation analysis. There was a positive correlation between mean zinc and mean leucocyte

Table 2. Comparison of attack frequency groups

Variable	Rare attacks n=22	Frequent attacks n=90	p-value
Gender (male) n (%)	13 (59)	45 (50)	0.487
Mean age at diagnosis (year)*	7.5 ± 4.7	7.7 ± 4.3	0.907
CRP (mg/dl)**			
Pre-treatment	4.5 (0.1-106)	4.2 (0.1-212)	0.725
Post-treatment	0.5 (0.2-149)	1.1 (0.1-69.5)	0.481
Sedimentation (mm/hr)**			
Pre-treatment	11 (5-40)	25 (4-83)	0.021
Post-treatment	11 (5-68)	14 (2-47)	0.419
Leucocyte count (/10³)**			
Pre-treatment	8130 (4480-16700)	8300 (4230-23820)	0.953
Post-treatment	8320 (4850-13210)	7550 (4600-20250)	0.382
Zinc (µg/dl) **			
Pre-treatment	110.67 ± 21.8	99.0 ± 16.8	0.147
Post-treatment	97.5 ± 15.4	104.4 ± 14.1	0.187

CRP: C-reactive protein, *Mean±Standard deviation, **Median (minimum-maximum)

count, CRP levels ($p=0.019$, $r=0.334$ and $p=0.016$, $r=0.344$ respectively), but not with sedimentation. There was positive correlation between sedimentation, leucocyte count, CRP, within each parameter (Table 3).

Table 3. Correlation of zinc with the mean acute phase reactants

Variable	Leucocyte	Sedimentation	CRP	Zinc
Leucocyte count		$p < 0.001$ $r=0.481$	$p < 0.001$ $r=0.463$	$p=0.019$ $r=0.334$
Sedimentation	$p < 0.001$ $r=0.481$		$p < 0.001$ $r=0.568$	$p=0.133$ $r=0.222$
CRP	$p < 0.001$ $r=0.463$	$p < 0.001$ $r=0.568$		$p=0.016$ $r=0.344$
Zinc	$p=0.019$ $r=0.334$	$p=0.133$ $r=0.222$	$p=0.016$ $r=0.344$	

CRP: C-reactive protein

DISCUSSION

In this study, we evaluated zinc levels in patients with FMF and investigated their association with inflammatory markers. This study appears to be one of the first to investigate zinc levels in pediatric patients with FMF.

Oxidative stress is known to contribute to the inflammatory episodes observed in FMF.⁹ Trace elements like zinc are crucial for defending cells and tissues against damage caused by free radicals.¹⁰ A decline in these elements can impair antioxidant defenses. Nevertheless, there is still limited understanding of how trace elements influence the inflammatory flares seen in FMF.

We did not find a significant difference between zinc levels, either in mutation groups and attack groups. Likely in a study comparing rheumatoid arthritis and osteoarthritis found no significant differences in zinc concentrations in plasma and synovial fluid between the patients groups and control groups.¹¹

We observed a positive correlation between zinc levels and CRP, leucocyte counts. Several studies have explored the link between dietary zinc and inflammatory markers. In the U.S., research involving healthy individuals identified a notable positive association between zinc intake and

CRP concentrations.² Similarly, Jung et al.¹² showed a comparatively clearer linear association was observed between serum zinc concentrations and inflammatory markers particularly in women. Conversely, investigations among older adults in Brazil found a negative correlation between serum zinc levels and CRP.³ Our interpretation emphasized that zinc may act as an acute-phase reactant under specific inflammatory conditions such as FMF, rather than serving as a simple anti-inflammatory indicator. We suggest that zinc concentrations may fluctuate in parallel with inflammatory activity, but this does not imply a causal relationship or confirm that zinc behaves as an acute-phase reactant.

Although zinc is generally described as inversely related to inflammatory activity, our finding of a positive correlation between zinc and CRP in FMF may reflect disease-specific metabolic responses rather than a simple anti-inflammatory relationship. During acute inflammatory episodes, cytokine-driven induction of metallothionein and hepatic redistribution of zinc can transiently alter serum zinc concentrations.¹³ In addition, frequent inflammatory attacks and colchicine therapy may modify zinc kinetics, leading to short-term elevations in circulating zinc despite chronic intracellular depletion.¹⁴ These mechanisms could explain the observed positive association without implying that zinc promotes inflammation.

Limitations

An important limitation of our study was, measurements of acute phase reactant and zinc were taken at two time points (pre and post-treatment); including more time points would have added value to our study. This factor restricts the ability to infer causality and generalize the findings. Nevertheless, this study is one of the first pediatric studies to investigate the association between zinc status and inflammatory markers in FMF.

