ANKARA EĞİTİM VE ARAŞTIRMA HASTANESİ

# TIP DERGİSİ

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# S.B. ANKARA EĞİTİM VE ARAŞTIRMA HASTANESİ TIP DERGİSİ

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Ankara Eğt. Arş. Hast. Derg. (Med. J. Ankara Tr. Res. Hosp.)

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"Dergimiz 2014 yılından itibaren TÜBİTAK - Ulakbim Türk Tıp Dizini' nde (TR-Dizin) dizinlenmektedir.

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## EDİTÖRDEN / EDİTORIAL

Değerli okuyucularımız,
Bilimsel bir derginin her yeni cildi, yalnızca sayıların ilerlemesi değil; bilgi birikiminin, emeğin ve meslektaş dayanışmasının sürekliliğinin de simgesidir. Bu anlayışla, dergimizin 59. cildine ulaşmış olmanın haklı gururunu sizlerle paylaşmaktan büyük mutluluk duyuyorum.
Tıp bilimi, doğası gereği dinamik, sorgulayıcı ve sürekli dönüşen bir alandır. Her yeni çalışma, var olan bilgiye bir katkı, kimi zaman da bir meydan okumadır. Bu nedenle bilimsel yayınlar, yalnızca bilgi aktarmanın değil; aynı zamanda bilginin güvenilirliğini, şeffaflığını ve etik zeminini korumanın da temel araçlarıdır. Dergimiz, kuruluşundan bu yana geçen onlarca yıl boyunca bu sorumluluğu taşımanın bilinciyle hareket etmiş, her sayısında nitelikli bilimsel üretimi sizlerle buluşturmayı ilke edinmiştir.

Her sayımızda olduğu gibi bu sayımızda da farklı alanlardan değerli araştırmacıların katkılarıyla hazırlanan özgün araştırmalar, olgu sunumları ve derlemeler yer alıyor. Bu çalışmaların her biri, bilimsel merakın ve disiplinler arası iş birliğinin bir ürünüdür. Kuşkusuz bu sürecin işlerliğinde, yazarlarımızın titiz emekleri kadar, hakemlerimizin özverili değerlendirmeleri ve yayın kurulumuzun kararlılığı da büyük rol oynamaktadır. Tüm paydaşlarımıza gönülden teşekkür ederim.

Özellikle vurgulamak isterim ki, 60. cilde doğru adım adım yaklaşmak, sadece sayısal bir ilerleme değil; onlarca yıllık bilimsel birikimin, sürekliliğin ve güvenin göstergesidir. Bu birikimin, yeni kuşak araştırmacılar için hem ilham kaynağı hem de bir sorumluluk mirası olduğuna inanıyoruz.

Dijitalleşmenin sunduğu olanaklar sayesinde, dergimizin erişilebilirliğini ve etki alanını her geçen gün daha da artırmak temel hedeflerimizden biridir. Bilimsel yayıncılıkta kaliteyi korumanın yanında hem ulusal hem de uluslararası endeksler düzeyinde görünürlüğümüzü artırmak, ülkemizin bilimsel katkılarını küresel ölçekte paylaşmak için yürüttüğümüz çalışmalar aralıksız devam etmektedir. Amacımız, ülkemizdeki tıp literatürünü dünya bilimine katkı sunan bir konuma taşımaktır.

Değerli okuyucularımız,

Yeni cildimizle birlikte araştırmacılarımızdan gelen yoğun istek üzerine çalışma metinlerinde kaynak gösterimi konusunda değişikliğe gidildi. Cümle sonunda üstel sayılar yerine parantez içinde sayı uygulamasına geçildi. Konuyla ilgili detaylı bilgiye dergimizin içinde ve internet sayfamızda yer alan "yayın kuralları" bölümünden ulaşılabileceğinizi belirtmek isterim.

Önümüzdeki süreçte, siz değerli meslektaşlarımızın katkı ve önerileriyle dergimizi daha da ileri taşıyacağımıza olan inancımız tamdır. Bilimsel dürüstlükten ödün vermeden, bilimsel merak ve eleştirel düşünceyi rehber edinerek sürdürdüğümüz bu yolculukta sizlerle birlikte olmaktan gurur duyuyorum.

Yeni cildimizin hepimiz için verimli, ilham verici ve yol gösterici olmasını diliyor; katkı sağlayan tüm araştırmacılara, hakemlere ve okuyucularımıza teşekkür ediyorum.

Dear Readers,
Every subsequent issue of a scientific publication is not just the advancement in numerical order but also the continuing buildup of knowledge, dedication to scholarship, and friendship among peers. In this vein, it is with great pleasure and a sense of pride that I herald the publication of the 59th volume of our journal.

The discipline of medical science is inherently dynamic, inquiring, and continually advancing. Each new research effort adds to the body of knowledge and occasionally challenges it. Thus, scientific journals are not just information dissemination vehicles but also vital means for ensuring integrity, transparency, and ethical practice that form the foundations of knowledge. Our journal has shouldered this responsibility since its beginning and endeavored incessantly to provide quality scientific research in each issue.

In line with our previous editions, this volume comprises original research pieces, case studies, and reviews from distinguished scholars across a variety of disciplines. Each of these offerings is a byproduct of scientific investigation and synergistic interdisciplinary collaboration. It goes without saying that the success of this project is due not just to the industrious efforts of our authors but also to the rigorous evaluations of our reviewers and the unfaltering commitment of our editorial board. I am deeply grateful to all our contributors.

I would like to note that nearing the 60th volume is not only a quantitative indicator but also serves as a milestone of decades-long scientific accumulation, continuity, and trust. We think that our heritage provides stimuli and a sense of responsibility to future generations of researchers.

Due to the potential created by digitalization, a prime aim is the constant expansion of our journal's accessibility and dissemination. Together with maintaining strict standards in scientific publishing, we are putting great effort into enhancing our journal's visibility on national as well as global indexing sites, as well as spreading the scientific output of our country at the global level. We hope to take national medical literature to a state of relevance that actually contributes to the world's science.

Dear Readers,

With our new volume, upon the request of our researchers, changes have been made in the citation of references in the study texts. Instead of exponential numbers at the end of a sentence, numbers in parentheses have been used. I would like to inform you that you can find detailed information on the subject in the "publication rules" section in our journal and on our website.

Looking ahead, we are optimistic in every sense that, with the additional encouragement and great feedback of you—our respected colleagues—we will be able to take our journal even further. I am honored to walk this journey with you, following scientific integrity, questioning, and thinking critically.

I hope that this new edition will be fruitful, thought-provoking, and enlightening to us all, and I extend my heartfelt thanks to all the researchers, reviewers, and readers who have participated.

**Prof. Dr. Mevüt Recep PEKCİCİ**
**Editör / Editor**

**S.B. Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi, 2025 Yılı; 58.Cilt, 1.Sayısı Nisan 2025 tarihinde yayımlanmıştır.**

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**Değerli Araştırmacılarımız;**

Sizlerle daha önce de paylaştığımız bazı hususları tekrar hatırlatmak istiyoruz;

2022 yılı ile birlikte Dergimize çalışma gönderiminde bazı yenilik ve değişiklikler yapılmıştır.

1. Dergimiz davetli derlemeler dışında derleme çalışmaları kabul etmemektedir.

2. Dergimize gönderilen çalışmalarla birlikte Turnitin ya da iThenticate programlarından elde edilen "benzerlik analizi"-raporunun da sisteme yüklenmesi gerekmektedir.

3. Çalışmalarda kaynak gösteriminde yaşanan sıkıntıları ortadan kaldırmak için "AMA" standartlarında kaynak gösterimi zorunludur.(Detaylı bilgiye "https://www.bcit.ca/files/library/pdf/bcit-ama_citation_guide.pdf" sayfasından ulaşılabilir)

Bu konuda detaylı bilgi dergimizin son kısmında yer alan yazım kuralları kısmında ve web sayfamızda yer almaktadır.

Çalışmalarınızı Dergimize gönderirken bu hususlara dikkat etmeniz değerlendirme süreçlerini kolaylaştıracaktır.

**Dear Researchers;**

We would like to remind you of some issues we shared with you before;
With the year 2022, some changes have been applied in the study submission rules for our Journal:

1. Our journal only accept invited reviews.

2. Along with the studies sent to our journal, the "similarity analysis" report obtained from Turnitin or iThenticate programs should also be uploaded to the system.

3. In order to eliminate the problems experienced in citing references in studies, it is obligatory to show references in "AMA"standards. (Detailed information can be found on "https://www.bcit.ca/files/library/pdf/bcit-ama_citation_guide.pdf")

Detailed information about these subjects can be found in the instructions to the authors section at the end of our journal and on our website.

Paying attention to these issues while submitting your studies to our Journal will facilitate the evaluation processes.

**Özgün Çalışma / Original Article**

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# Plastik Cerrahi Tarafından Değerlendirilen Travma Hastalarının Etiyolojik ve Demografik Özellikleri

# Etiological and Demographic Characteristics of Trauma Patients Evaluated by Plastic Surgery

Süleyman YILDIZDAL(1), Güven Ozan KAPLAN(2), Mert ÇALIŞ(3), Hakan UZUN(3), Figen ÖZGÜR(3)

## ÖZET

**AMAÇ:** Plastik rekonstrüktif ve estetik cerrahi travma hastalarının değerlendirilmesi ve tedavisinde önemli alanların başında gelir. İş kazalarının artışı, toplumun yaşlanması ile düşmelerin artışı ve günlük kullanıma giren makine ve aletlerin kullanım sıklığının artması travma insidansını arttırmaktadır. Bu çalışmanın amacı travma hastalarının demografik ve etiyolojik özelliklerini ortaya koymak ve plastik cerrahinin travma tedavisinde önemini vurgulamaktır.

**GEREÇ VE YÖNTEM:** Bu çalışmada 2018 kasım-2020 kasım arasında 2 yıllık süreçte plastik cerrahi tarafından değerlendirilen acil hastaları retrospektif olarak incelenmiştir. Hastaların yaş ve cinsiyet özellikleri kaydedilmiştir. Yaş grubu olarak 18 yaş altı pediatrik yaş grubu ve üstü erişkin yaş grubu olarak ayrılmıştır. Daha sonra klinik olarak hastalar el ve üst ekstremite travmaları ile maksillofasiyal travmalar (MFT) olarak ikiye ayrılmıştır. Daha sonra gruplardaki hastalar etiyolojik olarak ev kazaları, iş kazaları, düşmeler, trafik kazaları ve şiddet etiyolojisi olarak ayrılmıştır.

**BULGULAR:** Toplamda 3278 hasta çalışmaya dahil edildi. Bu hastaların 1327'si erişkin (898 erkek, 429 kadın) ve 1951'i pediatrik (1290 erkek,661 kadın) yaş grubundaydı. 1253 hasta (%38.2) el ve üst ekstremite travması, 2025 hasta (%61.8) MFT ile başvurdu. Erkek hastaların travma sonrasında acil servise başvurma oranı daha yüksek görüldü. Tüm hastalar içerisinde 1156 (%35.3) ev kazası, 1157 (%35.3) düşme, 402(%12.2) iş kazası, 318 (%9.7) trafik kazası ve 245 (%7.5) şiddet etiyolojisi saptandı. El ve üst ekstremite kazaları erişkin yaş grubunda daha sık görülürken, iş kazaları bu grubun büyük kısmını oluşturmaktadır. Çocuk yaş grubunda estetik ve fonksiyonel kaygıların daha fazla olması sebebiyle yüz bölgesindeki basit laserasyonlar bile plastik cerrahi tarafından değerlendirildiğinden bu grupta MFT daha sık görülmektedir. Şiddet etiyolojisi sıklıkla erişkin yaş erkek hastalarda görülmüştür.

**SONUÇ:** Travma hastaları plastik cerrahi acillerinin büyük bir kısmını oluşturur. Bu hastaların muayenesi ve ayrıntılı anamnezleri etiyolojiyi aydınlatmakta önemlidir. Erkek bireyler travma sonrasında daha fazla değerlendirilmektedir. Erişkin yaş grubunda iş kazaları el yaralanmalarında erkeklerde daha sıkken, kadınlarda ev kazaları sık görülmektedir. MFT daha sık çocuk hastalarda görülmektedir.

**Anahtar kelimeler:** Travma, şiddet, el ve üst ekstremite yaralanmaları, maksillofasiyal travma

## ABSTRACT

**AIM:** Plastic reconstructive and aesthetic surgery is one of the important areas in the evaluation and treatment of trauma patients. The increase in work accidents, the increase in falls due to the aging of the society, and the increase in the frequency of use of daily machines and tools increase the incidence of trauma. The aim of this study is to reveal the demographic and etiological characteristics of trauma patients and to emphasize the importance of plastic surgery in trauma treatment.

**MATERIAL AND METHOD:** In this study, emergency patients evaluated by plastic surgeons during a 2-year period between November 2018 and November 2020 were retrospectively examined. The age and gender characteristics of the patients were recorded. Age groups are divided into under 18 years of age, pediatric age group and above adult age group. Then, clinically, the patients were divided into two groups: hand and upper extremity traumas and maxillofacial traumas (MFT). Patients in these groups are divided etiologically into home accidents, work accidents, falls, traffic accidents and violence etiology.

**RESULTS:** A total of 3278 patients were included in the study. 1327 of these patients were in the adult (898 men, 429 women) age group and 1951 were in the pediatric age group (1290 men, 661 women). 1253 patients (38.2%) presented with hand and upper extremity trauma, and 2025 patients (61.8%) presented with MFT. Male patients had a higher rate of applying to the emergency department after trauma. Among all patients, 1156 (35.3%) home accidents, 1157 (35.3%) falls, 402 (12.2%) work accidents, 318 (9.7%) traffic accidents and 245 (7.5%) violence etiologies were detected.While hand and upper extremity accidents are more common in the adult age group, work accidents constitute the majority of this group. Since aesthetic and functional concerns are greater in the pediatric age group, even simple lacerations in the facial area are evaluated by plastic surgery, and MFT is more common in this group. The etiology of violence was frequently seen in adult male patients.

**CONCLUSION:** Trauma patients constitute a large portion of plastic surgery emergencies. Examination and detailed anamnesis of these patients are important in elucidating the etiology. Male individuals are evaluated more after trauma. In the adult age group, work accidents and hand injuries are more common in men, while home accidents are more common in women. MFT is seen more frequently in pediatric patients.

**Keywords:** Trauma, violence, hand and upper extremity injuries, maxillofacial trauma

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## INTRODUCTION

The incidence of trauma patients in society is increasing due to the rise in motor vehicle accidents, inadequacies in occupational safety, and many other factors. These injuries cause functional and aesthetic losses in individuals, reduce their quality of life, and consequently impose a socioeconomic burden on society and the state. The evaluation and treatment of these patients are therefore very important. Plastic surgery plays a crucial role in repairing hand and upper extremity injuries, maxillofacial traumas, and soft tissue injuries in any part of the body. It is also vital in treating damage to neurovascular structures, thanks to its microsurgical skills (1). For this reason, it has a critical role in the evaluation and treatment of all minor and major traumas.

There is insufficient data on trauma patients evaluated by plastic surgery in the literature. The aim of this study was to investigate the etiological and demographic characteristics of trauma patients evaluated by plastic surgery in a hospital with a high-level trauma centre.

## MATERIAL AND METHOD

This study was approved by Non-interventional Clinical Researches Ethics Board of Hacettepe University Hospital (Project Number: GO21/147). The medical records of patients admitted to high level trauma centre between November 2018 and November 2020 were retrospectively analyzed and their etiological characteristics were determined. Age (0-18, over 18 years) and gender were used as demographic features when grouping the patients. Patients in each group were evaluated according to their etiological and clinical features. In clinical evaluation, trauma areas were divided into two main regions; hand-upper extremity trauma and maxillofacial trauma (MFT). Other trauma patients were not included in the study. Neurovascular injuries and tendon injuries in hand and upper extremity injuries were evaluated. Etiological features were categorized as accidents, violence, and falls. The place of occurrence of accidents was specified as work, home and traffic. Patients in the violence group were classified as domestic violence, assaults, gunshot wounds and suicide attemps. Those subjected to violence by relatives were categorized as domestic violence, while those attacked by strangers were included in the assault category. Self-harm was categorised as attempt to suicide. Regardless of violence type, injuries after firearm use were considered as a gunshot group. Information was collected about the clinical pictures and prognosis of the patients.

## RESULTS

A total of 3278 patients admitted to our emergency service and evaluated by plastic surgery between November 2018 and November 2020 were included in the study. Of these, 898 (68%) were adult males, and 429 (32%) were adult females. Among pediatric patients, 1290 (66%) were male, and 661 (34%) were female. Male patients were statistically significantly more exposed to trauma than female patients ($p<0.05$). The mean age of adult male patients was 32 years, and the mean age of adult female patients was 36 years. The mean age of paediatric male patients was 8 years and the mean age of paediatric female patients was 7 years.

**Table 1.** Demographic Characteristics of Patients

| | Male | Female | Total |
|---|---|---|---|
| **Adults** | 898(41%) | 429(39.4%) | 1327(40.5%) |
| **Pediatric** | 1290(59%) | 661(60.6%) | 1951(59.5%) |
| **Total** | 2188(100%) | 1090(100%) | 3278(100%) |

Among all patients, there were 245 (7.5%) in the violence group, 402 (12.2%) in the work accidents group, 1156 (35.3%) in the home accidents group, 318 (9.7%) in the traffic accidents group, and 1157 (35.3%) in the falling group

**Table 2:** Trauma Types and Etiologies of All Patients

| | Hand and Upper extremity Trauma | MFT | Total |
|---|---|---|---|
| **Violence** | 133(10.6%) | 112(5.5%) | 245(7.5%) |
| **Work Accidents** | 332(26.5%) | 70(3.5%) | 402(12.2%) |
| **Home Accidents** | 573(45.8%) | 583(28.8%) | 1156(35.3%) |
| **Traffic Accidents** | 103(8.2%) | 215(10.6%) | 318(9.7%) |
| **Falling** | 112(8.9%) | 1045(51.6%) | 1157(35.3%) |
| **Total** | 1253(100%) | 2025(100%) | 3278(100%) |

1. Adult Patients

There were 573 (63.8%) hand-upper extremity traumas and 325 (36.2%) maxillofacial trauma cases in adult male patients. In order of frequency, work accidents, home accidents, violence, and traffic accidents were found to be the etiology of patients admitted with hand trauma. Work accidents were statistically significantly higher as an etiology of hand trauma in adult male patients ($p<0.05$). In MFT patients, the etiological factors in order of frequency were falls, traffic accidents, and violence

**Table 3:** Trauma Types and Etiologies of Adult Male Patients

| | Hand and Upper extremity Trauma | MFT | Total |
|---|---|---|---|
| **Violence** | 85(14.8%) | 59(18.2%) | 144(16%) |
| **Work Accidents** | 303(52.9%) | 8(2.5%) | 311(34.6%) |
| **Home Accidents** | 152(26.5%) | 3(0.9%) | 155(17.3%) |
| **Traffic Accidents** | 33(5.8%) | 127(39%) | 160(17.8%) |
| **Falling** | 0 | 128(39.4%) | 128(14.3%) |
| **Total** | 573(100%) | 325(100%) | 898(100%) |

In the evaluation of adult female patients, 278 (64.8%) had hand-upper extremity trauma, and 151 (35.2%) had MFT. The etiological characteristics of patients with hand trauma and maxillofacial trauma are given in

**Table 4:** Trauma Types and Etiologies of Adult Female Patients

| | Hand and Upper extremity Trauma | MFT | Total |
|---|---|---|---|
| **Violence** | 22(7.9%) | 29(19.2%) | 51(11.9%) |
| **Work Accidents** | 15(5.4%) | 4(2.7%) | 19(4.4%) |
| **Home Accidents** | 189(68%) | 7(4.6%) | 196(45.7%) |
| **Traffic Accidents** | 38(13.7%) | 44(29.1%) | 82(19.1%) |
| **Falling** | 14(5%) | 67(44.4%) | 81(18.9%) |
| **Total** | 278(100%) | 151(100%) | 429(100%) |

Home accidents were statistically significantly higher in hand injuries in female patients ($p<0.05$).

2. Pediatric Patients

Among male children, 284 (22%) presented with hand trauma, and 1006 (78%) presented with MFT. The etiological features of these patients are shown in

**Table 5**: Trauma Types and Etiologies of Pediatric Male Patients

| | Hand and Upper Extremity Trauma | MFT | Total |
|---|---|---|---|
| **Violence** | 19(6.7%) | 15(1.5%) | 34(2.6%) |
| **Work Accidents** | 12(4.2%) | 57(5.6%) | 69(5.4%) |
| **Home Accidents** | 152(53.5%) | 364(36.2%) | 516(40%) |
| **Traffic Accidents** | 21(7.4%) | 18(1.8%) | 39(3%) |
| **Falling** | 80(28.2%) | 552(54.9%) | 632(49%) |
| **Total** | 284(100%) | 1006(100%) | 1290(100%) |

In pediatric male patients, home accidents were statistically significantly higher in hand and upper extremity traumas, while falls were significantly higher in maxillofacial traumas (p<0.05).

Among female patients in the pediatric age group, 118 (17.9%) had hand trauma, and 543 (82.1%) had MFT. Etiological information is given in

**Table 6**: Trauma Types and Etiologies of Pediatric Female Patients

| | Hand-Upper extremity Trauma | MFT | Total |
|---|---|---|---|
| **Violence** | 7(5.9%) | 9(1.6%) | 16(2.4%) |
| **Work Accidents** | 2(1.7%) | 1(0.2%) | 3(0.5%) |
| **Home Accidents** | 80(67.8%) | 209(38.5%) | 289(43.7%) |
| **Traffic Accidents** | 11(9.3%) | 26(4.8%) | 37(5.6%) |
| **Falling** | 18(15.3%) | 298(54.9%) | 316(47.8%) |
| **Total** | 118(100%) | 543(100%) | 661(100%) |

In pediatric female patients, home accidents were statistically significantly higher in hand and upper extremity traumas, while falls were significantly higher in maxillofacial traumas (p<0.05).