CONCLUSION

Notably, in our current study, serum zinc levels were positively associated with inflammatory markers in FMF patients. Further research is required to explore the exact mechanisms connecting zinc and inflammation, and may also help to evaluate the effects of zinc supplementation in patients with FMF.

ETHICAL DECLARATIONS

Ethics Committee Approval

The ethics committee approval of the study was obtained from the Kırıkkale University Clinical Researches Ethics Committee (Date: 25.06.2025, Decision No: 2025.25.08).

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. Minihiene AM, Vinoy S, McArdle HJ, et al. Low-grade inflammation, diet composition and health: current research evidence and its translation. *Br J Nutr*. 2015;114(7):999-1012. doi:10.1017/S0007114515002093
2. de Oliveira Otto MC, Alonso A, Lee DH, et al. Dietary micronutrient intakes are associated with markers of inflammation but not with markers of subclinical atherosclerosis. *J Nutr*. 2011;141(8):1508-1515. doi:10.3945/jn.111.138115
3. De Paula R, Aneni EC, Costa APR, et al. Low zinc levels is associated with increased inflammatory activity but not with atherosclerosis, arteriosclerosis or endothelial dysfunction among the very elderly. *BBA Clin*. 2014;2:1-6. doi:10.1016/j.bbacli.2014.07.002
4. Michiels C, Raes M, Toussaint O, Remacle J. Importance of glutathione peroxidase, catalase, and Cu/Zn-SOD for cell survival against oxidative stress. *Free Radic Biol Med*. 1994;17(3):235-248. doi:10.1016/0891-5849(94)90079-5
5. Oteiza PI, Mackenzie GG. Zinc, oxidant-triggered cell signaling, and human health. *Mol Aspects Med*. 2005;26(4-5):245-255. doi:10.1016/j.mam.2005.07.012
6. Yao Q, Furst DE. Autoinflammatory diseases: an update of clinical and genetic aspects. *Rheumatology*. 2008;47(7):946-951. doi:10.1093/rheumatology/ken118
7. Keles M, Eyerici N, Uyanik A, et al. The frequency of familial Mediterranean fever related amyloidosis in renal waiting list for transplantation. *EJIM*. 2010;42(1):19-20. doi:10.5152/eajm.2010.06
8. Pras E, Livneh A, Balow JE Jr, et al. Clinical differences between North African and Iraqi Jews with familial Mediterranean fever. *Am J Med Genet*. 1998;75(2):216-219. doi:10.1002/(sici)1096-8628(19980113)75:2<216::aid-ajmg20>3.0.co;2-r
9. Kirkali G, Tunca M, Genc S, Jaruga P, Dizdaroglu M. Oxidative DNA damage in polymorphonuclear leukocytes of patients with familial Mediterranean fever. *Free Radic Biol Med*. 2008;44(3):386-393. doi:10.1016/j.freeradbiomed.2007.09.020
10. Tuncer S, Kamanli A, Akçil E, Kavas GO, Seçkin B, Atay MB. Trace element and magnesium levels and superoxide dismutase activity in rheumatoid arthritis. *Biol Trace Elem Res*. 1999;68(2):137-142. doi:10.1007/BF02784402
11. Yazar M, Sarban S, Kocyigit A, Isikan UE. Synovial fluid and plasma selenium, copper, zinc, and iron concentrations in patients with rheumatoid arthritis and osteoarthritis. *Biol Trace Elem Res*. 2005;106(2):123-132. doi:10.1385/BTER:106:2:123
12. Jung S, Kim MK, Choi BY. The relationship between zinc status and inflammatory marker levels in rural Korean adults aged 40 and older. *PLoS One*. 2015;10(6):e0130016. doi:10.1371/journal.pone.0130016
13. Cousins RJ. Metallothionein--aspects related to copper and zinc metabolism. *J Inherit Metab Dis*. 1983;6(Suppl 1):15-21. doi:10.1007/BF01811318
14. Choi BY, Lee BE, Kim JH, et al. Colchicine induced intraneuronal free zinc accumulation and dentate granule cell degeneration. *Metallomics*. 2014;6(8):1513-20. doi:10.1039/c4mt00067f

CALLY index in patients admitted in the intensive care unit with a diagnosis of decompensated heart failure

Elif Eygi¹, Sedat Sakallı², Bilge Durucu³, Engin Dondurmacı², Fulden Akyüz İnanç⁴, Esra Polat²

¹Department of Anesthesiology and Reanimation, Gaziantep City Hospital, Gaziantep, Türkiye

²Department of Cardiology, Gaziantep City Hospital, Gaziantep, Türkiye

³Department of Emergency Medicine, Gaziantep City Hospital, Gaziantep, Türkiye

⁴Department of Chest Disease, Faculty of Medicine, Kırıkkale University, Kırıkkale, Türkiye

Cite this article: Eygi E, Sakallı S, Durucu B, Dondurmacı E, Akyüz İnanç F, Polat E. CALLY index in patients admitted in the intensive care unit with a diagnosis of decompensated heart failure. *Ank Med J.* 2025;4(4):88-92.