3. MFT Patients

A total of 2025 MFT patients were admitted during the study period. The order of frequency was falls, home accidents, traffic accidents, violence etiology, and work accidents (Table 2). 76.5% of these patients were in the pediatric age group. The risk of maxillofacial trauma in the pediatric age group was 3.25 times higher than in the adult age group. While traffic accidents were the most common etiology of MFT in the adult age group, they were statistically significantly less common in the pediatric age group than in adults (p<0.05)

Among 2025 patients who underwent MFT, fractures were seen in 580 (28.6%). Fractures were present in 268 (17.3%) pediatric MFT patients. Fractures were seen in 312 (65.5%) adult MFT patients. The probability of fracture in the adult age group was statistically significantly higher than in the pediatric age group (p<0.05).

These fractures were classified as periorbital region, zygomaticomaxillary region, mandible, and nasal bone. A total of 729 maxillofacial fractures were seen in 580 patients. The most common fracture was in the nasal region (33.1%). The most common cause of fracture was falls (40%)

**Table 7**: Etiology of Fracture

| | Region | | | | |
|---|---|---|---|---|---|
| | **Periorbital** | **Mandible** | **Nazal** | **Zigomatic** | **Total** |
| **Violence** | 6 (2.9%) | 5 (2.8%) | 47 (19.5%) | 4(4.1%) | 62 (8.5%) |
| **Work Accidents** | 6 (2.9%) | 7 (3.9%) | 37 (15.4%) | 15(15.5%) | 65 (8.9%) |
| **Home Accidents** | 66 (31.4%) | 47 (25.9%) | 59 (24.5%) | 37(38.1%) | 209(28.7%) |
| **Traffic Accidents** | 11 (5.2%) | 32 (17.7%) | 42 (17.4%) | 16(16.5%) | 101(13.9%) |
| **Falling** | 121(57.6%) | 90(49.7%) | 56 (23.2%) | 25(25.8%) | 292(40%) |
| **Total** | 210(100%) | 181(100%) | 241(100%) | 97(100%) | 729(100%) |

4. Hand and Upper Extremity Trauma Patients

A total of 1253 hand and upper extremity trauma patients were admitted during the study period. The order of frequency was home accidents, work accidents, violence, falls, and traffic accidents (Table 2). Of these patients, 67.9% were in the adult age group and 32.1% in the pediatric age group. Work accidents were statistically significantly higher in adult male patients compared to other groups (p<0.05). Among all hand injuries, 264 hand bone fractures were observed in 113 patients. 12% of the fractures were closed fractures. The incidence of fractures after work accidents was 23.9%. The incidence of fractures after work accidents was statistically significantly higher than home accidents (p<0.05).

There were 822 flexor zone injuries in hand traumas. The most common injuries were caused by work accidents. A total of 391 (47.6%) tendon or neurovascular injuries were seen. The most common injury was seen in work accidents. The frequency of tendon or neurovascular injuries was 62.1% in patients with violence. The probability of injury to deep structures in flexor zones was statistically significantly higher in violence patients compared to other etiologies (p<0.05).

A total of 643 extensor zone injuries were observed. Tendon or neurovascular structure injuries were present in 237 injuries (36.8%). The most common deep tissue injuries were seen in home accidents.

5. Violence Patients

A total of 245 patients were evaluated within the aetiology of violence

**Table 10**: Patients and Clinical Applications in All Violent Etiologies

| | Hand and Upper Extremity Trauma | MFT | Total |
|---|---|---|---|
| **Domestic violence** | 64(48.1%) | 31(27.7%) | 95(38.8%) |
| **Assaults** | 32(24.1%) | 79(70.5%) | 111(45.3%) |
| **Suicide attemps** | 23(17.3%) | 0 | 23(9.4%) |
| **Gunshot injury** | 14(10.5%) | 2 (1.8%) | 16(6.5%) |
| **Total** | 133(100%) | 112(100%) | 245(100%) |

The frequency of the violence aetiology among the patients evaluated in the 2-year period of study was 7.5%

Of these 245 patients, 112 (54.3%) presented with MFT. In this group, 79 patients (70.5%) were assaulted by strangers, while the remaining 31 (27.7%) patients presented with domestic violence. 59 (52.7%) of these 112 patients were adult males

**Table 11**: Maxillofacial Trauma Patients in Violence Etiology

| | Adult male | Adult female | Pediatric male | Pediatric female | Total |
|---|---|---|---|---|---|
| **Domestic violence** | 13(22%) | 13(44.8%) | 4(26.7%) | 1(11.1) | 31(27.7%) |
| **Assaults** | 44(74.6%) | 16(55.2%) | 11(73.3%) | 8(88.9%) | 79(70.5%) |
| **Gunshot** | 2 (3.4%) | 0 | 0 | 0 | 2 (1.8%) |
| **Total** | 59(100%) | 29(100%) | 15(100%) | 9(100%) | 112(100%) |

Of these 245 patients, 133 (54.3%) presented with hand trauma. In this group, 85 (63.9%) of the patients were adult men. 46 (54.1%) of the patients were admitted due to domestic violence and 14 patients were admitted due to assaults in adult men. 11 patients presented with sucide attemp and 14 of adult males presented with gunshot injuries. In the aetiology of violence, 22 patients who presented with hand trauma were female patients in the adult age group. Adult women were mostly injuried with a cutting tool due to the theft. 19 male pediatric patients applied to the emergency department for violence-related injuries. Most of male pediatric patients came to the emergency department because of hitting a glass object after being angry with a family member. Only 7 female children applied for violence-related injuries, 3 of them were admitted because of sharp instruments injury during theft, and 4 of them were admitted because of suicide attempts.

Table 12: Hand and Upper Extremity Trauma in Violence Patients

| | Adult male | Adult female | Pediatric male | Pediatric female | Total |
|---|---|---|---|---|---|
| Domestic violence | 46(54.1%) | 5(22.7%) | 13(68.4%) | 0 | 64(48.1%) |
| Assaults | 14(16.5%) | 12(54.6%) | 3(15.8%) | 3(42.9%) | 32(24.1%) |
| Suicide attemps | 11(12.9%) | 5(22.7%) | 3(15.8%) | 4(57.1%) | 23(17.3%) |
| Gunshot injury | 14(16.5%) | 0 | 0 | 0 | 14(10.5%) |
| Total | 85(100%) | 22(100%) | 19(100%) | 7(100%) | 133(100%) |

## DISCUSSION

Trauma patients constitute a significant portion of those admitted to the emergency department. These trauma patients are mostly evaluated by orthopedics and general surgery. However, plastic surgery also plays an important role in their evaluation (2). The frequency of male patients was found to be 66.7% among all patients. Considering the gender distribution of the patients, 65.7% of the patients in MFT and 68.2% of the patients in hand and upper extremity trauma were male. In the literature, as in our study, male patients are exposed to statistically significantly more trauma than female patients in all age groups (3,4,5).

In the literature, the most common patients evaluated by plastic surgery are those with hand and upper extremity trauma (1,2,5). However, maxillofacial traumas are more prevalent than hand traumas among pediatric patients (6,7). Additionally, some studies focus on major facial injuries while overlooking minor soft tissue traumas in the adult age group (8). At our hospital, plastic surgeons evaluate all lacerations and maxillofacial traumas in pediatric patients rather than emergency doctors, resulting in 61.8% of all patients in our study presenting with maxillofacial injuries. Consequently, pediatric patients constituted 59.5% of all patients in this study. The lower incidence of maxillofacial traumas compared to hand injuries reported in the literature may be due to soft tissue injuries in pediatric patients being treated by emergency physicians rather than plastic surgeons. However, when considering all pediatric patients and soft tissue injuries, it can be concluded that maxillofacial traumas are more common than hand injuries.

In this study, the fall rate among maxillofacial trauma (MFT) patients was 51.6%. A similar fall rate of 47.4% was found in a study focusing on children, aligning with our results (7). According to a European multi-center study, the aetiology of maxillofacial injury varied from centre to centre, with assaults and falls being the most important etiological factor: assaults were the predominant cause in Plovdiv (Bulgaria), Tartu (Estonia), Oslo (Norway), Belgrad (Serbia), Kiev (Ukraine), London (England, UK), and Dundee (Scotland, UK). In contrast, falls were the leading cause in Turin (Italy), Nantes (France), Zagreb (Croatia), Bergen (Norway), Amsterdam (The Netherlands), and Ljubljana (Slovenia) (9).

In this study, 729 fractures were observed in a total of 580 (17.6%) patients. Fractures were seen in 6.9 % of the pediatric age group and 11.8% of adult age group. No additional injury was observed in 93.1% of pediatric patients, and only primary sutures and wound care were applied to the facial area. Previous studies have shown that fracture patients are more common in male and adults, and this study supports that conclusion (6). The most common cause of fracture was traffic accidents, which aligns with the literature where the second most common cause is interpersonal violence (6,7,8,9,10,11). In our study, 45.5% of patients had fractures due to traffic accidents. The second most common cause of maxillofacial fractures was falls (24.8%), followed by violence (16.6%). Similar etiologies have been observed in other studies. For instances, in United Arab Emirates, the most common cause of fractures was motor vehicle accident (75%), then followed by falls (12%) and then assaults (8%) (12). In India, similar rates were observed; Traffic accident related fractures occurred in 72.7%, falls at 14.1%, and assaults following (13). Multicenter trauma studies may provide clearer etiological information.

Previous studies have shown that the most common facial fractures occur in the nasal bone, and our study supports this finding (11). In some studies, mandibular fractures were also reported as the most common type. The reason for this discrepancy may be the lack of sufficient data on nasal traumas since nasal fractures often require less surgical intervention (12,14). In our study, the periorbital region was the second most common fracture site, likely because maxillary fractures were also included in this group. Additionally, fractures in this region were frequently seen in paediatric patients after falls and our clinic is a centre where pediatric patients are often evaluated. Mandibular fractures were the third most common type observed in this study.

Hand and upper extremity traumas are more frequent in most studies (4,15,16). These studies indicate that such injuries predominantly occur in male patients within the adult age group. While work accidents were the most common reason for presentation in all patients, home injuries were the primary cause for female patients (15,17). Statistically, work accidents were significantly higher in males, whereas home injuries were more prevalent in females, aligning with our results (15).This finding has been observed in other studies, although a small number of work accidents were also noted among females. This may be attributed to cultural factors, where women are more involved in domestic activities, and men are more active in business life. Regional etiological differences might also play a role, as some studies have found home accidents to be more common than work injuries among male patients, especially in Europe (18). Sport-related hand injuries were not seen in our study compared with a European study that indicated a high prevalence of these injuries (19). This discrepancy could be because high-level upper extremity traumas and isolated fractures are evaluated by the orthopedics department in our hospital.

Some hand injuries are isolated soft tissue injuries and may be overlooked without plastic surgery evaluation. In our clinic, simple or complicated hand traumas are evaluated by plastic surgeons. For this reason, the incidence of tendon or neurovascular injury was observed to be higher in our study than other studies (19). Regarding hand and upper extremity injuries, 42% of all patients underwent surgical exploration, while the remainder were explored and repaired in the emergency department. Although previous studies reported an incidence of fractures following hand injuries reaching 70%, our study found fractures in only 9% of patients (20). This discrepancy may be because only fractures of the metacarpal and digital bones were evaluated by the plastic surgery department in our clinic. Most of the fractures we observed were open fractures, as closed fractures are primarily assessed by the orthopedics department in our clinic. Therefore, our study reported a higher rate of open fractures compared to other studies (16).

Violence is gradually increasing, and some cases remain hidden (3,4,21). Although it is believed that there are numerous factors contributing to the incidence of violence, especially in cases of domestic injuries, patients admitted to the emergency department often conceal the true cause due to legal concerns. Additionally, while the likelihood of self-harm is higher among young adults, these patients sometimes hide the reasons for their injuries when they applied to hospital. Consequently, only 7.5% of the patients evaluated in emergency departments were reported to have been admitted due to violence-related causes.

The rates of violence in maxillofacial traumas have been well-documented in most studies, but the etiology of violence in hand traumas has not been sufficiently demonstrated (12,13). In adult males, 18.2% of maxillofacial trauma patients presented with an etiology of violence, whereas a similar rate (14.8%) was observed in the hand trauma group in this study. For female adults, the etiology of violence was seen in 11.9% of cases. As indicated by these rates, violence is less common among female patients (3,4,21,22). Overall, 14.7% of adults and 2.6% of children were admitted with a violent etiology. The relative risk of violence in children is 17.7% compared to adults.

The rate of violence varies according to the region and the characteristics of the patients. In Turkey, the most common etiology of MFT is traffic accidents, followed by violence (2.71%) (6). In the United Arab Emirates, violence accounts for 8% of all MFT cases (12). A study focusing on children and adolescents reported a violence rate in MFT of 14.9% (7). n a similar study conducted in India, violence was observed in 8.6% of patients (13). This rate may increase in younger patients with MFT; for instance, one study found that the rate of violence among individuals aged 21-30 was 23.1% (10). Another study reported that interpersonal violence was the primary mechanism of maxillofacial injury, accounting for 48.1% of 294 patients (14). In our study, violence was the etiology in 5.5% of maxillofacial trauma patients and 10.6% of hand trauma patients. Contrary to the literature, vi-

olence was a more common etiology in hand injuries compared to MFT in this study. The etiology of violence in trauma patients evaluated by plastic surgery has not been previously reported.

Violence was most common among male individuals in our study, a finding consistent with several other studies (6,7). When analyzing the nature of violence among patients, 95 (38.8%) were exposed to domestic violence

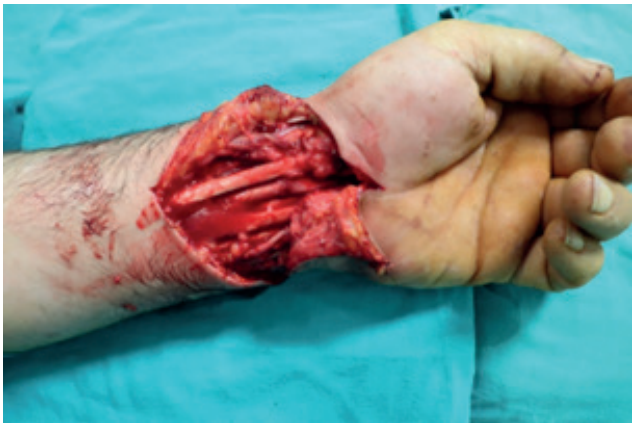

Figure 3: Spaghetti type wrist injury after suicide attempt

and 111 (45.3%) reported being attacked by unknown assailants. These findings suggest that violence is most often perpetrated by strangers. Although gunshot injuries are rare in most studies (4,17), their rates can be high in certain regions due to sociocultural factors. Most of our gunshot patients were injured while handling their own weapons, with 5 injuries occurring during hunting activities

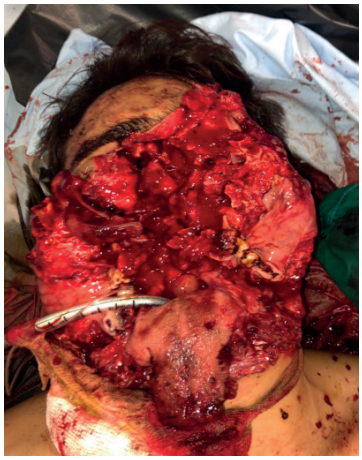

Figure 4: The patient who applied with a gunshot wound. Before the first intervention.

Of the patients exposed to domestic violence, 64 (48.1%) presented with hand and upper extremity trauma, with sharp instrument injuries being the most common

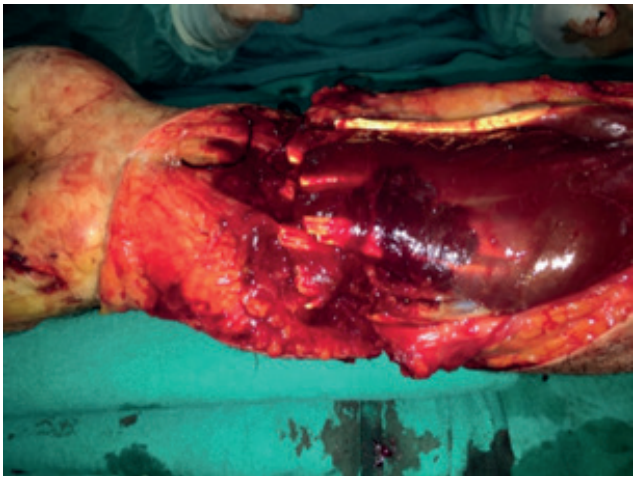

Figure 5: Patient injured during domestic violence

In maxillofacial trauma (MFT) cases, periorbital region traumas were the most frequent, followed by mandible fractures, in the domestic violence group in our study. The literature lacks sufficient information on domestic violence cases seen in plastic surgery emergencies (3,22).

Of the 111 patients who presented with assault-related injuries, 79 (71.1%) had maxillofacial trauma (MFT), while the remaining had hand and upper extremity trauma. In this group, the most common fracture pattern was the combination of mandibular body and mandibular condyle fractures. Lee et al. demonstrated that interpersonal violence often causes mandibular fractures, particularly angular fractures (3). Mandibular fractures were the most frequent type of fracture following assaults (12,13,14), a finding consistent with our study, where assault-related fractures were most common in the mandible. Conversely, fractures resulting from domestic violence were more frequently located in the periorbital region.

The age range of patients who attempted suicide was 14-32 years, consistent with the known trend of suicide attempts being more common among young individuals (22,21). All 23 patients who attempted suicide were trying to cut their wrists with sharp instruments, with only 4 of them presenting with spaghetti-type injuries. Five of the suicide attempts resulted in no neurovascular or tendon injuries. Among the remaining cases, suicide attempts involved injuries to the palmaris longus tendon and some degree of median nerve injury. It is likely that most patients ceased self-harming due to the pain caused by irritation of the median nerve.

## CONCLUSION

The majority of trauma patients evaluated by the plastic surgery department were males and children. Hand injuries were more common among adult patients, while maxillofacial traumas were predominant in the child age group. Falling was the most common cause of maxillofacial traumas, whereas home accidents were the leading cause of hand injuries. Among maxillofacial traumas, the most frequently fractured bone was the nasal bone. Regardless of age, gender, and trauma type, 7.5% of patients presenting to the plastic surgery department had an etiology of violence, with assaults being the most common cause of violence.

**Author contributions**:

Conception/Planning: SY, GOK, MÇ, HU, FÖ

Data collection/Processing: SY, GOK, MÇ, HU

Data analysis and interpretation: SY, GOK, MÇ, HU, FÖ

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**Özgün Çalışma / Original Article**

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# D vitamini ile Vitamin B12, Metilmelonik Asid, Homosistein ve Ferritin Düzeyleri Arasındaki İlişki

# Correlation Between Vitamin D and Ferritin, Vitamin B12, Homocysteine, and Methylmalonic acid

Recep ALANLI(1), Mustafa Kemal KILIÇ(1), Mehmet ŞENES(2)

## ÖZET

**AMAÇ:** D vitamini ile diğer vitamin düzeyleri arasında bir ilişki olup olmadığı tam olarak bilinmemektedir. Bu çalışmada D vitamini ile folat, ferritin, B12 vitamini, homosistein ve metilmalonik asit (MMA) düzeyleri arasındaki ilişki incelenmişdi.

**GEREÇ VE YÖNTEM:** Kasım 2022 ile Nisan 2023 tarihleri arasında iç hastalıkları polikliniğine başvuran 189 hastanın (18-65 yaş) laboratuvar sonuçları retrospektif olarak değerlendirildi. On sekiz yaş altı ve 65 yaş üstü, son 3 ay içinde D vitamini, B12 vitamini ve demir replasman öyküsü olan, kanser, akut enfeksiyon, gebelik, böbrek veya karaciğer hastalığı, çölyak hastalığı gibi malabsorbsiyon veya inflamatuar barsak hastalığı tanısı alan katılımcılar çalışma dışı bırakıldı.

**BULGULAR:** D vitamini ile hemoglobin ve ferritin arasında pozitif korelasyon vardı (sırasıyla r=0,219 p=0,003 ve r=0,262 p<0,001). Daha yüksek D vitamini çeyrekliklerinde yer alan hastaların hemoglobin ve ferritin düzeyleri, daha düşük çeyreklik dilimlere kıyasla daha yüksekti. D vitamini ile MMA seviyelerinin ilişkili olduğu belirlendi (OR= 4,576 %95 GA=1,506-13,903 p=0,007). D vitamini ile homosistein, folat ve B12 vitamini düzeyleri arasında ilişki saptanmadı.

**SONUÇ:** Serum MMA düzeylerinin doku düzeyinde B12 eksikliğini göstermede serum B12 ölçümünden daha duyarlı bir yöntem olduğu ve bu nedenle B12 vitamini seviyeleri normal bulunmuş olsa bile yüksek MMA düzeyleri saptanan hastalarda fonksiyonel vitamin B12 eksikliği düşünülmesi gerektiği ve vitamin D desteğinin verilmesinin uygun olabileceği düşünüldü. Vitamin D resplasmanının fonksiyonel B12 eksikliğine etkisinin inceleyecek randomize kontrollü çalışmalara ihtiyaç olduğu düşünüldü.

**Anahtar Kelimeler:** Ferritin, homosistein, metilmalonik asit, vitamin B12, vitamin D

## ABSTRACT

**AIM:** It is not well-known whether there is an association between vitamin D and other vitamin levels. In this study, potential interrelations between vitamin D and folic acid, ferritin, vitamin B12, homocysteine, and methylmalonic acid levels were examined.

**MATERIAL AND METHOD:** Laboratory results of 189 adult patients (18-65 years old) who admitted to Internal Medicine Outpatient Clinic of the hospital between November 2022 to April 2023 were retrospectively retrieved from hospital registry. Participants younger than 18 and older than 65 years old, with a history of vitamin D replacement within 3 months, diagnosed with cancer, acute infection, pregnancy, renal or hepatic disease, malabsorption like Celiac or inflammatory bowel disease were excluded.

**RESULTS:** There was a positive correlation between vitamin D and both hemoglobin and ferritin (r=0.219 p=0.003 and r=0.262 p<0.001 respectively). Patients in the higher vitamin D quartiles had higher hemoglobin and ferritin levels compared to lesser quartiles. Vitamin D and MMA were found to be associated (OR= 4.576 %95 CI=1.506-13.903 p=0.007). There were no association between vitamin D and homocysteine, folate, and vitamin B12 levels respectively.

**CONCLUSION:** Serum MMA is a more sensitive method than serum B12 measurement to reflect tissue level B12 deficiency, thus if the patient has elevated MMA levels but normal vitamin B12 levels, vitamin D supplementation might be beneficial to treat functional vitamin B12 deficiency. Prospective randomised controlled trials are required to reveal the effect of vitamin D replacement on functional B12 deficiency.

**Keywords**: Ferritin, homocysteine, methylmalonic acid, vitamin B12, vitamin D

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## GİRİŞ

Vitamin B12, folik asit, ferritin ve D vitamini oldukça önemli vitaminlerdir. Vitamin B12 ve folik asit; hücre çoğalması ve diferansiyasyonu, enerji ve lipid metabolizması, protein ve DNA sentezinde görev almaktadırlar.(1) Vitamin D ise, kas ve iskelet sistemi dışında da önemli görevleri olan bir vitamindir. Birçok dokuda D vitamini reseptörü bulunmaktadır. Vitamin D, hücre içine yerleşik reseptörleri aracılığıyla hedef genleri uyararak etki göstermektedir. D vitamininin binden fazla gene etki ettiği gösterilmiştir.(2) Bu reseptörlerin fonksiyonları anlaşıldıkça, D vitamininin çok iyi bilinen kemik ve kalsiyum metabolizmasındaki görevleri dışında farklı dokularda henüz bilinmeyen etkileri saptanacaktır.(3)

D vitamini ile folik asit, ferritin ve B12 düzeyi arasındaki ilişkiyi araştıran çalışmalarda çelişkili sonuçlar elde edilmiştir. D vitamini ile folik asit ve vitamin B12 düzeyleri arasında ilişki olduğu ve D vitamini eksikliğinin vitamin B12 ve folik asit emiliminde bozulmaya neden olabileceği bildirilmiştir. (4) Ancak D vitamini ile folik asit düzeyi arasında ilişki olmadığını gösteren çalışmalar da vardır.5,6 D vitamini eksikliğinin ferritin düşüklüğü ve anemi ile ilişkili olduğu çeşitli çalışmalarda gösterilmiştir.7,8

Hem homosistein hem de metilmalonik asit, B12 ve folik asit eksikliğini göstermede bu vitaminlerin doğrudan serum düzeylerinin ölçümüne kıyasla daha hassas parametrelerdir.(9) Yapılan çoğu çalışmada D vitamini ile ferritin, folik asit ve vitamin B12 düzeylerinin ilişkisine bakılmış olup, D vitamini ile metilmalonik asit ve homosistein ilişkisini gösteren çok az çalışma vardır. Kore'de yapılmış bir çalışmada D vitamini ile homosistein düzeyleri arasında negatif bir ilişki olduğu bildirilmiştir.(10) Başka bir çalışmada ise D vitamini düzeyi 21 ng/ml'nin altındaki düzeylerde homosisteinle ters ilişkili saptanmışken, bu düzeyin üstünde homosisteinle ilişkisiz bulunmuştur.(11) D vitamini düzeyiyle metilmalonik asit düzeyi arasındaki ilişki ise açıklığa kavuşturulamamıştır.

Yapılan bu çalışmada; D vitamini ile folik asit, ferritin, B12, homosistein ve metilmalonik asit düzeyi arasındaki ilişkiyi değerlendirmek hedeflenmiştir.

## GEREÇ VE YÖNTEM

Bu çalışma Ankara'daki üçüncü basamak bir hastanenin iç hastalıkları kliniğinde, Kasım 2022 ile Nisan 2023 tarihleri arasında başvuran 189 hastayla retrospektif olarak yapıldı. İç hastalıkları kliniğine; halsizlik, yorgunluk, kas ve sırt ağrısı gibi vitamin eksikliğini düşündüren şikayetlerle başvuran hastalar çalışmaya dahil edildi. On sekiz yaşından küçük ve 65 yaşından büyük olanlar, en az üç ay öncesinde D vitamini, B12 vitamini ve demir tedavisi alanlar, malignite, aktif enfeksiyon, gebelik, böbrek ve karaciğer hastalığı olanlarla çölyak ve inflamatuar bağırsak hastalığı gibi emilim bozukluğu olanlar çalışmaya dahil edilmedi. Ankara Eğitim ve Araştırma Hastanesi Etik Kurulunca 27.4.2023 tarih ve E-23-1281 karar numarası ile bu çalışmaya onay verilmiştir.

Hastaların yaş, cinsiyet, ferritin, vitamin B12, D vitamini, folik asit, hemogram, laktat dehidrogenaz (LDH), homosistein, metilmalonik asit (MMA), bilirubin değerleri kayıt altına alındı. Hemogram parametreleri Sysmex XN-300 Analyzer (ABD) cihazı ile ölçüldü. Metilmalonik asit; Shimadzu LCMS--8040 cihazı (Japonya) ile sıvı kromatografi-kütle spektrometresi/kütle spektrometresi yöntemiyle ölçüldü. Homositein, Shimadzu LC-2050C cihazı (Japonya ) ile yüksek performanslı sıvı kromatografisi yöntemi ile ölçüldü. Diğer parametreler Roche Hitachi Cobas 8000 Analyzer (İsviçre) ile ölçüldü. D vitamin değeri 20µg/L'den, vitamin B 12 191ng/L'den, ferritin 13µg/L'den ve folik asit 3,1µg/L'den düşük ise eksiklik olduğu kabul edildi. Hemoglobin değeri erkeklerde 13,5g/dl'den ve kadınlarda 12,5g/dL'den düşük ise anemi kabul edildi. LDH değerinin 223 U/L'den, total bilirubin 1.2 mg/dL direkt bilirubin 0.3mg/dL MMA 0,4Umol/l'den, homosistein 30µmol/L'den fazla ise yüksek olarak kabul edildi. Ayrıca B12 ve folik asit değeri normal ancak homositein veya metilmalonik asit düzeyi yüksek olan hastalar (fonksiyonel eksik) da ayrı bir grup olarak değerlendirilerek karşılaştırma yapıldı.(12)

İstatistiksel değerlendirme SPSS Statistics for Windows, version 15.0 (SPSS Inc., Chicago, Ill., USA) paket programı kullanılarak yapıldı. Değişkenlerin dağılımlarının normal olup olmadığı Kolmogorov-Smirnov testi ile belirlendi. Normal dağılım göstermeyen sayısal değişkenler için ortanca (minimum-maksimum) değerleri kullanıldı. D vitamini düzeyleri çeyreklik dilimlere ayrıldı. D vitamini grupları arasında sürekli değişkenlerin ortanca değerleri arasında fark olup olmadığını saptamak için Jonckheere-Terpstra testi kullanıldı. B12 ve folik asit seviyesi yeterli olan ve olmayan gruplar arasında sürekli değişkenlerin ortanca değerleri arasında fark olup olmadığını saptamak için Jonckheere-Terpstra testi kullanıldı. Sürekli değişkenler arasındaki ilişki için Spearman korelasyon yöntemi kullanıldı. Tek değişkenli analizde p değeri %20'ten küçük olan değişkenler alınarak çok değişkenli lojistik regresyon analizi yapıldı. Bu modeli oluştururken geriye doğru lojistik regresyon yöntemi kullanıldı. Her bağımsız değişken için rölatif risk oranı ve %95 güven aralığı hesaplandı. Çalışmada p değerinin 0,05'ten küçük olması istatiksel olarak anlamlı kabul edildi.

## BULGULAR

Çalışmaya alınan 189 katılımcının yaş ortalaması 34,88±0,76, yaş ortancası 34 (18-62) idi. Katılımcıların 55 (%29,1)'i erkek, 134 (%70,9)'ü kadındı. Katılımcıların değerlendirilen parametrelerin ortanca değerleri tablo 1'de gösterildi.

**Tablo 1. Katılımcıların Parametrelerin ortanca ve minimum maksimum değerleri**

| Parametre | Ortanca (Min-Max) |
|---|---|
| D vitamini (ng/ml) | 17,1 (5,1-53) |
| B12 vitamini (ng/L) | 317 (100-918) |
| Ferritin (µg/ml) | 32,1 (1,6-300) |
| Folik asit (µg/ml) | 6,6 (2-20) |
| Laktat Dehidrogenaz (U/L) | 199 (99-387) |
| Ortalama Eritrosit Hacmi (fL) | 86,7 (55-107) |
| Total Bilirubin (mg/dL) | 0,4 (0,1-2) |
| Direkt Bilirubin (mg/dL) | 0,2 (0,1-0,6) |
| Homosistein (µmol/L) | 10,8 (4-39) |
| Metilmalonik asit (Umol/l) | 0,22 (0,05-2,4) |
| Hemoglobin (g/dL) | 13,6 (5,8-19) |

Katılımcıların %32,8'inde D vitamini, %7,4'ünde B12, %26,5'inde ferritin ve %5,3'sinde folik asit eksikliği saptandı. En sık D vitamini eksikliği saptandı. Ayrıca katılımcıların %27,5'inde LDH, %24,9'unda MMA ve %5,3'ünde homosistein yüksekliği saptandı. Katılımcıların %21,8'inde anemi saptandı. Parametrelerin, D vitamini çeyreklik dilimlerine göre kıyasladığımızda, sadece ferritin ve hemoglobin değerinin anlamlı olduğu saptandı.

**Tablo 2. D vitamini çeyreklik dilimlerine göre parametrelerin kıyaslanması**

| Parametre | D vitamini <12,55 ng/ml (n=47) | D vitamini 12,55-17,1 ng/ml (n=46) | D vitamini 17,1-21,8 ng/ml (n=48) | D vitamini >21,8 ng/ml (n=48) | P değeri |
|---|---|---|---|---|---|
| Yaş | 33 (18-52) | 33 (18-59) | 33 (19-59) | 36 (18-62) | 0,185 |
| B12 vitamini (ng/L) | 313 (100-697) | 325,5 (114-700) | 299,5 (152-918) | 329 (155-704) | 0,15 |
| Ferritin (µg/ml) | 18,3 (2,4-140) | 27,7 (1,7-200) | 38,4 (2,5-300) | 43,2 (1,6-300) | **0,001** |
| Folik asit (µg/ml) | 6,65 (2-13) | 6,45 (2-13) | 7,1 (2-20) | 6,6 (3-20) | 0,798 |
| LDH (U/L) | 202 (131-296) | 206 (99-297) | 197,5 (134-307) | 181 (128-327) | 0,216 |
| MCV (fL) | 86,4 (59-107) | 86,5 (57-96,7) | 86,05 (62-96,7) | 87,15 (55-95) | 0,844 |
| Total Bilirubin (mg/dL) | 0,4 (0,1-1,6) | 0,4 (0,1-1,5) | 0,45 (0,2-1) | 0,4 (0,2-2) | 0,555 |
| Direkt Bilirubin (mg/dL) | 0,2 (0,1-0,5) | 0,2 (0,1-0,5) | 0,2 (0,1-0,5) | 0,2 (0,1-0,6) | 0,264 |
| Homosistein (µmol/L) | 11,2 (5,5-39) | 10,65 (4,9-22) | 11,15 (5,8-39) | 11,5 (4-28) | 0,991 |
| MMA (Umol/l) | 0,32 (0,08-2,4) | 0,2 (0,05-0,63) | 0,2 (0,1-2,4) | 0,23 (0,07-0,71) | 0,104 |
| Hemoglobin (g/dL) | 12,9 (6,7-18) | 13,6 (5,8-19) | 13,83 (8,6-18) | 14 (6,5-17) | **0,007** |

MCV=Mean corpuscular volüme, LDH=Laktat dehidrogenaz, MMA=Metilmalonik asit

Buna göre D vitamini düzeyi arttıkça, hemoglobin ve ferritin değeri de artmaktadır.

Hastalar B12 düzeylerine göre eksik (n=14), fonksiyonel eksik (B12 normal ancak MMA veya homosistein yüksek, n=56) ve normal (B12 ve diğer parametreler normal, n=119) olarak 3 gruba ayrıldı. Gruplar arasında D vitamini ve ferritin düzeyi açısından anlamlı bir fark saptanmadı (sırasıyla p=0,087 ve p=0,671).
Hastalar folik asit düzeyleri eksik (n=6), fonksiyonel eksik (folik asit normal ancak homosistein yüksek (n=64) ve normal (folik asit ve diğer parametreler normal (n=119) olarak 3 gruba ayrıldı. Gruplar arasında D vitamini ve ferritin düzeyi açısından anlamlı bir fark saptanmadı (p=0,152 ve p=0,946).
Parametreler normal dağılıma uymadığı için aralarındaki ilişki için Spearman korelasyonu hesaplandı. D vitamini ile hemoglobin ve ferritin değeri arasında korelasyon saptandı. (sırasıyla r=0,219 p=0,003 ve r=0,262 p<0,001). Ancak D vitamini düzeyi ile sırasıyla B12, folik asit, MMA ve homosistein arasında korelasyon saptanmadı (r= 0,125 p=0,088; r=0,009 p=0,904; r=-0,133 p=0,068 ve r= 0,066 p=0,364).
Vitamin D düzeyi ile bağımsız ilişkili saptanan parametrelerle çok değişkenli lojistik regresyon analizi yapıldı.

**Tablo 3. D vitamini ile ilişkili parametrelerin çok değişkenli regresyon analizi**

| Parametre | Odds Ratio (%95 GA) | P Değeri |
|---|---|---|
| Hemoglobin | 0,814 (0,697-0,951) | **0,010** |
| Metilmelonik Asid | 4,576 (1,506-13,903) | **0,007** |

Buna göre; MMA düzeyindeki 1 birim artış D vitamini eksikliği görülme olasılığını 4,5 kat artışa ve hemoglobin düzeyindeki 1 birim artış D vitamini eksikliği görülme olasılığında 0,8 kat azalışa neden olmaktadır.

## TARTIŞMA

Yapılan bu çalışmada D vitamini düzeyi ile hemoglobin ve ferritin düzeyleri arasında pozitif korelasyon saptandı. D vitamini çeyreklik dilimleri arttıkça hemoglobin ve ferritin değerleri artmaktadır. Ayrıca D vitamini ile MMA (vitamin B12 değil) seviyeleri arasında ters ilişki olduğu saptandı. D vitamini ile homosistein, folik asit ve vitamin B12 düzeyi arasında ilişki saptanmadı.

D vitamini birkaç yolla demir metabolizmasında rol oynamaktadır. Öncelikle D vitamininin eritropoezde önemli bir rolü olduğu ve D vitamini tedavisinin anemi tedavisinde katkı sağladığı gösterilmiştir. (13) Ayrıca, vitamin D reseptörlerinin kemik iliğinde plazmadan 100 kat fazla miktarda bulunmaktadır.(14) D vitaminin bir diğer etkisinin hepsidin düzeyini baskılayarak hemoglobin düzeyini arttırması olduğu gösterilmiştir.(15) Bunlara ek olarak D vitamini proinflamatuvar sitokin düzeyine etki ederek, demir metabolizmasında görev almaktadır.15,16 Hipotiroidi tanılı 500 hastayla yapılan bir çalışmada D vitamini eksikliği ile demir eksikliğinin birlikte görüldüğü saptandı.(17) Gebelik sırasında D vitamini eksikliğinin anemi gelişme riskini arttırdığı gösterilmiştir.(18) Başka bir çalışma D vitamini eksikliğinin anemi gelişme riskini arttırdığı gösterilmiştir.(19) Yapılan bu çalışmada yukarıdaki çalışmalarla benzer şekilde vitamin D düzeyi arttıkça, hemoglobin ve ferritin düzeylerinin arttığı gösterildi.
Çocuklarda yapılan bir çalışmada D vitamini eksikliği ile vitamin B12 eksikliği arasında ilişki olduğu saptandı.(20) USA'da yapılan bir çalışmada vitamin D düzeyi ile vitamin B12 arasında ilişki olduğu bildirildi.(21) D vitamini eksikliğinde mide mukozasında hasar geliştiği ve bu nedenle de vitamin B12'nin emilmesinde azalma olduğu ve bu yüzden vitamin D ve vitamin B 12 eksikliğinin birlikte görüldüğü iddia edilmektedir.(22) Başka bir açıklama da D vitamini eksikliğinin, kalsiyum düzeyine etki ederek terminal ileumdan vitamin B12 emilim oranının azaltmasıdır.(4) Ayrıca D vitamini eksikliğinin; gastrik asit ve intrensek faktör üretiminde azalma ve aşırı bakteriyel çoğalmaya yol açarak da vitamin B12 emilimini bozduğu düşünülmektedir.(3) Ancak yapılan bu çalışmada D vitamini düzeyi ile vitamin B12 düzeyi arasında ilişki saptanmadı. Bu durum serumda vitamin B12 ölçülmesinin, hücre içi vitamin düzeylerini tam olarak yansıtmamasıyla ilişkili olabilir. Serum vitamin B12 testi ile serumdaki total B12 düzeyi ölçülmekte olup, B12'nin aktif ve inaktif olan tüm formları hesaplanmaktadır. (23) Serum B12 düzeyi normal ancak MMA yüksekliği olan durumlara fonksiyonel B12 eksikliği olarak isimlendirilmektedir.(12) Yapılan bu çalışmada da fonksiyonel B12 eksikliği olanlar saptanmış olup, bu grup ile diğer gruplar arasında D vitamini düzeyi arasında fark saptanmamıştır.

MMA değeri, vitamin B12 eksikliğinde artmaktadır. MMA'nın vitamin B12 eksikliğinin tanısında kullanılması kılavuzlarca önerilmektedir. (24) Klinik şüphe olan durumlarda B12 düzeyleri normal iken tanı için MMA testinin kullanılması önerilmektedir.(25) Ayrıca vitamin B12 eksikliğini saptamada en iyi testin MMA olduğu da iddia edilmektedir.(23) Bir çalışmada MMA düzeyi kardiyovasküler nedenlere bağlı mortalite ile ilişkili bulunmuşken, serum B12 düzeyi ise ilişkisiz bulunmuştur.(26) Başka bir çalışmada ise Alzheimer hastalarındaki amiloid ve tau protein gibi belirteçlerle MMA seviyesi arasında ilişki saptanmışken bu ilişki serum B12 düzeyi ile saptanmamıştır.(27) Yapılan bu çalışmada benzer şekilde D vitamini eksikliği ile MMA düzeyi arasında ilişki saptanmışken, D vitamini ile vitamin B12 düzeyi arasında ilişki saptanmadı. Bu durum, MMA testinin serum B12 testine göre daha hassas olması ile açıklanabilir.

Yapılan bu çalışmada bazı kısıtlılıklar mevcuttur. Öncelikle tek merkezli ve retrospektif olarak yapılmıştır. Ayrıca katılımcıların beslenmelerindeki kalsiyum ve vitamin değerleri hesaba katılmamıştır. Çalışmadaki kesitsel desen nedeniyle D vitamini replasmanına diğer parametrelerin zaman içerisinde verdiği yanıt değerlendirilememiştir.

## SONUÇ

Yapılan bu çalışmada D vitamini düzeyi ile hemoglobin ve ferritin düzeyleri arasında pozitif, MMA arasında ise negatif bir ilişki saptandı. Vitamin B12 ile D vitamini ilişki saptanmamasının, MMA testinin B12 düzeyini daha iyi yansıtmasına bağlı olduğunu düşünüldü. Bu yüzden, serum vitamin B12 düzeyi normal bile olsa doku düzeyinde eksiklik olabileceğinin akla gelmelidir. Özellikle vitamin B12 eksikliği düşündürten yakınmaları olan ama B12 seviyeleri normal bulunan hastalarda serum MMA seviyelerinin tespitinin önemli olduğu ve MMA seviyelerinin yüksek saptanan hastalarda da vitamin D resplasmanının hastanın yakınmalarının azaltılmasına yardımcı olabileceği düşünüldü. D vitamini ile MMA ve vitamin B12 arasındaki ilişkiyi değerlendiren çok az çalışma olduğu için çalışmanın bu yönüyle literatüre katkı sağlayabileceği ve bu konuyu değerlendiren randomize kontrollü çalışmalara ihtiyaç olduğu düşünüldü.