Received: 25/09/2025

Accepted: 18/10/2025

Published: 19/10/2025

ABSTRACT

Aims: This study aimed to investigate whether the CALLY index is associated with mortality in patients admitted to intensive care due to decompensated heart failure.

Methods: In this retrospective study, 130 patients diagnosed with decompensated heart failure admitted to the intensive care unit between 15 October 2023 and 15 October 2024 were included. Demographic data, comorbidities, stages of heart failure, length of stay in the intensive care unit, and mortality status were examined. CALLY index were calculated, and their relationship with mortality was examined.

Results: The CALLY index was found to be statistically significant in distinguishing mortality ($p=0.018$). A higher mortality rate was observed in the group with a low CALLY index (≤ 0.12) (% 26.9% vs % 10.3%) ($p=0.013$).

Conclusion: In patients with decompensated heart failure followed in the intensive care unit, mortality was inversely related to the CALLY index. The CALLY index, a straightforward method for calculation, can serve as a guide for clinicians in determining prognosis.

Keywords: Heart failure, CALLY index, intensive care unit

INTRODUCTION

Heart failure is one of the most common reasons for admission to intensive care units from emergency departments worldwide.¹ According to the European Society of Cardiology (ESC) guidelines, heart failure is classified into three groups based on ejection fraction: heart failure with reduced ejection fraction, heart failure with mildly reduced ejection fraction, and heart failure with preserved ejection fraction (Figure).²

Admission to hospital for decompensated heart failure is frequently seen in patients with low ejection fraction, but it can be observed in all EF groups, regardless of ejection fraction.³ Decompensated heart failure is a clinical condition characterised by acute worsening of heart failure symptoms and haemodynamic instability, often requiring intensive care unit admission and having a risk of mortality.^{2,4}

Decompensated heart failure may also occur due to causes such as fluid overload, coronary ischaemia, arrhythmia, tachycardia, toxic damage, oxidative stress, thyroid dysfunction, anaemia, renal dysfunction, infection, and

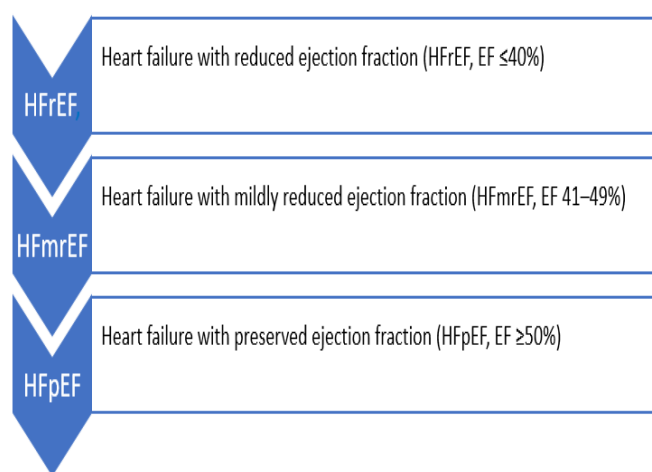


Figure. Classification of heart failure according to ejection fraction, based on the European Society of Cardiology Guidelines²

inflammation.^{3,5-9} Malnutrition, one of the factors affecting prognosis and mortality in intensive care units, is also one of the factors that lead to decompensated heart failure.^{10,11}

It is known that blood tests showing the immune system and inflammation status, such as albumin, lymphocyte, and C-reactive protein, can be used separately to evaluate malnutrition.^{12,13} Lately, the CALLY index, which is formed by combining these three components—CRP, albumin, and lymphocytes—has been used to assess the prognosis and mortality of cancer patients. It has been reported that the CALLY index can be used to predict poor prognosis and mortality in cancer patients.^{14,15}

This study investigated whether the CALLY index is associated with mortality in patients admitted to intensive care due to decompensated heart failure, thereby aiming to provide new evidence regarding the clinical value of this integrated biomarker in critical care practice.

METHODS

Ethics

The study was performed retrospectively. It was conducted in the coronary care units of a tertiary care hospital. Ethics committee approval has been obtained from the Ethics Committee for Non-interventional Clinical Researches at Gaziantep City Hospital (Date: 17.09.2025, Decision No: 2025/297). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Selection of Participants

Patients diagnosed with decompensated heart failure and who were hospitalised in the intensive care unit between 15 October 2023 and 15 October 2024 were included in the study. A total of 130 patients aged 18 years and older with complete medical records in the intensive care unit were included.