Yazar Katkıları
Çalışma konsepti ve tasarımı: RA, MKK
Veri toplama: RA, MKK, MŞ
Veri Analizi: RA, MKK, MŞ
Makale yazımı: RA,MKK
Makalenin düzenleme: RA, MKK, MŞ

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**Özgün Çalışma / Original Article**

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# Larenks skuamöz hücreli karsinomunda tedavi öncesi trombosit/lenfosit oranı, ortalama trombosit hacmi ve trombosit dağılım genişliğinin prognostik değeri: 594 hastanın analizi

# Prognostic value of the pretreatment platelet-to-lymphocyte ratio, mean platelet volume and platelet distribution width in laryngeal squamous cell carcinoma: Analyses of 594 patients

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## ÖZET

**AMAÇ:** Larenks skuamöz hücreli kanserli (LSCC) hastalarda tedavi öncesi tespit edilen trombosit-lenfosit oranı (PLR), ortalama trombosit hacmi (MPV) ve trombosit dağılım genişliğinin (PDW) hastalığın prognozu üzerine etkisini değerlendirmek

**GEREÇ VE YÖNTEM:** Çalışma popülasyonu iki gruba ayrıldı: sağ kalanlar (Grup 1) ve sağ kalmayanlar (Grup 2). Daha sonra, iki grup arasında yaş, cinsiyet, sigara içme durumu, lezyon lokalizasyonu, ön komissür tutulumu, tümör T evresi, N evresi, M evresi, erken/ileri evre ve tümör patolojik derecesi dahil olmak üzere çok sayıda değişken açısından kapsamlı bir karşılaştırma yapıldı. Genel sağkalımı (OS) tahmin etmek için ROC eğrisi analizi gerçekleştirildi. Daha sonra, kesme değerlerine göre gruplar oluşturuldu ve bu gruplar 3 ve 5 yıllık genel sağkalım (OS) oranları açısından karşılaştırıldı.

**BULGULAR:** Çalışmaya dahil edilme kriterlerini karşılayan 594 hasta alındı. Sağ kalan grup yaş ortalaması 59.8±9.18 yıl olan 419 (%70.5) hastadan (Grup 1) ve sağ kalmayan grup yaş ortalaması 62.4±11.17 yıl olan 175 (%29.5) hastadan (Grup 2) oluşuyordu. PDW (kesme değeri 16,35 fL) %78,3 duyarlılık ve %52,2 özgüllük ile kanser prognozunu öngörme potansiyeline sahipti. Ayrıca, PLR (kesme değeri 123.64) kanser prognozunu %70.2 duyarlılık ve %51.1 özgüllük ile öngörebildi.

**SONUÇLAR:** Tanı anında PDW >16.35 fL ve PLR >%123.64 olan LSCC hastalarının tedavi seçimi ve takibinde dikkatli olunmalıdır.

**Anahtar Kelimeler:** Kan Trombositleri, Laringeal neoplazmlar, Ortalama trombosit hacmi, Trombosit dağılım genişliği, Sağkalım Analizi

## ABSTRACT

**AIM:** The objective of this study was to evaluate the effect of platelet-to-lymphocyte ratio (PLR), mean platelet volume (MPV) and platelet distribution width (PDW) determined before treatment on the prognosis of patients with laryngeal squamous cell carcinoma (LSCC).

**MATERIAL AND METHOD:** The study population was divided into two groups: survivors (Group 1) and non-survivors (Group 2). Subsequently, we conducted a comprehensive comparison between the two groups with respect to a multitude of variables, including age, gender, smoking status, lesion localization, anterior commissure involvement, tumor T stage, N stage, M stage, early/advanced stage, and tumor pathological grade. ROC curve analysis was performed to estimate overall survival (OS). Then, groups were formed according to cut-off values and these groups were compared in terms of 3- and 5-year overall survival (OS) rates.

**RESULTS**: The study included 594 patients who met the inclusion criteria. The survivor group consisted of 419 (70.5%) patients with a mean age of 59.8±9.18 years (Group 1) and the non-survivor group consisted of 175 (29.5%) patients with a mean age of 62.4±11.17 years (Group 2). PDW (cut-off value 16.35 fL) demonstrated the potential to predict cancer prognosis with a sensitivity of 78.3% and specificity of 52.2%. Furthermore, PLR (cut-off 123.64) was able to predict cancer prognosis with a sensitivity of 70.2% and specificity of 51.1%.

**CONCLUSION:** It was suggested that LSCC patients with PDW >16.35 fL and PLR >123.64% at the time of diagnosis should be careful in treatment selection and follow-up.

**Keywords:** Blood Platelets, Laryngeal neoplasms, Mean platelet volume, Platelet distribution width, Survival Analysis

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## INTRODUCTION

Laryngeal cancer is one of the most common head and neck cancers (HNC). According to the 2018 cancer statistics, the estimated number of new laryngeal cancer cases annually is 177,000, approximately half of which die due to the laryngeal cancer (1) Although diagnosis and treatment options for laryngeal cancer have been improved in recent years, the increase in the 5-year relative survival rate over the past thirty years from 59.6% to 66.8% is not at a sufficient level (2) The current TNM staging system has been reported to be insufficient as patients with laryngeal squamous cell cancer (LSCC) at high-risk recurrence and prognosis are described purely on the anatomic extent of LSCC (3) Although many prognostic factors have been identified to predict the prognosis in LSCC, such as tumor size, grade, lymph node metastasis, and immunohistochemical marker, these factors can only be evaluated after surgical treatment (4) Therefore, there is a need for a simple, rapid, reliable and low-cost pre-treatment prognostic marker for LSCC.

Carcinogenesis is a multifactorial process and inflammation is known to play a role in tumorigenesis and tumor progression (5,6) Peripheral inflammatory cells, such as neutrophils, platelets (PLT), lymphoctes and monocytes have been shown to have prognostic value for the inflammation-tumorigenesis relationship in head and neck squamous cell cancers (HNSCC). Platelets (PLT) can stimulate tumor growth by increasing angiogenesis, microvascular permeability, and the extravasation of cancer cells. Mean platelet volume (MPV), the most commonly used measure of platelet size, is a surrogate marker of platelet activation (7) Altered MPV levels have been reported in gastric cancer, ovarian cancer, lung cancer, and breast cancer (8-11) In a study of 96 oral cavity squamous cell carcinoma patients and 96 healthy individuals, Anand et al. found no significant difference in PLR, MPV and PDW between the groups (12) In a retrospective study of 87 medullary thyroid cancer patients, Li et al. found that both PLR, MPV and PDW were significant in terms of clinicopathological features and postoperative calcitonin elevation (13) Platelet distribution width (PDW), another platelet index, indicates variation in platelet size, with increased levels having been shown to be significantly associated with poorer overall survival (OS) in LSCC patients (14) Many recent studies have stated that the pre-treatment neutrophil-to lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are closely associated with prognosis in patients with LSCC (15) Therefore, the aim of this study was to evaluate the effects of pre-treatment PLR, MPV, and PDW on the prognosis of patients with LSCC.

## MATERIAL AND METHOD

Approval for the study was granted by the Local Ethics Committee (decision no: 70/09, dated: 26.08.2019). A retrospective analysis was made of the data of patients who were diagnosed with LSCC and treated in our clinic between 2010- 2020. Venous blood samples were collected from all patients after a 12-hour overnight fast within 3 days prior to the diagnostic suspension-laryngoscopy procedure. The blood samples were withdrawn into EDTA-containing tubes and then processed within 30 minutes. White blood cell (WBC), haemoglobin, and platelet indices were measured by an autoanalyzer (Sysmex XE-2100, Kobe, Japan).The study inclusion criteria were as follows: (1) primary LSCC confirmed by pathology and classified according to the TNM-UICC/AJCC stage classification- 8th edition; (2) patients with a diagnosis of LSCC of any stage with the data available of a hemogram taken prior to diagnostic suspension-laryngoscopy procedure; (3) pre-treatment hemogram parameters (PLT, MPV, PDW, and PLR, which may be easily calculated); (4) complete clinical, imaging, and follow-up data.

The exclusion criteria were as follows: (1) patients with any inflammatory, autoimmune, acute or chronic infectious disease, hematological disorder, history of corticosteroid therapy or chronic renal insufficiency, medical treatment with anticoagulants, statins, or acetylsalicylic acid; (2) cancer of uncertain origin or probable metastatic LSCC determined on CT or MRI scans; (3) patients with unavailable pre-treatment hemogram parameters.
The patients were separated into two groups as survivors (Group 1) and non-survivors (Group 2). These groups were compared in respect of age, gender, smoking status, lesion localization, anterior commissure involvement, tumor T stage, N stage, M stage, early/ advanced stage, and tumor pathological grade. Groups were then formed according to cut-off values and were compared in terms of 3 and 5-year overall survival (OS) rates.

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS for Windows version 22.0 software. Continuous variables were presented as mean ± standard deviation values and categorical variables as frequency and percentage. Conformity of the numerical variables to normal distribution was assessed with the Kolmogorov-Smirnov test. Differences in quantitative data between the groups were determined using the Student's t-test. The Pearson chi-square test was applied to determine the associations between categorical variables. Survival analyses were performed with Kaplan Meier product limit estimation, and the Log rank test was used to determine the differences between groups. Cut off value was determined by ROC analysis to evaluate the effect of PLR and PDW on overall survival. A value of p<0 (05) was considered statistically significant.

## RESULTS

From a retrospective scan of the data of 620 patients, diagnosed with LSCC and treated in our clinic between 2010- 2020, 594 patients who met the inclusion criteria were included in the study. The survivors group comprised 419 (70 (5)%) patients with a mean age of 59 (8)±9 (18) years (Group 1), and the non-survivors group comprised 175 (29 (5)%) patients with a mean age of 62 (4)±11 (17) years (Group 2). The patients in Group 2 were seen to be significantly older (p=0.011). The data of both groups related to gender, smoking status, tumor localization, anterior commissure involvement, tumor stage (T1-4), lymph node stage (N0-3), presence of metastasis (M0-1), clinical stage (early/advanced), histopathology, PLT, MPV, PDW, lymphocyte, and PLR values, primary treatment (surgery/ chemotherapy [CT] and/or radiotherapy [RT]), and the recurrence rates of the groups are presented in Table 1.

**Table 1: Demographic data of the patients**

| Parameters | Group 1 (n=419) | Group 2 (n=175) | p value |
|---|---|---|---|
| Age (years) | 59.8± 9.18 | 62.4± 11.17 | 0.011 |
| Gender (Male/Female) | 392(66%)/ 27(4.5%) | 161(27.1%)/ 14(2.4%) | 0.49 |
| Smoking status (smoker/non-smoker) | 409(68.9%)/ 10(1.7%) | 160(26.9%)/ 15(2.5%) | 0.001 |
| Tumor localization (supraglottic/glottic/transglottic/ hypopharynx) | 34(5.7%)/ 235(39.6%) /124(20.9%)/ 26(4.4%) | 13(2.2%)/ 46(7.7%) /83(14%)/ 33(5.6%) | 0.0001 |
| Anterior commissure involvement (absent/present) | 268(45.1%)/ 151(25.4%) | 87(14.6%)/ 88(14.8%) | 0.001 |
| Tumor stage (T1/T2/T3/T4a/T4b) | 190(32%)/ 79(13.3%) /108(18.2%)/ 39(6.6%)/ 3(0.5%) | 34(5.7%)/ 29(4.9%) / 84(14.1%)/ 24(4%)/ 4(0.7%) | 0.0001 |
| Lymph node stage (N0/N1/N2a/N2b/N2c/N3) | 353(59.4%)/ 23(3.9%)/ 6(1%)/ 14(2.4%)/ 19(3.2%)/ 4(0.7%) | 115(19.4%)/ 24(4%)/ 4(0.7%)/ 8(1.3%)/ 21(3.5%)/ 3(0.5%) | 0.0001 |
| Metastasis (M0/M1) | 414(69.7%)/ 5(0.8%) | 166(27.9%)/ 9(1.5%) | 0.002 |
| Clinical stage (Early/Advanced) | 255(42.9%)/ 164(27.6%) | 51(8.6%)/124(20.9%) | 0.0001 |
| Histopathology (CIS/ well differentiated SCC/ moderately diff SCC/ poorly diff SCC) | 58(9.8%)/ 123(20.7%) /150(25.3%)/ 88(14.8%) | 6(1%)/ 44(7.4%) /69(11.6%)/ 56(9.4%) | 0.0001 |
| Platelet (x$10^3$/µL) | 256.7± 63.7 | 275± 79.5 | 0.0001 |
| Mean Platelet Volume (MPV)(fL) | 8.7± 1.1 | 8.3± 1.01 | 0.29 |
| Platelet Distribution Width (PDW)(fL) | 16.1± 1.7 | 16.7± 0.75 | 0.0001 |
| Lymphocytes (x$10^3$/µL) | 2.08± 0.6 | 1.78± 0.7 | 0.056 |
| Platelet-to-Lymphocyte Ratio (PLR) (%) | 140.3± 76.1 | 195.8± 136.2 | 0.0001 |
| Primary treatment (surgery/ CT and/or RT) | 241(40.6%)/ 178(30%) | 56(9.4%)/ 119(20%) | 0.0001 |
| Recurrence (absent/present) | 350(58.9%)/ 69(11.6%) | 98(16.5%)/ 77(13%) | 0.0001 |

ROC curve analysis was applied to estimate overall survival (OS). Using the cut-off value of 16 (35) fL

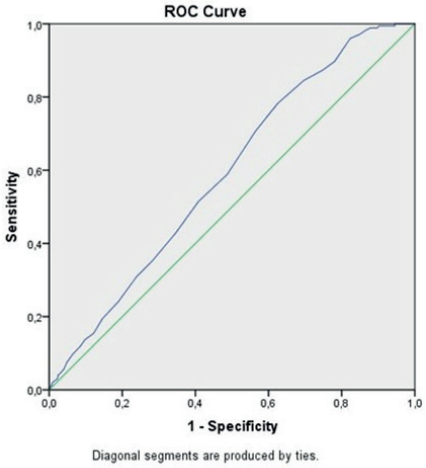


Figure 1: ROC curve for OS prediction, PDW (fL) (AUC=0.591, 95% CI: 0.543-0.638)

PDW was seen to be able to predict the cancer prognosis with 78 (3)% sensitivity and 52 (2)% specificity (AUC=0.591, 95% CI: 0.543-0.638, p<0.0001). The patients were separated into 2 groups of PDW≤16 (35) fL (n=195, 32 (8)%) and PDW>16 (35) fL (n=399, 67 (2)%). In the group with PDW≤16 (35) fL, 3-year OS was determined to be 84 (3)% and 5-year OS, 77 (2)%. In the patient group with PDW>16 (35) fL, these rates were determined to be 75 (1)% for 3-year OS and 63 (5)% for 5-year OS. The difference between these groups formed according to the cut-off value was determined to be statistically significant (p=0.006)

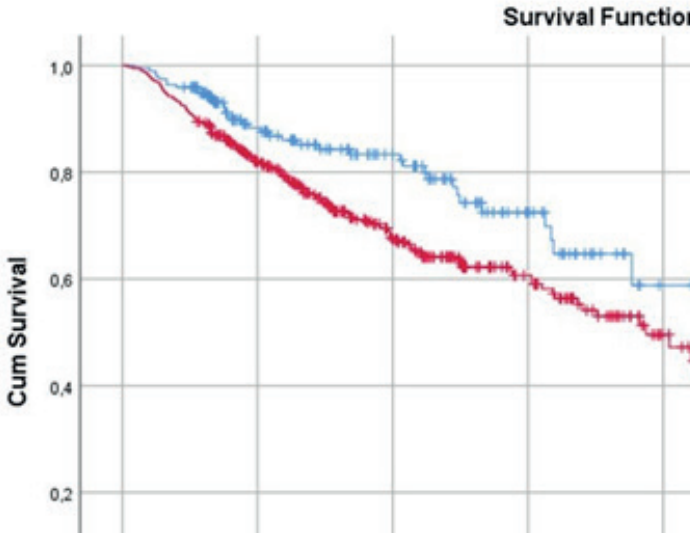


Figure 2: OS Kaplan-Meier curve according to the PDW cut-off value of 16.35 fL

In the ROC curve analysis for OS using the optimal cut-off value for PLR of 123 (64)%

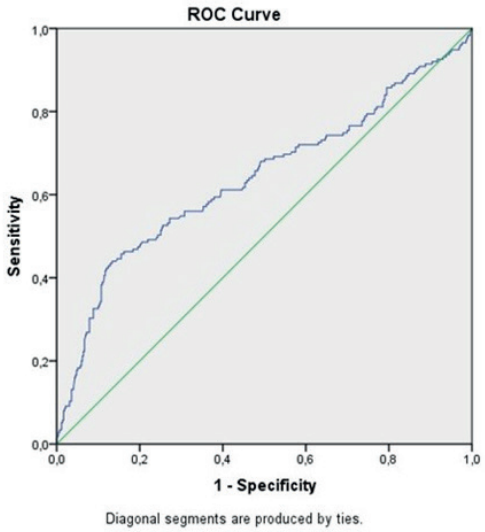


Figure 3: ROC curve for OS prediction, PLR (%) (AUC=0.639, 95 % CI: 0.586-0.692)

cancer prognosis was predicted with 70 (2)% sensitivity and 51 (1)% specificity (AUC=0.639, 95 % CI: 0.586-0.692, p<0.0001). The patients were divided into 2 groups of PLR≤123 (64)% (n=266, 44 (8)%) and PLR>123 (64)% (n=328, 55 (2)%). In the group with PLR≤123 (64)%, 3-year OS was 86 (1)%, and 5-year OS was 76 (3)%. In the group with PLR>123 (64) %, these rates were 71 (3)% for 3-year OS, and 60 (7)% for 5-year OS. The difference between these groups formed according to the PLR cut-off value was determined to be statistically significant (p=0.0001)

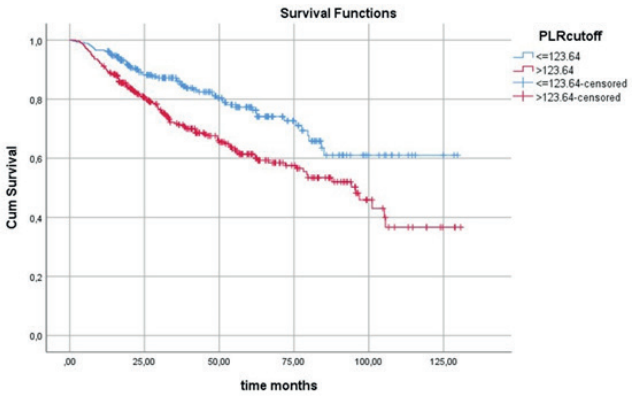


Figure 4: OS Kaplan-Meier curve according to the PLR cut-off value of 123.64%

## DISCUSSION

The results of this study demonstrated differences between the survivors and non-survivors groups in respect of the increase in platelet count, the increase in PDW showing platelet activation, and the increase in PLR increasing morbidity and mortality. This indicates that the disease course can be evaluated using hemogram examination, a low-cost, simple, and routinely used method in patients with laryngeal cancer. The aim of this study was to show that OS can be predicted at the time of first diagnosis of the disease, and that the treatment to be selected and follow-up can be provided with a preoperative hemogram test.

PLT plays a significant role in the emergence and development of malignant tumors (16) It has been stated that 30% to 60% of malignant tumors are associated with a rise in PLT, especially in the late stages of tumors, even when accompanied by thrombotic diseases (16,17) PLT can promote carcinogenesis through various means, such as providing mechanical protection to tumor cells during

transport in the circulation and promoting the transport and release of tumor molecules from their particles by enriching various biological activities in the tumor microenvironment (17)
Mean platelet volume (MPV), the most commonly used measurement of platelet size, is an important marker of platelet activation (18) MPV reflects platelet volume size, megakaryocyte proliferation, and platelet formation. Platelet distribution width (PDW), caused by fragmentation of megakaryocytes in varying sizes, is a measure of platelet heterogeneity and reflects the uniformity of platelet volume and the distribution of platelet volume in the blood (19,20)

Many studies have reported the role of platelet parameters in the progression and prognosis of LSCC. Ye et al (21) showed that pre-treatment PLT>248×109/L was a promising indicator of prognosis in patients with operable HNSCC. Pardo et al (22) reported that PLT was significantly associated with survival in univariate analysis, although prognostic capacity was lost in multivariate analysis, limiting its use as a prognostic marker in patients with HNSCC. Zhang et al (14) reported that PDW elevation may be a new prognostic marker in laryngeal cancer. Fu et al (23) stated that MPV decreased and PDW increased in patients with laryngeal cancer compared to patients without laryngeal cancer patients with laryngeal cancer. Additionally, MPV and PDW have been shown to play different roles in laryngeal cancer and benign laryngeal disease. Guo et al (24) reported that elevated PDW and decreased MPV may serve as independent biomarkers for worse survival in laryngeal cancer, while Sheng et al (25) came to the opposite conclusion that increased preoperative MPV was associated with decreased prognosis in patients with LSCC. Kara et al (26) concluded that caution should be exercised when using these new hematological parameters as they can be affected by many factors. In the current study, MPV was determined to be 8.7±1.1fL in the survivors group, and 8.3±1.01fL in the non-survivors group, and the difference between the groups was not found to be statistically significant (p=0.29). The PDW value was determined to be 16.1±1.7fL in the survivors group and this was seen to be statistically significantly increased to 16.7±0.75fL in the non-survivors group (p=0.0001). In the ROC curve analysis, the PDW cut-off value to be able to predict OS was found to be 16.35 fL, with 78.3% sensitivity and 52.2% specificity. Using this cut-off value, the 594 patients were grouped as 195(32.8%) with PDW≤16.35 fL, and 399(67.2%) with PDW>16.35 fL. A statistically significant difference was determined between these two groups in respect of the 3 and 5-year OS values (p=0.006). According to these results, it can be recommended that greater care should be taken in the treatment selection and follow-up of LSCC patients with PDW >16.35 fL at the time of diagnosis.