Measurements and Outcomes

The study examined patients' demographic data, comorbidities, stages of heart failure, EF, mortality, and length of intensive care unit stay. Routine biochemical and haematological blood parameters taken during admission to the intensive care unit were examined.

The CALLY index was calculated using the formula: $\text{CALLY index} = (\text{albumin (g/L)} \times \text{lymphocyte count (10}^9\text{/L)}) / \text{CRP (mg/dl)} \times 10^4$.¹⁶

Statistical Analysis

The data analyses were performed using 'IBM SPSS Statistics for Windows. Version 25.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA)'. Descriptive statistics were presented as n and %, for categorical variables, and mean±SD and median (min-max) for continuous variables. Independent t-tests were used for binary group comparisons. Pearson Chi-square tests were used for comparisons of categorical variables. ROC curve analysis was used for CALLY score mortality discrimination. $p < 0.05$ was considered statistically significant.

RESULTS

The mean age of the patients included in the study was 67.59 ± 12.40 . The mean intensive care unit stay was 5.27 ± 4.44 days. The patients were 50.8% male ($n=66$). The prevalence of

diabetes mellitus (DM) was 63.1% ($n=82$), hypertension (HT) was 83.8% ($n=109$), coronary artery disease (CAD) was 58.5% ($n=76$), and hyperlipidemia was 36.9% ($n=48$). The prevalence of chronic kidney disease (CRF) was 50.0% ($n=65$). In terms of cardiac function, those with an ejection fraction (EF) < 40 were 78.5% ($n=102$), those between 40-49 were 6.9% ($n=9$), and those ≥ 50 were 14.6% ($n=19$). The rate of patients with a history of stroke was determined to be 2.3% ($n=3$). When mortality was considered, 83.1% ($n=108$) of patients were alive during the follow-up period, while 16.9% ($n=22$) had an exitus (Table 1).

Table 1. Distribution of clinical data of patients

Variables	n	%
Age		
Mean±SD	67.59±12.40	
Median (min-max)	68.5 (35-95)	
Length of hospital admission (day)		
Mean±SD	5.27±4.44	
Median (min-max)	4.0 (1.0-25.0)	
Gender		
Male	66	50.8
DM		
Yes	82	63.1
HT		
Yes	109	83.8
CAD		
Yes	76	58.5
Hyperlipidaemia		
Yes	48	36.9
CRF		
No	65	50.0
CRF present, no dialysis	54	41.5
CRF present, irregular dialysis	7	5.4
CRF present, regular dialysis	4	3.1
HF		
EF<40 %	102	78.5
EF:40-49 %	9	6.9
EF≥50 %	19	14.6
Stroke		
Yes	3	2.3
EF %		
Mean±SD	32.31±11.61	
Median (min-max)	30.0 (15.0-55.0)	
Mortality		
Exitus	22	16.9
DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CRF: Chronic renal failure HF: Heart failure, EF: Ejection fraction, SD: Standard deviation, Min: Minimum, Max: Maximum		

DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CRF: Chronic renal failure, HF: Heart failure, EF: Ejection fraction, SD: Standard deviation, Min: Minimum, Max: Maximum

Table 2 shows the statistics regarding the patients' laboratory parameters. The mean albumin level was 35.42 ± 5.20 , the mean lymphocyte count was 1.80 ± 0.87 , and the mean CRP level was 33.03 ± 38.28 (Table 2).

As shown in Table 3, the CALLY score was found to be statistically significant in discrimination mortality ($p=0.018$).

The study was divided into two groups based on the CALLY index: ≤ 0.12 ($n=52$) and > 0.12 ($n=78$). A significant difference

Table 2. Patients' biochemical and haematological data

Variables	Min	Max	Avg.	SD
Glukose (mg/dl)	50.00	535.00	191.10	100.79
Urea (mg/dl)	21.80	181.00	70.24	35.27
Serum creatinine (mg/dl)	0.37	8.10	1.47	1.06
Sodium (mmol/L)	115.00	145.00	136.36	5.07
Potassium (mmol/L)	3.02	6.88	4.52	0.71
Albumin (g/L)	19.60	45.90	35.42	5.20
ALT (U/L)	5.00	468.00	39.72	70.46
AST (U/L)	10.00	726.00	57.45	105.44
ALP (U/L)	20.00	584.00	118.01	89.75
GGT (U/L)	9.00	1107.00	102.31	147.87
Total cholestrol (mg/dl)	82.00	352.00	173.80	53.09
TG (mg/dl)	47.00	819.00	131.10	88.90
LDL (mg/dl)	26.00	244.00	106.79	41.86
HDL (mg/dl)	17.00	119.00	42.60	16.01
WBC (10 ⁹ /L)	2.10	28.30	11.35	4.92
PLT (10 ⁹ /L)	40.00	750.00	282.39	121.15
HB (g/dl)	6.40	17.30	11.79	2.25
Lymphocyte (10 ⁹ /L)	0.10	17.00	1.81	1.82
Neutrophil (10 ⁹ /L)	1.50	26.90	8.69	4.67
CRP (mg/L)	0.30	215.60	33.03	38.28
CALLY index	0.10	1.89	.30	0.29