The increase of PLR value was first related to the increase of platelet ratio. A large body of evidence has shown that tumor cells can induce platelet activation, and thus, activated platelets can also promote the growth of tumor cells (27) The mechanisms of this are that platelets can induce tumor dissemination and invasion by increasing angiogenesis, microvascular permeability and promoting tumor cell extravasation,7,28 while the interaction between platelets and tumor cells can also promote the proliferation of tumor cells and protect tumor cells from apoptosis (29) From another perspective, high PLR levels in peripheral blood may also indicate a decrease in lymphocyte ratio. Lymphocytes and neutrophils constitute the majority of total leukocytes and play an important role in systemic inflammation. They can inhibit or promote the progression of malignant tumors by regulating immune interactions in the microenvironment. It is well known that lymphocytes play an important role in the immune surveillance of malignant tumors, and can inhibit the proliferation and metastasis of tumor cells. The relative decrease of lymphocytes will create an immunosuppressive state in the body, which inhibits the proliferation and metastatic activity of tumor cells, while the relative increase of neutrophils can provide the host with a microenvironment to promote tumor growth. Changes in either of these may indicate that the body has an inadequate immune response to the tumors. Several studies have reported the prognostic value of preoperative evaluation of the PLR, with a high PLR level has been shown to be associated with poor CSS and DFS (15,30) The cut off value for PLR varies from 106 to 193.55 Kara et al (31) reported that pretreatment high PLR is a predictive factor of survival rates in patients with LSCC, and a high PLR increases mortality in these patients. Wang et al (32) stated that PLR was a reliable prognostic factor in patients with LSCC, and Zhong et al (33) reported that change in the PLR may be a useful prognostic marker for patients with T3-T4 LSCC. In the current study, the PLR was determined to be 140.3±76.1% in the survivors group and 195.8±136.2% in the non-survivors group (p=0.0001). In the ROC analysis the cut-off value for PLR to be able to determine OS was found to be 123.64% with 70.2% sensitivity and 51.1% specificity. According to this cut-off value the 594 patients were grouped as 266 (44.8%) with PLR≤123.64% and 328 (55.2%) with PLR>123.64%. The difference in the 3 and 5-year OS values of these two groups separated according to the cut-off value was determined to be statistically significant (p=0.0001). Similarly, greater attention should be paid to the treatment and follow-up of LSCC patients with a PLR value >123.64% at the time of diagnosis.

There are still limitations to research on this subject, primarily the fact that the majority of studies in the literature are retrospective, single-center and small-sample studies may lead to bias in retrospective studies. Although detailed data and follow-up results have been recorded in many studies, prospective studies will help to better evaluate the prognostic factors of patients with laryngeal cancer. Therefore, the current study results still need to be confirmed by prospective studies with larger sample sizes. A second limitation of this study could be said to be that since many other factors, such as acute undetected infections and hematological diseases, affect hematological markers, this may affect the accuracy of prognosis prediction based on hematological markers. In addition, there is a lack of a clear method to obtain the best cut-off value of hematological markers, and the current recommended critical values are empirical and determined by the simplicity of the calculation and the relatively good balance between the number of patients in the upper and lower groups. Therefore, there is a need to develop uniform classification criteria with consensus for the use of these hematological markers in clinical settings. Based on the observations of this retrospective study, there can be seen to be a need for further large prospective studies on this topic to be able to further investigate the relationship between hematological markers and laryngeal squamous cell carcinoma.

## CONCLUSION

It can be recommended that greater care should be taken in the treatment selection and follow-up of LSCC patients with PDW >16.35 fL at the time of diagnosis. In the same way as for PDW, greater attention should be paid to treatment and follow-up for LSCC patients with a PLR value >123.64% at the time of diagnosis. For these patients, closer follow-up and more aggressive treatment should be chosen.

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# Laparoscopic colorectal surgery for cancer in a regional service hospital: single surgeon experience

# Bölgesel bir hizmet hastanesinde kansere yönelik laparoskopik kolorektal cerrahi: tek cerrah deneyimi

Serdar ŞENOL(1), Mustafa KUŞAK(2)

## ÖZET

**AMAÇ**:Kanıtlanmış avantajlarına rağmen bölge hizmet hastanelerinde laparoskopik kolorektal cerrahi yeterince kullanılmamaktadır. Türkiye'nin Orta Karadeniz Bölgesi'ndeki bir hizmet hastanesinde bir gastroenteroloji cerrahı tarafından laparoskopik cerrahi ile tedavi edilen kolorektal kanserli hastaların sonuçlarının değerlendirilmesi amaçlanmıştır.

**GEREÇ ve YÖNTEM:** Laparoskopik kolorektal cerrahi uygulanan ardışık her hastanın verileri prospektif olarak kaydedildi ve retrospektif olarak analiz edildi. Kaydedilen parametreler demografik özellikler, teşhis çalışmaları, cerrahi olaylar, ameliyat sonrası morbidite, mortalite ve sonuçları içeriyordu.

**BULGULAR:** Kırk aylık bir süre içinde 75 hastaya kolorektal kanser nedeniyle laparoskopik cerrahi uygulandı. Ortalama yaş 66,4 olup erkeklerin kadınlara oranı 11:4'tür. Rektum kanseri oranı %65,3, kolon kanseri oranı yüzde 34,6 idi. Bir hastada senkron kolorektal kanser tespit edildi. Ortalama ameliyat süresi 276 dakika ve ortalama kanama hacmi 75 ml idi. Açık rezeksiyona geçiş oranı %6,6 idi. Ortalama hastanede kalış günü altı gündü. Ameliyat sonrası komplikasyon oranı (Clavien-Dindo derecesi ≥ III) %8,5 idi. Takip sırasında iki sistemik nüks gözlendi.

**SONUÇ:** Sonuçlarımız ve araştırmada sunulan diğer çalışmalar doğrultusunda, yüksek vaka sayısına sahip eğitimli bir cerrah, gelişmekte olan bir ülkenin bölge hizmet hastanesinde güvenli ve yeterli onkolojik laparoskopik kolorektal prosedürü gerçekleştirebilir. Sağlık politikalarının ve bölgesel koşulların ilimizdeki ve ülkemizdeki cerrahi uygulamalar üzerine olan etkisini göstermesi açısından da sonuçlarımız değerlidir. Özellikle kalabalık hizmet hastanelerinde uzun amaliyat süresi uygulamanın dezavantajıdır. Mevcut şartlarda cerrahların özverisi ve ilgili her türlü destek gereklidir.

**Anhtar Kelimeler:** Cerrah, Hastane, Kapasite, Kolorektal kanser, Minimal invazif cerrahi

## ABSTRACT

AIM: In spite of the demonstrated advantages, laparoscopic colorectal surgery is not adequately utilised in regional service hospitals. Purpose of the research was to document the findings of patients managed by a gastroenterological surgeon for colorectal neoplasms using laparoscopic surgery at a service hospital of the Central Black Sea Region, Turkey.

**MATERIAL AND METHOD**: Every sequential patient having laparoscopic colorectal surgery was registered prospectively and analysed retrospectively. Recorded parameters consisted of demographic characteristics, diagnostic work-up, surgical events, post-surgical morbidity, mortality and outcomes.

**RESULTS:** Seventy-five patients each underwent laparoscopic colorectal surgery for colorectal neoplasm within a period of forty months. Average age was 66.4 years and ratio of males to females was 11:4. Rectal cancer rate was 65.3%. Colon cancer rate was 34.6%. One patient had synchronous colorectal cancer. Mean time of surgery was 276 min and mean volume of haemorrhage was 75 ml. Conversion to open resection rate was 6.6%. Median day of hospitalization was six days. Postoperative complication rate (Clavien–Dindo grade ≥ III) was 8.5%. Two systemic recurrences were observed during the surveillance.

**CONCLUSION:** Based on our results and those of other studies presented here, a trained surgeon with a high caseload can perform safe and adequate oncological laparoscopic colorectal resections in a regional service hospital of a developing country. The longer operative time is the drawback of the procedure, especially in crowded service hospitals. The results are also valuable in terms of showing the effect of health policies and regional conditions on surgical practices in our city and country. Under the current conditions, surgeons' dedication and all relevant supports are required.

**Keywords:** Colorectal cancer, Hospital, Minimally invasive surgery, Surgeon, Volume

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## INTRODUCTION

The minimally invasive approach for colorectal diseases has been used since 1991. After initial concerns, which were overcame by the results of several trials, the laparoscopic approach has progressively gained popularity.1-4 Especially, high-volume and/or academic centers currently prefer this approach. The majority of the supporting informations were acquired from these centers.5-8 Although researches favour the surgical method, it can not be applied easily due to factors predicting the outcomes with surgery, such as the surgeon,9-12 case volume of a hospital,6 the development level of a country.13,14 Therefore, success of the researches may not be possible in all hospitals. We hypothesized that a standard surgical procedure, which has started with surgical gastroenterology training in high-volume central hospitals and continuated in low-medium volume regional hospitals can balance the predictive factors that are stated to be effective on surgical results. So, results of our study were compared with outcomes of high volume tertiary centres and/or multi-centres.

## MATERIAL and METHOD

This research was approved by the ethics committee (Decision number: 2023/9/4). The hospital is a 600-bed, tertiary hospital, in The Middle Black Sea Region. The General Surgery Clinic consists of nineteen experts, 7 of them are in the training staff. Also clinic consists of two inpatient services with twenty-six patient capacity. Based on a recent study,6 the hospital was classified as an intermediate-volume hospital for colorectal cancer because there were fewer than 135 annual non-urgent minimally invasive surgery. The study involved sequential patients who had laparoscopic surgery for colorectal malignancies performed by a single gastroenterological surgeon over a forty-month period from May 2019 to October 2022. Data were collected prospectively over this period and analyzed retrospectively. Emergency surgeries, open surgeries and laparoscopic surgeries performed by other specialists were excluded from the study.

Preoperative colonoscopy was performed in all patients and the diagnosis of carcinoma was confirmed by biopsy. Perioperative evaluation consisted of physical examination and standard laboratory test. Colonoscopy was done to investigate the characteristics of the tumour. All patients had abdominal and chest computed tomography scans to exclude metastatic disease. Pelvic MRI was utilised in rectal cancer patients to obtain further information on tumour depth and lymph node status.

All patients had preoperative mechanical bowel cleansing on the day before surgery. Intravenous broad-spectrum antibiotics were administered at induction of anaesthesia. Low molecular weight heparin and antithrombotic stockings were used in all patients in the perioperative period and continued for 10 days after the patient was discharged. Any patient suffering from colorectal cancer was assumed to be appropriate for laparoscopic surgery if there were no specific contraindications.

Surgical Technique:
We maintained pneumoperitoneum with 12-14 mmHg carbon dioxide. The basic rules of medial to lateral dissection and proximal ligation of the lympho-vascular pedicle were exactly obeyed for all patients.

Surgery for the left colon and rectum: Inferior mesenteric vein (IMV) is identified at the lower border of pancreas and dissected from surrounding structures. IMV is then held up and the peritoneum incised. The Toldt fascia is dissected free from the prerenal fascia. The IMV is clipped and divided . The transverse mesocolon is held up and the mesocolon is lifted off the anterior surface of the pancreas. After the enterance to the lesser sac dissection proceeds along the upper border of the pancreas. The greater omentum is then divided above the transverse colon and the splenic flexure is taken down. The rectosigmoid is held up and the peritoneum on the right leaf of the rectal mesentery is incised just posterior to the inferior mesenteric artery (IMA) at the level of the sacral promontory. A larger plane is established and left ureter and gonadal vessels are visualised as well as retroperitoneal structures. Nodal dissection is then completed at the root of the IMA and IMA is clipped and divided. Holding up the IMA, and IMV, separation of the Toldt from the fascia of Gerota is completed. The posterior mesorectal plane is determined at the level of the promontorium and dissected. The total mesorectal excision (TME) is performed. Rectal wall is dissected circumferentially and the dividing of the distal border is carried out with linear staplers. Pfannenstiel incision is made and the distal end is pulled out after placement of a wound protector. An intracorporeal side-to-end anastomosis is fashioned using a circular stapler (usually 31 mm). In case of a Miles procedure is performed, the splenic flexure is not fully mobilized and the specimen is extracted through the perineum. A protective ileostomy is created in patients with previous chemo-radiotherapy or TME and low colorectal-coloanal anastomosis.

Surgery fort he right colon: The root of the right colon mesentery is held up to identify the ileocolic vessels. Following the vascular division, the mesocolon is dissected from the retroperitoneum. Dissection plane is keeped away from the head of pancreas, left ureter and gonadal vessels. The right branches of the middle colic vein are ligated and the hepatic flexure is freed from the lateral peritoneal attachments. The proximal bowel margin is labelled in the distal ileum and then the distal bowel margin is determined in the transverse colon. A midline incision is made to exteriorise the colon. The mesentery is divided. Distal and proximal bowel margins is transected with endoscopic lineer stapler. A side to side ileocolic anastomosis is made by using a circular stapler (usually 28 mm).
Surgery for isolated transverse colon: IMV is identified at the lower border of pancreas and dissected from peritoneal attachments. IMV is then held up and the peritoneum incised. The Toldt fascia is dissected free from the prerenal fascia. The IMV is clipped and divided . The transverse mesocolon is held up and the mesocolon is lifted off the anterior surface of the pancreas. After the enterance to the lesser sac dissection proceeds along the lower border of the pancreas. The middle colic trunk is identified and the vascular pedicle divided just distal to the inferior aspect of the pancreas. The greater omentum is then divided above the transverse colon. Hepatic flexure is freed from the lateral peritoneal attachments. A midline incision is made to exteriorise the colon. The mesentery is divided. Distal and proximal bowel margins is transected with endoscopic lineer stapler. A side to side colo-colic anastomosis is made by using a circular stapler (usually 28 mm).
Postoperative care: On the third postoperative day, oral fluids were allowed and started on a diet after the patients had flatulence or bowel movements. On the fourth postoperative day, parenteral analgesics were discontinued and urinary catheters were withdrawn. Patients who tolerated the diet were frequently discharged on the fifth or sixth postoperative day.
Postoperative complications: Morbidity and mortality occurring during hospitalization or within 90 days after surgery were defined as postoperative complications. They were classified using the Clavien-Dindo (CD) system.15
Subsequent to pathological examination, patients were staged according to the 8th edition of the American Joint Committee on Cancer staging system.16
Recorded parameters consisted of demographic characteristics, diagnostic work-up, surgical events, post-surgical morbidity, mortality and outcomes. The data were entered into a Microsoft Excel worksheet and analyzed retrospectively.

## RESULTS

Over the study period, there were sixty eight emergency surgery, one hundered ninety six elective open surgery and, twelve laparoscopic elective surgery performed by other specialists and these were excluded. The study included seventy-five sequential patients who had laparoscopic surgery by a gastroenterological surgeon for colorectal malignancy. Case-load for laparoscopic colorectal surgery was 23 operations per year. The median age of the patients was 65 years (range 31-91 years) with a male:female ratio of 11:4. In the preoperative work-up, 46 (61,3%) patients were ASA grade 3, 27 (36%) were ASA grade 2, and 2 (2,7%) were ASA grade 4. Thirty seven patients had low anterior resection, fourteen had right hemicolectomy, eleven had anterior resection and ten had left hemicolectomy, two had isolated transverse colon resection, one had abdominoperineal resection. One patient had minimally invasive laparoscopic total abdominal colectomy for synchronous colorectal cancer. Conversion to open surgery was required in five patients (6.6%). Difficulty in identifying the lesion due to extensive adhesions after hysterectomy, appendectomy and subtotal gastrectomy was the reason in three of them. Others were bleeding and locally advanced disease.
Mean time of surgery and mean operative blood loss were 275±51 min and, 75.6±44.6 ml, respectively. Median day of hospitalization was six (range 4-21 days). Six patients underwent simultaneous laparoscopic procedures; three cholecystectomies, one gastric wedge

resection, one unilateral salpingoophorectomy and one liver metastasectomy. Clavien-Dindo complications ≥Grade III complications were observed in 6 (8.5%) patients; Grade III in 4 (5.7%) patients, Grade V in 2 (2.8%). Preperitoneal hematoma at the pfannenstiel incision occurred in two (2.8%) patients who used anticoagulants for coronary artery disease, ileus in one (1.4%), anastomotic leak in one (1.4%), anastomotic stenosis in one (1.4%). There were one Hartmann's procedure for anastomotic leak, one balloon dilatation for anastomotic stenosis, and one percutaneous drainage and antibiotic treatments for preperitoneal hematoma at the pfannenstiel incision site. The ninety-day postoperative mortality rate was %2.8. One patient died after a suicide attempt in the 2nd month, while another one died in the intensive care unit due to multiple organ failure within 24 hours after the emergency surgery for brid ileus in the 1st month. The final histologic diagnosis of the resected specimens revealed: The mean number of harvested lymph nodes was 17.3±10 and there was only one positive circumferential resection margin. Fourty-six of cases were categorized as stage 0, I or II colorectal cancers on final histopathological review as per TNM classification, 28 were stage III, and the remaining 1 patient had a single incidental liver metastasis at the time of surgery (stage IV). She refused adjuvant chemotherapy. According to a mean follow-up of 18.6±10.8 months, she was diagnosed with multi-metastatic liver cancer 5 months after the surgery, but still alive for 24 months, and one patient who was underwent low anterior resection developed metachronous cecum tumor and peritoneal carcinomatosis. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy were applied. Also, there were any local recurrences for the follow up period.

## DISCUSSION

A number of important conclusions emerge from this study. These should be interpreted in the context of a study of 75 sequential unselected patients with colorectal cancer operated on by a single gastroenterological surgeon in a regional service hospital. In order to qualify as a high-volume surgeon, a precise minumum number of cases per year per surgeon is not defined.17-19 However, according to a recent study,20 assessing the value of the surgeon's caseload in predicting result after elective minimally invasive colorectal surgery, high-caseload is defined as surgeon who perform >20 procedures per year. Our surgery clinic is classified as a mid-volume, with 85 elective colorectal cancer surgeries annually.6 The operating surgeon's case-load for laparoscopic colorectal surgery as a member of this clinc was 22 elective operations annually. However, it is not sufficiently utilised among other members of surgical clinic. The longer operative time is the drawback of the procedure, especially in a regional service hospital of developing country due to case burden is a current problem.21 If the learning curve is optimised, operative time can be decreased. Unfortunately overcoming this curve is not so easy in a crowded service hospital.22 Because, as a consequence of high patient-load, broad spectrum of surgical procedures may prevent adequate specialization. A training which has started with surgical gastroeneterology fellowship in a high-volume central hospital can balance the time required for achieving learning curve and allow focus on specific interests, like minimally invasive colorectal surgery. Other possible reasons that make laparoscopic procedures less attractive: As a consequence of working in a large surgical team, number of monthly elective surgical days per surgeon is limited; in a developing country, health policies make remuneration based on performance; older surgeons are reluctant to learn new techniques. In our opinion, surgeons' sacrifice, health policies' and hospital managers' support are required to overcome these reasons.
As compared the other sudies

| Outcomes | Şenol et al. n=75 | Huscher et al.[30] n= 1832 | Veldkamp et al.[23,29] n=627/534[a] | Nelson et al.[25] n=435 | D'Annibale et al.[26] n=302 | Hewett et al.[27] n=294 | Yamamoto et al.[29] n=529 | Biondi et al.[28] n=207 |
|---|---|---|---|---|---|---|---|---|
| Age (year) Mean ± SD /Median (range) | 65 (31-91) | 67.5±10.9 | 71 (27–92) | 70 (28–96) | 66.1±11.3 | 71.1± 10.4 | 64 (28-75) | 65.7±12.89 |
| BMI (kg/m$^2$) Mean ± SD /Median (range) | 26 (16-40) | 25.4±3.1 | 24.5 (12.1-37.1) | ND | ND | 25.8± 4.5 | 22.9 (14.8-36.1) | 24.16±3.06 |
| ASA score 1-2 | 36% | 69% | 82% | 86% | ND | 71.8% | ND | 65.2% |
| 3-4 | 64% | 31% | 16% | 14% | | 28.2% | ND | 34.8% |
| Tumor stage 0-1-2 | 61.3% | 57% | 65% | 71% | 63% | 70.9% | 53.1% | 48.4% |
| 3-4 | 38.7% | 43% | 34% | 28% | 37% | 28.6% | 46.9% | 51.6% |
| Operative time (minute) Mean ± SD /Median (range) | 275±59 | 211.4 ± 83 | 202 (50–540) | 150 (35-450) | 226±71 | 158(49-365) | 211 (80-616) | 165.3±37 |
| Blood loss (ml) Mean ± SD /Median (range) | 75.6±44.6 | ND | 100 (0–2700) | ND | 59±100 | 100 (0-1400) | 30 (0-4080) | 108.71±93.91 |
| Postoperative length of stay (day) Mean ± SD /Median (range) | 6 (4-21) | 10±7.1 | 8.2 ±6.6 | 5 (4-6) | 11±5 | 9.5 ±7.4 | 10 (8-13) | 8.72±3.2 |
| Anastomotic leak | 1.4% | 8.3% | 3% | ND | 5% | 1.4% | 3.6% | 0 |
| Conversion to open | 6.6% | 10.5% | 17% | 21% | 10% | 14.6% | 5.4% | 15.9% |
| 30-day mortality | 1.4% | 1.2% | 1% | <1% | ND | 1.4% | 0 | 0 |
| 90-day mortality | 2.8% | ND | ND | 14% | 1.3% | ND | ND | 0 |
| Amount of lymph nodes resected | 17.3±10 | 15.4±9.2 | 10 (3–20) | 12 (ND) | 14±8 | 13 (1-74) | 21 (2-85) | 12.36±4.36 |
| Follow-up (month) Mean ± SD /Median (range) | 18.6±10.8 | 54.2±14.7 | 52±17 | 52.8 (ND) | 21(0-75) | 60[a] | 60[a] | 53[a] |
| Cancer Recurrence | 2.6% | 13.3% | 19.6% | 17.4% | ND | 13.7% | ND | 29% |
| Definitive stoma | 0 | 2.8% | ND | ND | ND | ND | ND | ND |

ND:not defined; *: standart deviation or range is not defined

23-30 we determined a slightly longer operating time. It was thought that approximately 80% of the patients in our study consisted of left colon and rectal cancer, also approximately 70% of the rectal cancers located in the middle and lower rectum. So that mobilisation of the splenic flexure, which is a more technically demanding procedure, might have caused this difference.
In this study, the rate of conversion to open surgery was 6.6%, which was comparable to reported in other studies,23-30 included accredited surgeons, which ranged between 5.4% to 21%. Six patients (8.5%) had Clavien-Dindo complications ≥Grade III complications. The 30-day mortality rate and anastomotic leak rate (one case of anterior resection) were 1,4%. This rate was comparable with the studies.23-30 and ranged between 0% to 1.4% for the 30-day mortality and 0% to 8.3% for the anastomotic leak. In our study the mean blood loss and the median postoperative hospital stay were 75.6±44.6 ml and 6 (4-21) days, respectively. Although some studies reported23, 24, 27, 28 more blood loss, the others26,29 were better (Table 1). The postoperative hospital stay was comparable with the studies23-30 (Table 1).
The oncological results of laparoscopic colorectal surgery is very significant. It's represented by negative surgical margins and sufficient number of retrieved lymph nodes. The mean value of harvested lymph nodes for the study group was comparable to others26,28,30 ( 17.3±10 vs. 15.4±9.2, 14±8 and, 12.3±4.3). Also, reported median values ranged between ten to twenty one.23-25,27,29 Only one patient who underwent laparoscopic total abdominal colectomy for synchronous colorectal cancer had positive circumferential surgical margins. No local recurrence was observed in a mean follow-up of 18.6±10.8 months, however two systemic systemic recurrences were detected: one multi-metastatic liver cancer; one metachronous cecum tumor and peritoneal carcinomatosis. Table 1 summarises that the results produced at high volume centres and/or multi-centres might be repeated in a regional service hospital by a single surgeon with a sufficient surgical volume.23-30 As the limitations of the study, we are aware that these results should be cautiously analysed because of the limited participants and follow-up period.