SD: Standard deviation, Min: Minimum, Max: Maximum, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, LDL: Low-density lipoprotein cholesterol, HDL: High-density lipoprotein cholesterol, PLT: Platelet, WBC: White blood cell, Hb: Hemoglobin, CRP: C-reactive protein

Table 3. Analysis of the predictive value of the CALLY index in predicting mortality in patients

Variables	AUC	95% CI	Cut-off	Sensitivity (%)	Specificity (%)	p
CALLY	0.661	0.534-0.787	≤0.12	54.7	54.4	0.018

AUC: Area under the curve, 95% CI: Confidence interval

was found in terms of mortality; the mortality rate was 26.9% in the group with a low CALLY index (≤0.12), while it was 10.3% in the group with a high CALLY index (>0.12) (p=0.013). There was no difference between the groups in terms of intensive care hospitalisation days (5.23±5.22 vs. 5.30±3.88; p=0.923). When heart failure (HF) staging was examined, EF<40 values were predominant in both groups, and no statistically significant difference was observed in terms of distribution (p=0.339). When comparing ejection fraction (EF) values, the mean EF was 30.05±11.49 in the low CALLY group and 33.82±11.51 in the high CALLY group, with a borderline significant difference between the two (p=0.070) (**Table 4**).

DISCUSSION

In this study, which examined the relationship between the CALLY index and mortality in patients admitted to intensive care due to decompensated heart failure, it was observed that the CALLY index was statistically significant in distinguishing mortality. It showed that mortality was higher in the group with a low CALLY index.

The CALLY index, which provides information about patients' immune status, nutritional status, and inflammation

Table 4. Comparison of different variables according to CALLY groups

	CALLY		p
	≤0.12 (n=52)	>0.12 (n=78)	
Mortality			
Survivor	38 (73.1)	70 (89.7)	0.013 ^a
Exitus	14 (26.9)	8 (10.3)	
Length of hospital admission (day)	5.23±5.22	5.30±3.88	0.923 ^b
HF-EF %			
<40%	44 (84.6)	58 (74.4)	0.339 ^a
40-49%	2 (3.8)	7 (9.0)	
≥50%	6 (11.6)	13 (16.7)	
EF %	30.05±11.49	33.82±11.51	0.070 ^b

HF: Heart failure, EF: Ejection fraction, a: Pearson Chi-Square test, b: Independent t-test, p<0.05 statistically significant

status based on CRP, albumin, and lymphocyte parameters, was first used in cancer patients.¹⁷ In cancer patients with a low CALLY index, increased preoperative complications, increased infection and increased mortality have been observed.^{17,18}

Later, it has been used in other diseases related to inflammation. A study conducted on 17,946 asthma patients showed a negative correlation between asthma and CALLY index.¹⁹ In another inflammatory disease, rheumatoid arthritis, a negative relationship has been demonstrated between disease activity and the CALLY index.²⁰

According to studies performed in intensive care units, the CALLY index can be used to predict one-month mortality in sepsis patients admitted to intensive care units.²¹ It has also been reported that the CALLY index can predict mortality in patients admitted to intensive care units due to stroke.²²

Regarding the CALLY index, looking at cardiac patients, a study involving 16,291 patients with angina pectoris, in which inflammation also plays a role in the formation mechanisms, observed a negative correlation between angina pectoris and the CALLY index.²³ CALLY index has also been shown to be useful in predicting major adverse cardiovascular events (MACE) and mortality in patients with ST-elevation myocardial infarction (STEMI) undergoing percutaneous intervention.²⁴ The CALLY index has been shown to be useful in predicting atrial fibrillation (AF) recurrence in patients undergoing AF ablation.²⁵ Candemir et al.²⁶ reported in a retrospective study that there was a negative correlation between length of hospital stay and CALLY index in patients hospitalised with decompensated heart failure.

In our study, consistent with the literature, it was determined that the CALLY index can be used to predict mortality in patients admitted to the intensive care unit with the diagnosis of decompensated heart failure, and that higher mortality was seen in patients with a low CALLY index.

Limitations

Our study has several limitations. Firstly, the nutritional parameters of the patients are unknown. The body mass index of the patients is unknown for subgroup analysis. The nutritional status of patients who died during the period of intubation is unknown.

CONCLUSION

The CALLY index was negatively associated with mortality in patients with decompensated heart failure monitored in the intensive care unit. This index, which is easy to calculate in the intensive care unit and does not require any additional costs, can be automatically calculated by software programmes and used by clinicians as a guide for prognosis in patients with heart failure.

ETHICAL DECLARATIONS

Ethical Committee Approval

Ethics committee approval has been obtained from the Ethics Committee for Non-interventional Clinical Researches at Gaziantep City Hospital (Date: 17.09.2025, Decision No: 2025/297).

Informed Consent

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

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

- Sheehan M, Sokoloff L, Reza N. Acute heart failure: from the emergency department to the intensive care unit. *Cardiol Clin*. 2024;42(2):165-186. doi:10.1016/j.ccl.2024.02.005
- McDonagh TA, Metra M, Adamo M, et al. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: developed by the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J*. 2023;44(37):3627-3639. doi:10.1093/eurheartj/ehad195
- Kurmani S, Squire I. Acute heart failure: definition, classification and epidemiology. *Curr Heart Fail Rep*. 2017;14(5):385-392. doi:10.1007/s11897-017-0351-y
- Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur J Heart Fail*. 2016;18(8):891-975. doi:10.1002/ehf.592
- O'Connor CM, Stough WG, Gallup DS, Hasselblad V, Gheorghiade M. Demographics, clinical characteristics, and outcomes of patients hospitalized for decompensated heart failure: observations from the IMPACT-HF registry. *J Card Fail*. 2005;11(3):200-205. doi:10.1016/j.cardfail.2004.08.160
- Nieminen MS, Brutsaert D, Dickstein K, et al. EuroHeart Failure Survey II (EHFS II): a survey on hospitalized acute heart failure patients: description of population. *Eur Heart J*. 2006;27(22):2725-2736. doi:10.1093/eurheartj/ehl193
- Anker SD, Negassa A, Coats AJ, et al. Prognostic importance of weight loss in chronic heart failure and the effect of treatment with angiotensin-converting-enzyme inhibitors: an observational study. *Lancet*. 2003;361(9363):1077-1083. doi:10.1016/S0140-6736(03)12892-9
- Wróbel-Nowicka K, Wojciechowska C, Jacheł W, Zalewska M, Romuk E. The role of oxidative stress and inflammatory parameters in heart failure. *Medicina*. 2024;60(5):760. doi:10.3390/medicina60050760
- Fonarow GC, Abraham WT, Albert NM, et al. Factors identified as precipitating hospital admissions for heart failure and clinical outcomes: findings from OPTIMIZE-HF. *Arch Intern Med*. 2008;168(8):847-854. doi:10.1001/archinte.168.8.847
- Brogi D, Espinosa E, Lilli A, Bovenzi FM, Battino M. Nutrizione e malnutrizione in terapia intensiva cardiologica. Nozioni di base per il cardiologo clinico. [Nutrition and malnutrition in the intensive coronary care unit. Fundamentals for the clinical cardiologist]. *Giornale Italiano di Cardiologia*. 2016;17(4):259-267. doi:10.1714/2214.23898
- Brinza E, Flint K. Malnutrition in heart failure with preserved ejection fraction: more than meets the eye. *J Am Geriatr Soc*. 2023;71(11):3354-3356. doi:10.1111/jgs.18593
- Zouridakis EG, Garcia-Moll X, Kaski JC. Usefulness of the blood lymphocyte count in predicting recurrent instability and death in patients with unstable angina pectoris. *Am J Cardiol*. 2000;86(4):449-451. doi:10.1016/s0002-9149(00)00963-2
- Sun L, Huo X, Jia S, Chen X. Association between the aggregate index of systemic inflammation and albuminuria: a cross-sectional study of National Health and Nutrition Examination Survey 2007-2018. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2024;55(3):671-679. doi:10.12182/20240560108
- Sakurai K, Kubo N, Hasegawa T, et al. Clinical significance of the CALLY index in patients with gastric cancer undergoing gastrectomy. *World J Surg*. 2024;48(11):2749-2759. doi:10.1002/wjs.12357
- Liu XY, Zhang X, Zhang Q, et al. The value of CRP-albumin-lymphocyte index (CALLY index) as a prognostic biomarker in patients with non-small cell lung cancer. *Support Care Cancer*. 2023;31(9):533. doi:10.1007/s00520-023-07997-9
- Xu Z, Tang J, Chen X, Jin Y, Zhang H, Liang R. Associations of CALLY index with cardiorenal syndrome: insights from a population-based study. *Heliyon*. 2024;10(17):e37197. doi:10.1016/j.heliyon.2024.e37197
- Zhu D, Lin YD, Yao YZ, Qi XJ, Qian K, Lin LZ. Negative association of C-reactive protein-albumin-lymphocyte index (CALLY index) with all-cause and cause-specific mortality in patients with cancer: results from NHANES 1999-2018. *BMC Cancer*. 2024;24(1):1499. doi:10.1186/s12885-024-13261-y
- Okugawa Y, Ohi M, Kitajima T, et al. Clinical feasibility of the preoperative C-reactive protein-albumin-lymphocyte index to predict short-and long-term outcomes of patients with gastric cancer. *J Gastrointest Surg*. 2024;28(7):1045-1050. doi:10.1016/j.gassur.2024.04.016
- Liu Y, Wei Y. Association between the CALLY index, vitamin D, and asthma: insights from NHANES. *Front Allergy*. 2025;6:1557677. doi:10.3389/falgy.2025.1557677
- Kılıç Ö, Tecer D, Canbaş M, Kaya MN, Çınar M, Yılmaz S. Immune nutrition indices are associated with disease activity in rheumatoid arthritis: a cross-sectional study. *Biomark Med*. 2024;18(24):1093-1102. doi:10.1080/17520363.2024.2430942
- Zhang J, Zhao Q, Liu S, Yuan N, Hu Z. Clinical predictive value of the CRP-albumin-lymphocyte index for prognosis of critically ill patients with sepsis in intensive care unit: a retrospective single-center observational study. *Front Public Health*. 2024;12:1395134. doi:10.3389/fpubh.2024.1395134
- Altuntaş G, Yıldırım R, Demirel İ. Superiority of pan-immune inflammation value, systemic inflammation index, and CALLY scores prognostic value for mortality of ischemic stroke patients followed in intensive care unit. *BMC Immunol*. 2025;26(1):49. doi:10.1186/s12865-025-00730-7
- Ye J, Chen L, Xu D, et al. Inverse association between CALLY index and angina pectoris in US adults: a population-based study. *BMC Cardiovasc Disord*. 2025;25(1):94. doi:10.1186/s12872-025-04544-8