## CONCLUSION

Based on our results and those of other studies presented here, a trained surgeon with a high caseload can perform safe and adequate oncological laparoscopic colorectal resections in a regional service hospital of a developing country. The longer operative time is the drawback of the procedure, especially in crowded service hospitals. The results are also valuable in terms of showing the effect of health policies and regional conditions on surgical practices in our city and country. Under the current conditions, surgeons' dedication and all relevant supports are required.

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# Hidradenitis Süpürativalı Hastaların Klinik Özellikleri ve Laboratuvar Bulgularının Değerlendirilmesi

# Evaluation of Clinical Features and Laboratory Findings of Patients with Hidradenitis Suppurativa

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## ÖZET

**AMAÇ:** Hidradenitis suppurativa (HS), intertriginöz bölgelerde tekrarlayan inflame foliküler lezyonlar, nodüller, apseler ve daha sonraki evrelerde drene olan sinüs yolları ve skarlarla prezente olan kronik inflamatuar bir deri hastalığıdır. Hastalığın kronik, tekrarlayan seyri, ağrılı, kötü kokulu lezyonlar, fistül/skar oluşumu ve eşlik eden komorbiditeler nedeniyle HS, yaşam kalitesini önemli ölçüde azaltır ve psikolojik bozukluklar ile ilişkilidir. Bu çalışmada, HS'li hastaların genel özelliklerini ve hastalık şiddetini ve hastaların psikososyal durumlarını etkileyen faktörleri değerlendirmeyi amaçladık.

**GEREÇ VE YÖNTEM:** Bu retrospektif tanımlayıcı çalışmada HS'li 30 hastanın tıbbi kayıtları analiz edildi. Sosyodemografik veriler, hastaların genel özellikleri, HS'nin klinik özellikleri ve laboratuvar bulguları kaydedildi. Hastalardan Hastane Anksiyete ve Depresyon Ölçeği (HADÖ) ve Dermatoloji Yaşam Kalitesi İndeksini doldurmaları istendi.

**BULGULAR:** Hidradenitis süpürativali 30 hastanın 16'sı (%53,3) kadın, 14'ü (%46,7) erkek olup yaş ortalaması 36,86 ± 12,62 yıl idi. Hurley evreleme sistemine göre hastaların %26,7'si evre I, %60'ı evre II ve %13,3'ü evre III hastalığa sahipti. Perineal/skrotal ve perianal tutulumu olan hastalarda Hurley evreleme sistemine göre hastalık şiddeti istatistiksel olarak anlamlı şekilde artmıştı. Hurley evreleme sistemine göre hastalık şiddeti ile medyan CRP düzeyleri arasında istatistiksel olarak anlamlı ilişki bulundu. Hurley evre III hastalığı olan hastalarda CRP düzeyleri Hurley evre I hastalığı olanlara göre anlamlı şekilde yüksekti. İnguinal tutulumu olan hastalarda ortalama HADS-A ve HADS-D skorları inguinal tutulumu olmayanlara göre anlamlı şekilde yüksekti. Ayrıca perianal tutulumu olan hastaların ortalama HADS-D skorları perianal tutulumu olmayanlara göre anlamlı şekilde yüksekti.

**SONUÇ:** Bu çalışma, perineal/skrotal ve perianal tutulumu olan hastaların, hastalık şiddetinin anlamlı şekilde arttığını göstermektedir. Üstelik, inguinal ve perianal tutulumu olan hastaların anksiyete ve depresyon skorları anlamlı şekilde daha yüksekti. Klinisyenler HS'li hastalarda depresyon ve anksiyete riskinin farkında olmalıdır.

**Anahtar kelimeler:** anksiyete, depresyon, HADS, hidradenitis süpürativa, laboratuvar bulguları

## ABSTRACT

**AIM:** Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that clinically presents with recurrent inflamed follicular lesions, nodules, abscesses, and, in later stages, draining sinus tracts and scars in intertriginous areas. Due to the chronic, recurrent course of the disease, painful, malodorous lesions, fistula/ scar formation, and accompanying comorbidities, HS significantly reduces the quality of life and is associated with psychological impairment. In this study, we aimed to evaluate the general characteristics of patients with HS and the factors influencing their disease severity and psychosocial status.

**MATERIAL AND METHOD:** This retrospective descriptive study analyzed the medical records of 30 patients with HS. Sociodemographic data, general characteristics of the patients, clinical features of HS, and laboratory findings were noted. The patients were asked to fill out Hospital Anxiety and Depression Scales (HADS) and Dermatology Life Quality Index.

**RESULTS:** Of 30 patients with HS, 16 (53.3%) were females, and 14 (46.7%) were males, with a mean age of 36.86 ± 12.62 years. According to the Hurley staging system, 26.7% of the patients had stage I, 60% had stage II, and 13.3% had stage III disease. The patients with perineal/scrotal and perianal involvement had a statistically significantly increased disease severity according to the Hurley staging system. A statistically significant relationship was found between the disease severity according to the Hurley staging system and the median CRP levels. CRP levels in the patients with Hurley stage III disease were significantly higher than those with Hurley stage I disease. The mean HADS-A and HADS-D scores in the patients with inguinal involvement were significantly higher than those without inguinal involvement. Also, the mean HADS-D scores of the patients with perianal involvement were significantly higher than those without perianal involvement.

**CONCLUSION:** This study shows that the patients with perineal/scrotal and perianal involvement had significantly increased disease severity. Moreover, the patients with inguinal and perianal involvement had significantly higher anxiety and depression scores. Clinicians should be aware of the risk of depression and anxiety in patients with HS.

**Keywords:** anxiety, depression, HADS, hidradenitis suppurativa, laboratory findings

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## INTRODUCTION

Hidradenitis suppurativa (HS) is a chronic inflammatory skin disease that clinically presents with recurrent inflamed follicular lesions, nodules, abscesses, and, in later stages, draining sinus tracts and scars in intertriginous areas.1 The most commonly involved sites are axillary, inguinal, anogenital, perineal, and inframammary regions.2 The age of onset is usually between 30 and 40 years of life.3,4 HS is also reported to be associated with several comorbidities, such as metabolic syndrome, inflammatory bowel disease, cardiovascular diseases, and axial spondyloarthritis.5-7

HS is diagnosed clinically. Skin biopsy is not routinely taken, and no confirmatory laboratory tests are needed. The Hurley staging system is still the most commonly used system to determine the severity of the disease, as it is easy to apply in outpatient settings. The disease is divided into three stages in the Hurley staging system: mild, moderate, and severe.8 Studies in the literature reported that male gender, smoking, and obesity were associated with severe disease.9, 10 Although there is no confirmatory laboratory test for diagnosing hidradenitis suppurativa, complete blood count, ESR, CRP, complete urine test, serum iron level, and serum electrophoresis are recommended to manage patients.11, 12

Due to the chronic, recurrent course of the disease, painful, malodorous lesions, fistula/ scar formation, and accompanying comorbidities, HS significantly reduces the quality of life (QoL) and is associated with psychological impairment.1 Moreover, involvement of the anogenital region was reported to cause an additional emotional and physical burden.13

In the present study, we aimed to evaluate the general characteristics of patients with HS and the factors influencing their disease severity and psychosocial status.

## MATERIAL AND METHOD

This retrospective descriptive study was carried out over one year in the medical archives of the Department of Dermatology in a tertiary care hospital. The Institutional Ethics Committee gave approval for the study (25/03/2015, No:0588). The study was performed in accordance with the latest version of the 'Helsinki Declaration' and 'Guidelines for Good Clinical Practice'.

The medical records of consecutive patients admitted to a dermatology outpatient clinic and/or received inpatient treatment with the diagnosis of HS were compiled and analyzed. The data of 30 patients were examined for the study. Sociodemographic data and general characteristics of the patients, such as age, sex, body mass index (BMI), and smoking habit, were recorded. Patients' medical history, the age of disease onset, the duration of the disease, and accompanying other diseases were noted. The involvement sites were determined using dermatological examination findings, and the disease severity was assessed using the Hurley stage. Hurley staging is a well-known, easy-to-apply, and most commonly used staging system in clinical practice. It divides the disease into 3 stages: mild to severe. Self-limiting inflammatory lesions resolving without scarring are seen in stage I disease. Stage II disease presents with single or multiple lesions with normal-appearing skin between them and discrete lesions of recurrent abscesses with tunnels and scars. Lastly, tunnels, scars, and inflammatory abscesses coalesce to form characteristic chronic inflammatory lesions seen in stage III disease.8

The patients were evaluated for axial and peripheral arthropathy by a specialist from the Physical Medicine and Rehabilitation Department. Characteristic symptoms and signs such as pain, swelling, tenderness, increased temperature, and joint redness were questioned to assess the joint involvement. On physical examination, joint range of motion was checked for peripheral arthropathy. For axial arthropathy, spinous and paraspinous sensitivity, spinal mobility were evaluated, and sacroiliac compression and distraction tests, as well as the Mennel and the Gaenslen tests, were performed. In the radiological examination, hand, foot, and knee radiographs, cervical-thoracic-lumbar two-way vertebra radiographs, and standard anteroposterior pelvis radiographs were evaluated.

The patients were asked to fill out Hospital Anxiety and Depression Scales (HADS) and Dermatology Life Quality Index (DLQI) to evaluate their psychological status and quality of life. The validated Turkish version of the HADS was used to question symptoms of anxiety and depression [14]. HADS is a self-administered questionnaire consisting of 14 items scored with a 4-point Likert scale (0-3 points), and it has 2 subscales as HADS-Anxiety (HADS-A) and HADS-Depression (HADS-D) evaluated separately with 7 questions for each.15 The cut-off scores for depression and anxiety were determined to be 7 and 10, respectively.14 The validated Turkish version of the DLQI, which is a 10-item self-rating questionnaire with a 4-point Likert scale (0-3 points), was used to assess the QoL of the patients.16, 17 DLQI score ranges from 0-30. As the score increases, quality of life worsens, and scores >10 indicate that quality of life is moderate-to-severely affected.

### Statistical Analysis

The statistical analyses were conducted using the IBM SPSS Statistics for Windows, Version 20.00 (Armonk, New York, USA: IBM Corp.), and $p<0.05$ was statistically significant. The distribution of the variables was determined by the Shapiro-Wilk tests. The chi-square test was employed to compare categorical independent data, while the Fischer's exact test was utilised when one or multiple cells had an expected count of less than 5. The Student's T and ANOVA tests were used to compare continuous independent data with parametric distribution. The Mann-Whitney U and Kruskal-Wallis tests were used to compare continuous independent data with non-parametric distribution. Correlation analyses of quantitative independent data with non-parametric distribution were performed by the Spearman test. The power of the correlations was defined by r value, ranged as follows: very weak: r<2; weak: r=0.2-0.39; moderate: r=0.4-0.59; strong: r=0.6-0.8; very strong: r>0.8.

## RESULTS

Of 30 patients with HS, 16 (53.3%) were females, and 14 (46.7%) were males, with a mean age of 36.86 ± 12.62 years. Demographic and clinical features of the patients with HS are presented in Table 1.

**Table 1.** Demographic and clinical features of the patients with HS

| **HS group (n=30)** | |
|---|---|
| **Sex (n/%)** | |
| Female | 16 (53.3%) |
| Male | 14 (46.7%) |
| **Age (Mean±SD, years)** | 36.86 ± 12.62 |
| **Body mass index (Mean±SD, kg/m²)** | 28.64 ± 5.60 |
| **Body mass index classification (n/%)** | |
| Normal weight (18.5-24.99 kg/m²) | 11 (36.7%) |
| Overweight (25-29.99 kg/m²) | 6 (20%) |
| Obesity (≥30 kg/m²) | 13 (43.3%) |
| **Smoking Habit (n/%)** | |
| Yes | 21 (70%) |
| No | 9 (30%) |
| **Medical History (n/%)** | |
| None | 11 (36.7%) |
| Present | 19 (63.3%)<br>Diabetes mellitus: 8 (26.6%)<br>Hypertension: 8 (26.6%)<br>Metabolic syndrome: 7 (23.3%)<br>Hyperlipidemia: 6 (20%)<br>Acne vulgaris 6 (20%)<br>Hirsutism: 3 (10%)<br>Crohn disease: 2 (6.7%)<br>Familial Mediterranean fever: 2 (6.7%)<br>Ulcerative colitis: 1 (3.3%)<br>Major depression: 1 (3.3%)<br>Bipolar affective disorder: 1 (3.3%) |
| **Follicular occlusion tetrad (n/%)** | HS, acne conglobata, dissecting cellulitis of the scalp and pilonidal sinus: 2 (6.7%)<br>HS, acne conglobata, dissecting cellulitis of the scalp: 1 (3.3%)<br>HS, acne conglobata: 1 (3.3%)<br>HS, pilonidal sinüs: 5 (16.5%) |
| **Age of disease onset [Median, (IQR), years]** | 27 (16.75) |
| **Duration of disease [Median, (IQR), months]** | 72 (135) |
| **Hurley Staging System (n/%)** | |
| Stage I | 8 (26.7%) |
| Stage II | 18 (60%) |
| Stage III | 4 (13.3%) |
| **Sites of involvement (n/%)** | |
| Axillary | 23 (76.7%) |
| Inguinal | 18 (60%) |
| Perineal/scrotal | 9 (30%) |
| Perianal | 6 (20%) |
| Gluteal/Intergluteal | 8 (26.7%) |
| Inframammary | 8 (26.7%) |
| Intermammary | 5 (16.5%) |
| **Number of sites of involvement (n/%)** | |
| One-site involvement | 9 (30%) |
| Two-site involvement | 7 (23.4) |
| Three or more-site involvement | 14 (46.6%) |
| **Axial and peripheral arthropathy (n/%)** | 0 |

IQR: Interquartile range, HS: Hidradenitis Suppurativa, SD: Standard deviation

**Table 2.** Laboratory measurements of patients with HS

| Hidradenitis Suppurativa (n=30) | |
|---|---|
| **Laboratory Parameters** | |
| WBC (mean ± SD, x10$^9$/L) | 8.97 ± 2.90 |
| RBC (mean ± SD, x10$^{12}$/L) | 4.81 ± 0.51 |
| Hb (mean ± SD, gr/dl) | 13.04 ± 1.89 |
| Platelet [median, (IQR), x10$^9$/L] | 274.5 (122) |
| Glucose [median, (IQR), mg/dl] | 101 (45.75) |
| Urea (mean ± SD, mg/dl) | 29.26 ± 7.94 |
| Creatinine (mean ± SD, mg/dl) | 0.87 ± 0.16 |
| AST [median, (IQR), U/L] | 20 (8.25) |
| ALT [median, (IQR), U/L] | 18.5 (8.25) |
| Iron (mean ± SD, µg/dl) | 65.53 ± 27.81 |
| UIBC (mean ± SD, µg/dl) | 312.99 ± 82.78 |
| TIBC (mean ± SD, µg/dl) | 373.70±74.73 |
| Ferritin [median, (IQR), µg/ml] | 20 (37.03) |
| Total cholesterol (mean ± SD, mg/dl) | 180.46 ± 40.82 |
| TG (mean ± SD, mg/dl) | 144.56 ± 65.62 |
| LDL (mean ± SD, mg/dl) | 111.56 ± 32.61 |
| HDL (mean ± SD, mg/dl) | 40.13 ± 8.53 |
| ESR [median, (IQR), mm/hour] | 13 (24.25) |
| CRP [median, (IQR), mg/dl] | 0.71 (3.08) |
| **Laboratory Parameters Classification** | |
| Leukocytosis (n/%) | 7 (23.3%) |
| Anemia (n/%) | 8 (26.7%) |
| High glucose (n/%) | 16 (53.3%) |
| Low iron (n/%) | 16 (53.3%) |
| High UIBC (n/%) | 17 (56.7%) |
| High TIBC (n/%) | 6 (20%) |
| Low ferritin (n/%) | 7 (23.3%) |
| High total cholesterol (n/%) | 11 (36.7%) |
| High TG (n/%) | 6 (20%) |
| High LDL (n/%) | 6 (20%) |
| Low HDL (n/%) | 16 (53.3%) |
| High ESR (n/%) | 14 (46.7%) |
| High CRP (n/%) | 13 (43.3%) |

ALT: Alanine transaminase, AST: Aspartate aminotransferase, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, HDL: High-density lipoprotein, IQR: Interquartile range, LDL: Low-density lipoprotein, SD: Standard deviation, TIBC: Total iron binding capacity, TG: Triglyceride, UIBC: Unsaturated iron binding capacity
Data were expressed as mean ± SD and median (IQR) in continuous variables according to normality distribution and n (%) in categoric variables.

Laboratory measurements of patients with HS are also shown in Table 2. None of the patients in the study showed signs of axial or peripheral arthropathy based on physical examination and direct radiographs.

The psychosocial status of the patients with HADS and DLQI scores is given in Table 3.

**Table 3.** Evaluation of psychosocial status of the patients with HADS and DLQI scores

| HS group (n=30) | |
|---|---|
| DLQI [median, (IQR)] | 10 (11.25) |
| HADS-A (mean ± SD) | 10.60 ± 4.88 |
| **HADS-A classification (n/%)** | |
| Anxiety Present | 18 (60%) |
| Anxiety Absent | 12 (40%) |
| HADS-D (mean ± SD) | 8.86 ± 5.55 |
| **HADS-D classification (n/%)** | |
| Depression Present | 19 (63.3%) |
| Depression Absent | 11 (36.7%) |

HAD-A: Hospital anxiety and depression-anxiety, HAD-D: Hospital anxiety and depression-depression, IQR: Interquartile range, SD: Standard deviation
Data were expressed as mean ± SD and median (IQR) in continuous variables according to normality distribution and n (%) in categoric variables.

There were statistically significant positive correlations between the patients' DLQI scores and HADS-A/HADS-D scores (r=0.598, p<0.001, r=0.551, p=0.002, respectively). However, there was no statistically significant correlation between the disease severity according to Hurley Stage and the scores of DLQI, HADS-A and HADS-D (p=0.171, p=0.225, p=0.114, respectively).
Disease Severity and Related Factors According to Hurley Staging

System:
There was no statistically significant relationship between disease severity determined by the Hurley staging system and age, age of onset, BMI, smoking, number of areas involved, and accompanying metabolic syndrome (p>0.05). A statistically significant relationship was found between disease severity and duration of disease (p=0.024). The disease duration was significantly longer in Hurley stage III patients than in Hurley stage I patients (p=0.020). In addition, a statistically significant positive correlation was found between the duration and severity of the disease (r=0.489, p=0.006).
There was no statistically significant difference in the disease severity according to the Hurley staging system between the patients with and without axillary, inguinal, gluteal/intergluteal, inframammarian, intermammarian involvement (p=0.489, p=0.130, p=0.065, p=0.617, p=0.645, respectively). The patients with perineal/scrotal and perianal involvement had a statistically significantly increased disease severity according to the Hurley staging system compared to those without perineal/scrotal and perianal involvement (p=0.002, p=0.021, respectively).

No statistically significant relationship was found between the disease severity determined by the Hurley staging system and the median DLQI scores, mean HADS-A and HADS-D scores (p=0.205, p=0.416, p=0.210, respectively).

No statistically significant relationship was found between the disease severity according to the Hurley staging system and the mean Hb and median ESR levels (p=0.247, p=0.269, respectively). However, a statistically significant relationship was found between the disease severity according to the Hurley staging system and the median CRP levels (p=0.007) (Table 4).