24. Ji H, Luo Z, Ye L, et al. Prognostic significance of C-reactive protein-albumin-lymphocyte (CALLY) index after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction. *Int Immunopharmacol.* 2024;141:112860. doi:10.1016/j.intimp.2024.112860
25. Deng Y, Huang J, Deng L, et al. C-reactive protein-albumin-lymphocyte (CALLY) index as an independent risk factor for postoperative atrial fibrillation recurrence. *Clin Cardiol.* 2025;48(6):e70157. doi:10.1002/clc.70157
26. Candemir M, Kızıltunç E, Yamak BA. Association between the C-reactive protein-albumin-lymphocyte (CALLY) index and length of hospital stay in patients with heart failure. *Angiology.* 2025;33197251338416. doi:10.1177/00033197251338416

Complex spinal case associated with Angelman syndrome

 Murat Baloğlu

Department of Neurosurgery, Eskişehir City Hospital, Eskişehir, Türkiye

Cite this article: Baloğlu M. Complex spinal case associated with Angelman syndrome. *Ank Med J.* 2025;4(4):93-94.

Received: 02/10/2025

Accepted: 18/10/2025

Published: 19/10/2025

Keywords: Angelman syndrome, complex spine surgery, intraoperative neuromonitoring, neuromuscular disorder, scoliosis

Dear Editor,

We would like to share a rare and challenging case of rapidly progressive scoliosis in a pediatric patient with Angelman syndrome, which may contribute to the clinical understanding of spinal deformities associated with neuromuscular disorders. A 14-year-old female patient diagnosed with Angelman syndrome presented with a rapidly worsening spinal deformity over the past three months. Her gait, previously ataxic and unsteady, deteriorated significantly, and she developed marked weakness in the right lower extremity. Caregivers also reported a decline in her motor performance at her special education school, and she became unable to ambulate without assistance. On neurological examination, the patient was non-verbal and appeared apathetic, with severe cognitive impairment. Muscle strength was assessed using the medical research council (MRC) 0–5 scale. Preoperatively, the upper extremity strength was 5/5 bilaterally, the left lower extremity was 4/5, and the right lower extremity was 2/5.