**Table 4.** Relationship between the disease severity according to Hurley staging system and ESR and CRP levels

| Patients with HS (n=30) | | | |
|---|---|---|---|
| | ESR (mm/hour) | | |
| Hurley Stage | Median | IQR | p |
| Stage I | 12 | 23.25 | 0,269 |
| Stage II | 12.5 | 15.25 | |
| Stage III | 92 | 97.25 | |
| | CRP (mg/dl) | | |
| Hurley Stage | Median | IQR | p |
| Stage I | 0,33 | 0.62 | 0,007* |
| Stage II | 0,71 | 2.34 | |
| Stage III | 9 | 6.16 | |

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, HS: Hidradenitis suppurativa
Data with non-parametric distribution were expressed as median (IQR).
Kruskal Wallis test was used. *p<0.05

CRP levels in the patients with Hurley stage III disease were significantly higher than those with Hurley stage I disease (p=0.005). The median ESR and CRP levels were statistically significantly higher in patients with perianal involvement, while CRP levels were statistically significantly higher in those with inguinal, perineal/scrotal, and intergluteal involvement compared to those without such involvement (p=0.001, p=0.001, p=0.491, p=0.028, p=0.137, p=0.017, p=0.170, p=0.008, respectively). There was no difference in the median ESR and CRP levels between patients with axillary, inframammary, and intermammary involvement and those without such involvement (p>0.05).

Dermatology life quality index, HADS-A, HADS-D Scores and Related Factors:

There was no statistically significant difference between the patients with and without axillary, perineal/scrotal, gluteal/intergluteal, inframammarian, intermammarian involvement in terms of DLQI, HADS-A, and HADS-D scores (p>0.05).
A statistically significant difference was found between the mean HADS-A and HADS-D scores of the patients with and without inguinal involvement (p=0.048, p=0.004). HADS-A and HADS-D scores in the patients with inguinal involvement were higher than those without inguinal involvement. There was no statistically significant difference in the median DLQI scores between the patients with and without inguinal involvement (p=0.053). A statistically significant difference was found between the mean HADS-D scores of the patients with and without perianal involvement (p=0.021). HAD-D scores in the patients with perianal involvement were higher than in the patients without perianal involvement. There was no statistically significant difference in the median DLQI and mean HADS-A scores between patients with and without perianal involvement (p=0.705, p=0.116).

No statistically significant correlation was found between the number of sites of involvement in the patients and DLQI scores(r=0.294, p=0.115). A statistically significant positive correlation was found between the number of sites of involvement and HADS-A/HADS-D scores (r=0.440, p=0.015; r=0.414, p=0.023).

**Table 5.** Correlation of the number of sites of involvement and HADS-A, HADS-D and DLQI scores in patients with HS

| Patients with HS (n=30) | | | | | | |
|---|---|---|---|---|---|---|
| | HADS-A Score | | HADS-D Score | | DLQI Score | |
| Number of sites of involvement | r | 0,440 | r | 0,414 | r | 0,294 |
| | p | 0,015* | p | 0,023* | p | 0,115 |

HADS-A: Hospital anxiety and depression scale-anxiety, HADS-D: Hospital anxiety and depression scale-depression, DLQI: Dermatology life quality index
Spearman Rho correlation was used. *p<0.05

As the number of sites of involvement increased, mean scores of HADS-A and HADS-D increased.

## DISCUSSION

Hidradenitis suppurativa is a multidimensional, chronic, debilitating skin disease. Firstly, it is associated with systemic comorbidities such as metabolic syndrome and inflammatory bowel disease and requires systemic evaluation of these conditions.5, 6 Besides, the involvement of intertriginous regions with nodules, abscesses, and draining sinus tracts increases the level of inflammatory biomarkers in the body and necessitates investigating laboratory values. Last but not least, it significantly negatively impacts the patient's QoL.
In the present study, we aimed to elucidate the clinical features and laboratory findings of patients with HS. Another purpose of the study was to assess the relationship between disease severity, depression, anxiety, and QoL in patients with HS. First of all, the patients with perineal/scrotal and perianal involvement had a statistically significantly increased disease severity. Furthermore, the mean HADS-A and HADS-D scores of the patients with inguinal involvement and HADS-D scores of the patients with perianal involvement were significantly higher than those without these involvements. However, the involvement of these regions had no significant impact in the QoL.
With regard to the studies evaluating the factors affecting the disease severity in the literature, Schrader et al. reported that 45.5% of the patients were Hurley stage I, 41.5% were Hurley stage II, and 13% were Hurley stage III in their retrospective study with 846 Dutch patients. In addition, male gender, obesity, smoking (package/year), disease duration, and axillary, perianal, and mammarian involvement were found to be associated with HS severity. However, age of onset, family history, severe acne, and diabetes mellitus were not found to be associated with disease severity.9 Vazquez et al. conducted a population-based study in Olmsted County, Minnesota, to investigate the potential associations of HS with other diseases and factors. Of the 268 patients with HS, 59.7% had Hurley stage I, 38.1% had Hurley stage II, and 2.2% had Hurley stage III disease. Age, male gender, and smoking were found to increase disease severity. However, no association was found between disease severity and BMI, depression, acne, or pilonidal disease.18 In this study, 26.7% of the patients had stage I, 60% had stage II, and 13.3% had stage III disease. In line with previous studies, the findings of our study revealed that the relationship between disease severity and duration, as well as perineal/scrotal and perianal involvement, was significant.

Considering the laboratory findings of HS, inflammatory markers such as ESR and CRP are elevated. A recent study evaluated the inflammatory biomarkers in 102 patients with HS and found that CRP level, neutrophil, lymphocyte, monocyte, and platelet count were significantly higher in patients with HS than in the control group.19 In another recent study, Andriano et al. evaluated serum inflammatory markers and white blood cell profiles in a retrospective cohort study of 404 patients with HS and reported that CRP, ESR, and IL-6 levels were significantly elevated among patients with severe disease.20 Jiménez-Gallo et al. investigated the relationship between CRP, ESR, and the clinical inflammatory activity of 74 patients with HS. They reported that serum CRP and ESR levels were significantly higher in HS patients and associated with disease activity.21 Riis et al. investigated the systemic inflammatory burden in 50 patients with HS and found that CRP levels were statistically significantly higher in the HS group and positively correlated with the Hurley stage. In addition, the mean leukocyte count in HS patients was 9656 x109/L, which was significantly higher than in the control group.22 This study found leukocytosis in 23.3% of the patients, elevated ESR and CRP levels in 46.7%, and 43.3% of the patients. In accordance with the literature, a statistically significant relationship was found between the severity of the disease and CRP levels according to the Hurley staging system. With these findings, it can be concluded that CRP and ESR levels are effective indicators of active, severe disease and can be used in treatment monitoring.
The psychosocial impact of HS is a well-established issue. Numerous studies in the literature evaluate the psychological comorbidities of patients with HS, and these studies were analyzed in various meta-analyses. In 2019, Patel et al. analyzed data from 27 studies in their meta-analysis. They found higher frequencies of depression (26.5%) and anxiety (18.1%) in the HS patient group. Moreover, patients with HS had higher odds of depression (OR:2.54) and anxiety (OR:2).23 Also, in 2019, Machado et al. evaluated 10 observational studies to find out the prevalence and odds of depression and anxiety in patients with HS. The prevalence of depression and anxiety was 16.9% and 4.9%, respectively. The OR for depression in patients with HS was 1.84, but the OR for anxiety could not be determined due to insufficient data.24 In 2020, Jalenques et al. included 28 articles on depression and 12 articles on anxiety in their meta-analysis. They calculated a prevalence of 21% of depression and 12% of anxiety in patients with HS, with vast variations due to diagnostic tools used (self-administered questionnaires, medical records, etc). Patients with HS had a 1.99 and 1.97-fold increased risk for depression and anxiety, respectively.1 In this study, symptoms of depression and anxiety were detected in 63.3% and 60% of the patients. These frequencies were higher than the frequencies reported in the literature. The small study population, the use of self-administered questionnaires rather than thorough psychiatric evaluation, and the higher ratio of patients with severe disease may have led to this result. Considering that increased depression and anxiety scores reflect disease-related psychological morbidity, depression, and anxiety scores can be used as a morbidity assessment tool in future studies. There were other noteworthy findings in this study. Patients with inguinal and perianal involvement had significantly higher scores of depression and/or anxiety. These patients also had higher levels of inflammatory parameters in their blood. Ooi et al. conducted a study with 45 patients to assess the psychosocial burden of HS and reported that higher objective disease severity scores (such as Hurley stage, modified Sartorius score) correlated with poorer QoL and increased anxiety and depression. In addition, they found that inguinal, gluteal, and suprapubic involvements resulted in poorer QoL, whereas inguinal and gluteal involvements were correlated with anxiety/depression.25 From another point of view, it is widely known that patients with HS experience sexual disturbances, and the involvement of genital regions may contribute to it. Kurek et al. investigated the impairment of sexual life in 44 patients with HS and 41 controls. They reported that patients with HS had sexual dysfunctions and sexual distress in comparison to controls.26 In light of these findings, clinicians should be aware of the psychological comorbidities of patients with HS and screen them at routine intervals.

The present study has several limitations. The main limitation was that it was a retrospective study without a control group containing a small number of patients. The sample size might not be enough to determine the true prevalence of psychological comorbidities. Additionally, the psychological status of the study population was measured by self-administered questionnaires that were widely used in clinical practice. Still, these comorbidities were not diagnosed through a detailed psychiatric evaluation by a psychiatrist.

## CONCLUSION

Our study indicates that the patients with perineal/scrotal and perianal involvement had significantly increased disease severity. Moreover, the patients with inguinal and perianal involvement had significantly higher anxiety and depression scores. Further prospective studies with large population-based samples are needed to evaluate the relationship between the areas of involvement of HS, the number of sites affected, the severity of the disease, and the psychological state. However, for the immediate future, clinicians should be conscious of the risk of depression and anxiety in patients with HS and manage these patients from a holistic perspective. Rather than focusing only on the disease severity and treatment of the lesions, all the patient's physical, emotional, and functional symptoms should be questioned and addressed in the treatment schedule.

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# Evaluation of PLEVA and PLC Patients: Two Decades of Clinical Experience

# PLEVA ve PLK Hastalarının Değerlendirilmesi: Son 20 Yıllık Deneyimlerimiz

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## ÖZET

**AMAÇ:** Bu çalışmanın amacı, pityriasis likenoides tanısı alan hastaların klinik ve demografik özellikleri ile histopatolojik bulgularını değerlendirmek; pediatrik ve erişkin hasta grupları arasındaki farklılıkları analiz etmektir.

**GEREÇ VE YÖNTEM:** 01.08.2004-01.08.2024 tarihleri arasında Ankara Eğitim ve Araştırma Hastanesi Dermatoloji Polikliniği'nde takip edilen 47 pityriasis likenoides hastasının verileri retrospektif olarak incelendi. Hastalar pityriasis likenoides kronika ve pityriasis likenoides et varioliformis akuta olarak sınıflandırıldı. Klinik, demografik ve histopatolojik özellikler ile tedavi yanıtları değerlendirildi. Hastalar pediatrik (<18 yaş) ve erişkin (≥18 yaş) gruplarına ayrılarak karşılaştırıldı. İstatistiksel analizlerde p<0.05 anlamlı kabul edildi.

**BULGULAR:** Hastaların %66'sı kadın, %34'ü erkek olup yaş ortalaması 35.28±18.96 yıl idi. Medyan hastalık süresi 14 ay, medyan tanı süresi 3 ay olarak belirlendi. En sık etkilenen bölgeler gövde ve ekstremitelerdi (%68.1). Hastaların %42.6'sında relaps görüldü. En sık saptanan histopatolojik bulgular perivasküler lenfosit infiltrasyonu (%87.8) ve lenfosit ekzositozu (%80.5) idi. Hastaların tümüne topikal kortikosteroid tedavisi verildi; %95.7'sine dar bant UVB fototerapisi uygulandı. Tam yanıt %40.4, kısmi yanıt %51.1 olup %8.5'inde tedaviye yanıt alınamadı. Pediatrik hastalarda hastalık süresi erişkinlere göre anlamlı olarak daha kısa iken (p=0.026), tanıya kadar geçen süre erişkinlere kıyasla anlamlı derecede kısa bulundu (p=0,039).

**SONUÇ**: Pityriasis likenoides hastalığının erişkinlerde daha uzun sürdüğü, pediatrik hastaların daha erken tanı aldığı saptandı. Topikal kortikosteroid ile dar bant UVB fototerapisi kombinasyonu ve gerekli olgularda tedaviye antibiyoterapi eklenmesi, hem çocuk hem erişkinlerde etkili bir tedavi seçeneğidir. Pityriasis likenoides yönetimi için daha fazla prospektif çalışmaya ihtiyaç duyulmaktadır.

**Anahtar Kelimeler:** Pityriasis likenoides, fototerapi, doksisiklin

## ABSTRACT

**AIM:** The aim of this study is to evaluate the clinical and demographic characteristics, as well as the histopathological findings, of patients diagnosed with pityriasis lichenoides, and to analyze the differences between pediatric and adult patient groups.

**MATERIAL AND METHOD:** The data of 47 patients with pityriasis lichenoides, followed up at the Dermatology Clinic of Ankara Training and Research Hospital between 01.08.2004 and 01.08.2024, were retrospectively analysed. The patients were classified as pityriasis lichenoides chronica and pityriasis lichenoides et varioliformis acuta. Clinical, demographic, and histopathological characteristics, as well as treatment responses, were evaluated. The patients were divided into pediatric (<18 years) and adult (≥18 years) groups for comparison. In statistical analyses, a p-value of <0.05 was considered significant.

**RESULTS:** Sixty-six percent of the patients were female, and 34% were male, with a mean age of 35.28±18.96 years. The median disease duration was 14 months, and the median time to diagnosis was 3 months. The most commonly affected areas were the trunk and extremities (68.1%). Relapses were observed in 42.6% of the patients. The most frequently detected histopathological findings were perivascular lymphocytic infiltration (87.8%) and lymphocytic exocytosis (80.5%). All patients were treated with topical corticosteroids, and 95.7% received narrow-band UVB phototherapy. The complete response rate was 40.4%, the partial response rate was 51.1%, and no response was observed in 8.5% of the patients. In pediatric patients, the disease duration was significantly shorter than in adults (p=0.026) and time to diagnosis was significantly shorter compared to adults (p = 0.039).

**CONCLUSION:** Pityriasis lichenoides has a longer duration in adults, while pediatric patients are diagnosed earlier. The combination of topical corticosteroids with narrowband UVB phototherapy, along with the addition of antibiotic therapy when necessary, is an effective treatment option for both children and adults. More prospective studies are needed for the management of pityriasis lichenoides.

**Keywords:** Pityriasis lichenoides, phototherapy, doxycycline

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## INTRODUCTION

Pityriasis lichenoides (PL) is the broad term given to a group of papulosquamous skin diseases which includes pityriasis lichenoides chronica (PLC) and pityriasis lichenoides et varioliformis acuta (PLEVA). PLC presents with multiple erythematous-brownish papules with mica-like scale, which often heal with postinflammatory hypopigmentation. The trunk, buttocks and proximal extremities are the most common sites of involvement. Although PLC is usually asymptomatic, pruritus may occur in some cases. Patients with PLC follow a relapsing and remitting course lasting for months to years 1. PLEVA generally presents with acute erythematous papules and papulovesicles with haemorrhagic or necrotic crusts. In PLEVA, lesions are symmetrically distributed on the trunk, buttocks and proximal extremities. Varioliform scars and post-inflammatory hyper- and hypopigmentation may form after healing. Patients may describe burning and pruritus as symptoms. Both PLC and PLEVA tend to affect children and young adults 2. Infectious agents, inflammatory response to an underlying T-cell dyscrasia and immune-complex mediated hypersensitivity are proposed theories for pathogenesis 2,3.
Treatment options include topical corticosteroids, oral antibiotics including erythromycin, azithromycin, clarithromycin, minocycline and tetracycline, phototherapy, and systemic immunosuppressants such as methotrexate and cyclosporine 2,4. When the present literature was examined, most of them were determined to be limited to case reports and reviews. Only a few retrospective studies were detected, and there was no prospective studies evaluating the clinical course and treatment strategies for the disease 4-7.
In this retrospective study, the clinical and demographic characteristics, histopathological findings, and the treatment agents given to PL patients over the last 20 years will be discussed. Additionally, the characteristics of the disease in different age groups and treatment responses will be evaluated. The main purpose of the study was to contribute to the clinical diagnosis and treatment approach of the disease, including clues for the clinicians in their clinical practice.

## MATERIAL AND METHOD

The study included 47 PL patients, who presented to the Dermatology Outpatient Clinic of the Ankara Training and Research Hospital between 01.08.2004 and 01.08.2024. The institutional ethics committee of Ankara Training and Research Hospital approved the study (E-24-215). The study was performed following the latest version of the Helsinki Declaration and Guidelines for Good Clinical Practice.
The study included all of the patients' data who were diagnosed as PLEVA or PLC during the past 20 years. Age, sex, accompanying diseases, drug usage, clinical features, duration of the disease, time to diagnosis, detailed analysis of histopathological findings, and treatment agents were investigated and recorded. The patients under 18 years of age were categorized as the pediatric group, and the remaining as adult group. The clinical presentation was detailed in terms of distribution of the lesions such as trunk and extremity involvement. Histopathological findings of 41 patients were classified and examined in detail. Major histopathological findings included parakeratosis, hyperkeratosis, acanthosis, lymphocyte exocytosis, basal vacuolar degeneration and perivascular lymphocyte infiltration. The diagnosis of PL was established based on both clinical presentation and histopathological findings. Treatment agents were analyzed, including topical steroids, systemic antibiotics and phototherapy. Treatment responses were categorized as complete, partial and no response. As the disease may have a relapsing course, the history of relapse was also evaluated. All data obtained were compared in terms of any significant differences between pediatric and adult patients.

Statistical Analysis
All analyzes were performed using IBM SPSS Statistics for Windows, Version 20.00 (IBM Corp.), and a p-value of less than 0.05 was considered statistically significant. The normality of the data was tested with the Kolmogorov Smirnov test. Continuous variables were expressed as mean ± standard deviation and median (minimum-maximum), interquartile range (IQR) with parametric and non-parametric distribution, respectively. Categorical variables were expressed as numbers and percentages. Mann-Whitney U test was used to compare independent samples. Pearson's chi-square test was applied for categorical variables, and if any cell had an expected count below 5, Fisher's Exact test was used instead.

## RESULTS

A total of 47 patients were included in this study. Thirty-one (66%) of them were female and 16 (34%) were male. The age of the patients ranged from 6 to 78 years old, and the mean age was 35.28±18.96 years. The median duration of the disease was 14 months (IQR=16), and the median time to diagnosis was 3 months (IQR=3). Thirty seven (78.7%) patients had no additional disease while 10 (21.3%) patients had other accompanying diseases. Forty patients (85.1%) were diagnosed with PLC and 7 patients (14.9%) with PLEVA. The disease was located mostly on both trunk and extremities (68.1 %). While 27 patients (57.4 %) had no relapse, 20 of them (42.6 %) had a relapsing course. The demographic and clinical characteristics of patients with PLC and PLEVA are presented in Table 1.

**Table 1.** The demographic and clinical features of patients with PLC/PLEVA

| | **PLC/PLEVA group (*n*=47)** |
|---|---|
| **PLC/PLEVA (*n*/%)** | |
| **PLC** | 40 (85.1%) |
| **PLEVA** | 7 (14.9%) |
| **Sex (*n*/%)** | |
| Female | 31 (66%) |
| Male | 16 (34%) |
| **Age [Mean±SD, years]** | 35.28±18.96 |
| **Duration of disease [Median, (IQR), months]** | 14 (16) |
| **Time to diagnosis [Median, (IQR), months]** | 3 (3) |
| **Medical History (*n*/%)** | |
| None | 37 (78.7%) |
| Present<br>There were 15 disease diagnoses in 10 patients with PLC/PLEVA<br>Hypertension<br>Diabetes mellitus<br>Coronary artery disease<br>Asthma<br>Hypothyroidism<br>Multiple sclerosis | 10 (21.3%)<br><br>5 (10.6%)<br>3 (6.4%)<br>2 (4.3%)<br>2 (4.3%)<br>2 (4.3%)<br>1 (2.1%) |
| **Locations of involvement (*n*/%)** | |
| Trunk | 11 (23.4%) |
| Extremities | 4 (8.5%) |
| Trunk&Extremities | 32 (68.1%) |
| **History of relapse (*n*/%)** | |
| None | 27 (57.4%) |
| Present | 20 (42.6%) |
| PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta<br>IQR: interquartile range, SD: standard deviation,<br>Data were expressed as mean±SD or median and IQR in continuous variables and n (%) in categorical variables. | |

Although the study included 47 patients, histopathological findings of 6 patients were inaccessible since they received their diagnoses at external healthcare institutions. Therefore, histopathological examination results of 41 (87.2%) patients were examined. Perivascular lymphocyte infiltration (n=36, 87.8%) and lymphocyte exocytosis (n=33, 80.5%) were the most frequently reported histopathological findings. Histopathological findings of the patients are summarized in Table 2.