Angelman syndrome (first described by Dr. Harry Angelman in 1965) is a neurogenetic disorder caused by abnormalities in the maternal chromosome 15q11-q13 region (loss of maternal UBE3A gene function), with an estimated incidence of approximately 1 in 15,000–30,000 live births.¹ Clinically, Angelman syndrome is characterized by severe developmental delay, profound speech impairment (minimal to no spoken language, though receptive comprehension is often better), gait and balance difficulties (ataxic movements), microcephaly, abnormal electroencephalography findings, disordered sleep, and a characteristically happy demeanor with frequent laughter.² Notably, scoliosis is a common comorbidity in Angelman syndrome, reported in roughly 10–20% of affected children and up to 30–50% of adults as they age.^{3,4} Given the progressive nature of her scoliosis and associated neurological deficits, surgical intervention was considered. In such complex spinal cases, intraoperative neuromonitoring plays a critical role in reducing the risk of neurological complications.

Intraoperative neuromonitoring included somatosensory evoked potentials (SEP), motor evoked potentials (MEP), and free-run electromyography, with total intravenous anesthesia (TIVA) used to optimize signal quality, avoiding inhalational agents and minimizing neuromuscular blockade. Baseline SEP and MEP responses were obtained in the supine position after induction and intubation, and monitored continuously after turning the patient prone and throughout all stages of correction. Postoperatively, posterior segmental pedicle-screw instrumentation resulted in correction and improved coronal alignment (**Figure**).

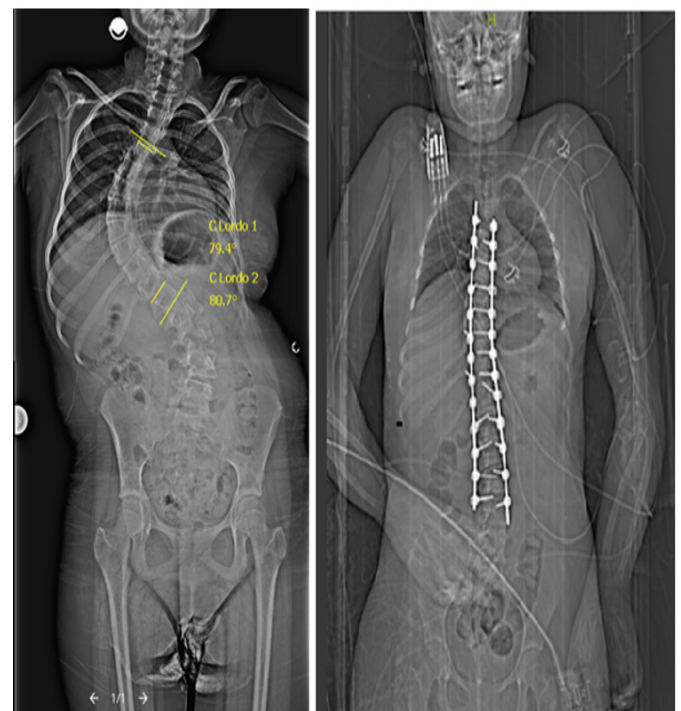


Figure. Pre- and immediate postoperative whole-spine radiographs in a 14-year-old girl with Angelman syndrome. (A) Standing AP film shows severe double-curve neuromuscular scoliosis with Cobb angles of 79.4° and 80.7°. (B) Postoperative AP film demonstrates posterior segmental pedicle-screw instrumentation with correction and improved coronal alignment

This case underscores the need for early recognition and individualized surgical planning for spinal deformity in Angelman syndrome. Intraoperative neuromonitoring is indispensable—baseline values should be obtained in the supine position, re-verified after prone positioning, and neurophysiological signals interpreted throughout corrective maneuvers in close coordination with anesthesia—to minimize risk in these high-risk patients.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

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

Author Contributions

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

REFERENCES

1. Gilmore RB, Gorka D, Stoddard CE, Sonawane P, Cotney J, Chamberlain SJ. Generation of isogenic models of Angelman syndrome and Prader-Willi syndrome in CRISPR/Cas9-engineered human embryonic stem cells. *PLoS One*. 2024;19(11):e0311565. doi:10.1371/journal.pone.0311565
2. Angelman H. 'Puppet'children a report on three cases. *Developmental Med Child Neurol*. 1965;7(6):681-688.
3. Sachdeva R, Donkers SJ, Kim SY. Angelman syndrome: a review highlighting musculoskeletal and anatomical aberrations. *Clinical Anatomy*. 2016;29(5):561-567. doi:10.1002/ca.22659
4. Prasad A, Grocott O, Parkin K, Larson A, Thibert RL. Angelman syndrome in adolescence and adulthood: a retrospective chart review of 53 cases. *Am J Med Genet A*. 2018;176(6):1327-1334. doi:10.1002/ajmg.a.38694