**Table 2**. Histopathological features of patients with PLC/PLEVA

| | **PLC/PLEVA group (*n*=41)** |
|---|---|
| **Histopathological findings (*n*/%)** | |
| Parakeratosis | 22 (53.7%) |
| Hyperkeratosis | 23 (56.1%) |
| Acanthosis | 18 (43.9%) |
| Lymphocyte exocytosis | 33 (80.5%)) |
| Basal vacuolar degeneration | 16 (39%) |
| Perivascular lymphocyte infiltration | 36 (87.8%) |
| PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta<br>Data were expressed as n (%) in categorical variables. | |

All of the 47 patients had received topical corticosteroid treatment. In addition to topical steroids, 11 (23.4%) patients were given systemic antibiotic treatment while 45 (95.7%) patients received narrow-band UVB phototherapy. Doxycycline was the most frequently preferred systemic antibiotic therapy followed by erythromycin. The median total cumulative dose of phototherapy was 16.55 Joule/ cm2. While 19 (40.4%) patients had a complete response, 24 (51.1) had a partial response. Only 4 (8.5%) of the patients had no response to the treatment. Of the four patients who did not respond to treatment; two were adults, two were from the pediatric group, and all were patients who received phototherapy. The treatment agents administered to the patients and treatment response are given in Table 3.

**Table 3.** Treatment history of patients and their response to these agents

| | PLC/PLEVA group (*n*=47) |
|---|---|
| **Treatment history (*n*/%)** | |
| Topical corticosteroid | 47 (100%) |
| Systemic antibiotics<br>Doxycycline<br>Erythromycin | 11 (23.4%)<br>9 (19.1%)<br>2 (4.3%) |
| Narrow-band UVB Phototherapy | 45 (95.7%) |
| Total cumulative dose of phototherapy [Median, (IQR), Joule/cm$^2$] | 16.55 (36.63) |
| **Treatment Response (*n*/%)** | |
| Complete response | 19 (40.4%) |
| Partial response | 24 (51.1%) |
| No response | 4 (8.5%) |
| PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta<br>Data were expressed as n (%) in categorical variables. | |

Patients under 18 years of age were categorized as pediatric, over or equal to 18 years of age were categorized as adult group. Eleven patients were pediatric and 36 were classified as adult patients. Among the 11 pediatric patients, 7 (63.6%) were diagnosed with PLC and 4 (36.4%) with PLEVA. Of the 36 adult patients, 33 (91.7%) were diagnosed with PLC and 3 (8.3%) with PLEVA. The proportion of PLEVA cases was significantly higher in the pediatric group compared to the adult group (p = 0.042). The median disease duration was 8 months (IQR=17) for pediatric patients and 16 months (IQR=14) for adult patients. Disease duration for pediatric patients was statistically significantly lower compared to adult patients (p=0.026). The median time to diagnosis was 2 months (IQR = 2) for pediatric patients and 3 months (IQR = 4) for adult patients. This difference was statistically significant (p = 0.039), indicating that pediatric patients received an earlier diagnosis compared to adults. Histopathological examination revealed that parakeratosis was statistically significantly more common in adult patients (64.5%) compared to pediatric patients (20%) (p=0.026). No statistically significant difference was detected between the two groups in the remaining parameters. Comparison of the demographic and disease characteristics, treatment modalities and histopathological results between patients under 18 years and adult patients are demonstrated in Table 4.

**Table 4.** Comparison of the demographic and disease characteristics, treatment modalities and histopathological results between patients under 18 years and adult patients

| | Patients under 18 years of age (n=11) | Adult patients (n=36) | p |
|---|---|---|---|
| **PLC/PLEVA** | | | |
| **PLC** | 7 (63.6%) | 33 (91.7%) | 0.042[f]* |
| **PLEVA** | 4 (36.4%) | 3 (8.3%) | |
| **Sex (*n*/%)** | | | |
| Female | 7 (63.6%) | 24 (66.7%) | 0.853[x] |
| Male | 4 (36.4%) | 12 (33.3%) | |
| **Duration of disease [Median, (IQR), months]** | 8 (17) | 16 (14) | 0.026[m]* |
| **Time to diagnosis [Median, (IQR), months]** | 2 (2) | 3 (4) | 0.039[m]* |
| **Locations of involvement (*n*/%)** | | | |
| Trunk | 1 (9.1%) | 10 (27.8%) | 0.556[f] |
| Extremities | 1 (9.1%) | 3 (8.3%) | |
| Trunk&Extremities | 9 (81.8%) | 23 (63.9%) | |
| **History of relapse (*n*/%)** | | | |
| None | 8 (72.7%) | 19 (52.8%) | 0.310[f] |
| Present | 3 (27.3%) | 17 (47.2%) | |
| **Treatment history (*n*/%)** | | | |
| Topical corticosteroid | 11 (100%) | 36 (100%) | 1 |
| Systemic antibiotics<br>Doxycycline<br>Erythromycin | 3 (27.3%) | 8 (22.2%) | 0.056[f] |
| Narrow-band UVB Phototherapy | 10 (90.9%) | 35 (97.2%) | 0.417[f] |
| **Treatment Response (*n*/%)** | | | |
| Complete response | 6 (54.5%) | 13 (36.1%) | 0.523[f] |
| Partial response | 4 (36.4%) | 20 (55.6%) | |
| No response | 1 (9.1%) | 3 (8.3%) | |
| **Histopathological findings (*n*/%)** | **Patients under 18 years of age (n=10)** | **Adult patients (n=31)** | p |
| Parakeratosis | 2 (20%) | 20 (64.5%) | 0.026[f]* |
| Hyperkeratosis | 6 (60%) | 17 (54.8%) | 1[f] |
| Acanthosis | 3 (30%) | 15 (48.4%) | 0.467[f] |
| Lymphocyte exocytosis | 8 (80%) | 25 (80.6%) | 1[f] |
| Basal vacuolar degeneration | 4 (40%) | 12 (38.7%) | 1[f] |
| Perivascular lymphocyte infiltration | 10 (100%) | 26 (83.9%) | 0.310 |
| PLC: Pityriasis lichenoides chronica, PLEVA: Pityriasis lichenoides et varioliformis acuta<br>UVB: Ultraviolet B<br>IQR: interquartile range, SD: standard deviation,<br>Data were expressed as mean±SD or median and IQR in continuous variables and n (%) in categorical variables. *p<0.05., [m]Mann-Whitney U test, [x] Chi-Square test, [f]Fisher's Exact Test | | | |

## DISCUSSION

PL is the general term for a group of disorders with PLEVA and PLC regarded as two ends of the same disease spectrum, sharing overlapping clinical and histopathological features while differing in their presentation and course. PLEVA is characterized by acute, inflammatory papules, vesicles, and necrotic crusts, often accompanied by pruritus or burning. In contrast, PLC typically presents with chronic, scaly, and erythematous-brownish papules that evolve slowly and may heal with post-inflammatory pigmentary changes. Despite these differences, both conditions are thought to arise from a similar underlying pathogenesis, potentially involving immune dysregulation, T-cell-mediated inflammation, infections or hypersensitivity reactions 2.

The sex distribution among PL patients has shown considerable variability in the literature. In a randomised study involving 15 PLC patients, 53% of the patients were male while 47% were female 8. In another retrospective study involving 25 PLC patients, 56% were male and 44% were female 4. In a review involving pedatric PL cases, a slight (%61) male predominance was noted out of a total of 393 patients 3. On the other hand, in an observational retrospective study including 20 PL patients, more than half (55%) of the patients were female 5. In a retrospective study investigating the differences between pediatric and adult PL, male: female ratio was 1.5 : 1 for children and 1 : 1 for adults with no statistically significant difference in sex distribution between two groups 7. In this study, the majority of the patients was female (66% vs 34%) with no significant difference in sex distribution between pediatric and adult patients.

The age distribution of PL patients has been widely documented in the literature, with varying median and mean ages reported across different studies. In a retrospective study with 75 PL patients, the median age was found 16 and 26 years for PLEVA and PLC, respectively 9. In another retrospective study including PL patients collected during a 8-year period, the median age was 8 years for children (age range: 2-18 years) and 40 years for adults (20-65 years) 7. Agaoglu et al reported a mean age of 30.3 years in their retrospective study on 20 PL patients 5. In this study, the mean age was 35.28 years, and the proportion of PLEVA patients was higher in the pediatric group compared to adults, consistent with findings in the literature.

The duration of disease in PL patients has been a subject of interest in the literature, with studies reporting varying disease durations across different patient populations. In a retrospective review with 24 PL patients, median disease duration was reported as 11 months 6. Ersoy-Evans et al reported a median duration of 18.5 months in their retrospective study involving 124 PL patients 10. Wahie et al compared pediatric and adult PL patients and found that 80% of pediatric cases had active disease after a median duration of 30 months while 78% of adult patients had achieved remission by this time 7. In this study, the median disease duration was 14 months which was similar to the results in the literature. In contrast to the literature, the median disease duration of adults was significantly longer when compared with the pediatric patients.

The duration from symptom onset to diagnosis is highly variable. In a retrospective study on 75 PL patients, the median time to diagnosis was 5 weeks for PLEVA patients and 12 weeks for PLC patients 9. In a study by Fatturi et al, the mean time from symptom onset to diagnosis was 5 months with a maximum delay of up to 10 years 11. Similarly, a previous series reported a mean diagnostic delay of 1 year, with some cases taking as long as 3 years 12. Wahie et al reported 6 months and 24 months as the median time until consultation in children and adults, respectively 7. In our study, the median time to diagnosis was 3 months with children getting a diagnosis significantly earlier than adults.

Numerous studies have reported the coexistence of diseases in patients with PL. For instance, febrile tonsillitis was reported in a 3-year-old male patient diagnosed with PLEVA 13. Tsai et al reported accompanying alopecia areata in a 5-year-old male patient with PL while Saltik-Temizel et al reported autoimmune hepatitis in a 13-year-old male patient with PLC 14,15. Moreover, granulomatous chronic variable immunodeficiency was reported in a 8-year-old female patient with PL 16. Hodgkin's lymphoma, mitochondrial disorder, asthma, hereditary hemorrhagic telangiectasia and atopic dermatitis were reported in pediatric PL patients whereas hypertension, rheumatoid arthritis, ischemic heart disease, psoriasis, atopic dermatitis, immune thrombocytopenic purpura and hepatitis B were reported in adult patients 7. In our study, the majority of the patients (78.7%) had

no additional disease. The remaining patients had diseases such as hypertension, diabetes, coronary artery disease, asthma, hypothyroidism and multiple sclerosis, with hypertension being the most common associated disease.

PL typically affects trunk and proximal extremities. However, involvement of the face and inguinal regions have also been reported. For example, in a retrospective study by Agaoglu et al., involvement of the face, trunk, and inguinal region was classified as central, involvement of the extremities as peripheral, and whole-body involvement as diffuse. The study reported that the majority of patients exhibited diffuse involvement, followed by central and acral involvement, respectively 5. Ersoy-Evans noted that peripheral and diffuse involvement was noted in 48% and 44% of PL patients while only 8% had trunk involvement 4. In our study, the majority of patients had involvement of both the trunk and extremities, followed by those with only trunk involvement and those with only extremity involvement, respectively; with no significant difference in location of involvement between children and adults.

Both PLC and PLEVA have relapsing and remitting disease course and highly variable relapse rates have been reported so far, ranging from 18.9% to 42.8% 17,18. In a prospective study, relapse occurred in 43% of PLC patients within the first six months after narrowband ultraviolet B phototherapy 18. Conversely, research involving pediatric PL patients treated with oral erythromycin reported a relapse rate of 12.5% 6. In our study, relapse was observed in 42.6% of the patients. No difference was observed in relapse rates between pediatric and adult patients.

Histopathology of PLEVA and PLC has some overlapping features as well as certain differences. In PLEVA, parakeratosis, spongiosis, acanthosis, basal layer vacuolization, lymphocyte exocytosis and epidermal necrosis are observed. Perivascular lymphohistiocytic infiltrate, dermal edema and subepidermal vesicles can also be found as well as vascular dilation, erythrocyte extravasation and vasculitis. In PLC, focal parakeratosis, mild acanthosis, spongiosis, mild epidermal necrosis, and mild dermal edema with perivascular infiltration, occasional erythrocyte extravasation and vessel dilation are observed. Vasculitis is not an expected finding of PLC 2. In our study, parakeratosis and hyperkeratosis were present in over half of the patients, while lymphocyte exocytosis and perivascular infiltrate were noted in the majority of the patients. Notably, spongiosis, erythrocyte extravasation, epidermal necrosis, subepidermal vesicles, vascular dilation, vasculitis, and dermal edema were not detected. Parakeratosis was noted significantly more common in adult patients compared to pediatric patients.

Different treatment approaches for PL are available, with topical corticosteroids, oral antibiotics, and phototherapy being the most commonly used modalities, demonstrating differing rates of efficacy and response among pediatric and adult patients. Wahie et al. reported that 64% of pediatric and 56% of adult cases received topical corticosteroids, with symptom relief in 50% and 56%, respectively. Oral antibiotics were used in 32% of children and 13% of adults, resulting in full/partial resolution in 25% and 75% of children and adults, respectively. Phototherapy was administered to 32% of children and 64% of adults, with improvement observed in 88% and 71%, respectively 7. Ozdol et al. reported that 17%, 29%, and 23% of PLEVA patients received topical corticosteroids, oral antibiotics, or phototherapy, compared to 15%, 15%, and 55% of PLC patients, respectively 9. In our study, all patients received topical corticosteroid treatment, nearly a quarter underwent systemic antibiotic therapy, and all except two patients were treated with narrowband UVB phototherapy with a median cumulative dose of 16.55 Joule/cm2. More than half of the patients achieved a partial response, 40% achieved complete resolution, while 8.5% showed no response to treatment. No significant difference was noted in the treatment history and response rates between pediatric and adult patients. It can be concluded that narrow-band UVB therapy is a safe, well-tolerated treatment option in both pediatric and adult patients, with high rates of treatment success.

Limitations

This study has a few limitations. Firstly, there may be potential biases in data collection. Since the study was retrospective, patients with PL could not be prospectively evaluated regarding treatment responses over a period of time. Additionally, treatment responses for individual treatment options (topical corticosteroids, narrow band UVB, systemic antibiotics) could not be assessed, which is a drawback of this study.

## CONCLUSION

In conclusion, PL tends to have a longer duration in adults, while pediatric patients are typically diagnosed earlier. The combination of topical corticosteroids, narrowband UVB phototherapy and antibiotic therapy, when indicated, has proven to be an effective treatment approach for both children and adults. However, further prospective studies are essential to refine and optimize management strategies for PL.

**Yazarlık Katkıları:**
**Author Conributions:** Concept and design: NK, Data collection: BD, İY, ZA, Data analysis: PÖÇ, Literature research and collection: NK, İK, Writing: NK, İK, Review and assessment: NK, İK, BD, ZA, İY, PÖÇ

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**Özgün Çalışma / Original Article**

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# Comparison of Maternal and Neonatal Outcomes in Cases of Pre-Viable Preterm Premature Rupture of Membranes (pPPROM) According to Weeks of Gestation

# Pre-Viable Preterm Prematür Membran Rüptürü (pPPROM) Olgularında Gebelik Haftalarına Göre Maternal ve Neonatal Sonuçların Karşılaştırılması

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## ABSTRACT

**AIM:** The rupture of the amniotic membrane before 24 weeks gestation is defined as pre-viable preterm premature rupture of membranes (pPPROM). This study aims to compare the maternal and neonatal outcomes of cases of pPPROM detected before and after 22 weeks of gestation.

**MATERIAL AND METHOD:** This retrospective study evaluated singleton pregnancies with pPPROM between 2014 and 2019. The pPPROM cases were divided into two groups: Group 1 consisted of cases between 12+0 and 21+6 weeks of gestation, while Group 2 consisted of cases between 22+0 and 23+6 weeks of gestation. The obstetric outcomes, maternal complications, and neonatal intensive care unit (NICU) admission rates were compared in both groups. Furthermore, the neonatal outcomes of fetuses with a birth weight of over 500 grams were compared in both groups.

**RESULTS:** A total of 181 cases of pPPROM were identified, with 45 (24.8%) occurring in Group 2. The latent period duration, age at birth, and maternal complications were found to be higher in Group 2 ($p < 0.05$). Twenty percent of cases resulted in viable outcomes (15/136 vs. 22/45, $p < 0.001$). Higher termination rates were observed in Group 1 ($p<0.001$). However, ongoing pregnancies in this group reached more than 500 grams, these fetuses had higher Apgar scores and lower NICU admission rates ($p < 0.05$).

**CONCLUSION:** In cases of pPPROM after 22 weeks gestation, the incidence of maternal morbidity was higher, and the NICU admission rate was higher in fetuses born over 500 grams in this group.

**Keywords:** Pre-viable preterm premature rupture of membranes, neonatal outcomes, maternal outcomes, neonatal intensive care unit, termination of pregnancy

## ÖZET

**AMAÇ:** Amniyotik membranın 24. gebelik haftasından önce rüptüre olması, pre-viable preterm prematüre membran rüptürü (pPPROM) olarak tanımlanır. Bu çalışma, 22. gebelik haftasından önce ve sonra tespit edilen pPPROM olgularının maternal ve neonatal sonuçlarını karşılaştırmayı amaçlamaktadır.

**GEREÇ VE YÖNTEM:** Bu retrospektif çalışmada 2014-2019 yılları arasında pPPROM'lu tekil gebelikler değerlendirildi ve pPPROM vakaları iki gruba ayrıldı: 12+0 ile 21+6 gebelik haftaları arasındaki vakalardan oluşan Grup 1 ve 22+0 ile 23+6 gebelik haftaları arasındaki vakalardan oluşan Grup 2. Her iki grupta latent dönem süresi, obstetrik sonuçlar, maternal komplikasyonları ve yenidoğan yoğun bakım ünitesine (YYBÜ) yatış oranları karşılaştırıldı. Ayrıca 500 gramın üzerinde ağırlıkla doğan fetüslerin neonatal sonuçları iki grup arasında karşılaştırıldı.

**BULGULAR:** Grup 2'de 45 (%24,8) olgu olmak üzere toplam 181 pPPROM vakası tespit edildi. Grup 2'de latent dönem süresi, doğum yaşı ve maternal komplikasyonları daha yüksek bulundu ($p <0,05$). Gebeliklerin %20,4'si viable sonuçlandı (15/136 vs. 22/45, $p<0,001$). Grup 1'de daha fazla terminasyon oranları gözlemlendi ($p<0.001$). Ancak, bu grupta devam eden gebelikler 500 gramın üzerine çıktığında, bu fetüslerin Apgar skorları daha yüksekti ve NICU'ya kabul oranları daha düşüktü ($p < 0,05$).

**SONUÇ:** 22 haftalık gebelikten sonra pPPROM vakalarında, maternal morbidite insidansı daha yüksekti ve bu grupta 500 gramın üzerinde doğan fetüslerde NICU'ya kabul oranı daha yüksekti.

**Anahtar Kelimeler:** Pre-viable Preterm Premature Membran Rüptürü, neonatal sonuçlar, maternal sonuçları, yenidoğan yoğun bakım ünitesi, terminasyon

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## INTRODUCTION

Pre-viable preterm premature rupture of membranes (pPPROM) occurs in 0.4% to 1% of pregnancies before 24 weeks gestation and is defined as a rupture of the amniotic membranes before the onset of labor (1,2). PPROM is associated with high rates of maternal and neonatal morbidity and mortality, including infection-related problems and other associated problems such as pulmonary hypoplasia, fetal malformations, and abruption of placentae. The probability of neonatal death and morbidity associated with premature rupture of membranes (PROM) decreases with prolonged latency and increasing gestational age (1,2,3). Therefore, the gestational week in which PROM occurs affects both neonatal and maternal morbidity and mortality, as well as the management of these cases by clinicians (3).

In the case of pregnancies complicated by pPPROM, the options for women include termination of a pre-viable fetus or expectant management to achieve the viability of the fetus. Although it rarely occurs, critical maternal complications after pPPROM, unfortunately, maternal morbidity is experienced in approximately 14% of cases, which renders expectant management challenging (4). Nevertheless, in cases of PROM detected in the second trimester, the latent periods were observed to be longer than those observed in later gestational ages, however, it was observed that 40-50% of these cases resulted in delivery within the first week, and approximately 70-80% of them resulted in delivery after 2-5 weeks (2,5,6). Furthermore, the survival rates were significantly higher when the rupture of membranes was followed by expectant management after 22 weeks of gestation compared to the rupture of membranes before 22 weeks of gestation (57.7% versus 14.4%, respectively) (2).

The management of PROMs in pre-viable fetuses presents a variety of challenges and crucial processes for the mother, fetus, and obstetrician and one of the most prominent parameters in this process is the rupture of the membranes at which gestational week (1,2,3). This study aims to compare the maternal and neonatal outcomes of these two groups of pPPROM cases detected before and after 22 weeks of gestation.

## MATERIAL AND METHOD

This retrospective study identified singleton pregnancies with pPPROM who were admitted to the early pregnancy service between January 2014 and October 2019. The study was conducted on the hospital admission records at our hospital. The study was approved by the local ethics committee on 14/05/2020, with approval number 07. Informed consent was received from all participants.
The study included singleton pregnancies with a definitive clinical diagnosis of pPPROM between 12+0 and 23+6 gestational weeks. The visualization of amniotic fluid passing from the cervical canal or posterior fornix accumulation in cases diagnosed as pPPROM by speculum examination, and pregnant women presenting with a history of vaginal observation of amniotic flow, were included in the study. However, amniotic fluid was not visually observed in speculum examination, but placental alpha microglobulin-1(PAMG-1) test (amniosure) positive and diagnosed as pPPROM were also included. In our clinic, we manage pPPROM cases by the recommendations of the American College of Obstetricians and Gynecologists (ACOG) (1). Multiple pregnancies, cases with PROM detected at <12 and ≥24 weeks gestation, women with labor within 24 hours of rupture, uncertain date of membrane rupture, oligohydramnios or anhydramnios without membrane rupture, membrane rupture within 48 hours of amniocentesis, chorionic villous sampling, or fetal selective reduction, and cases with missing maternal and neonatal data were excluded.

The pregnancies included in the study were divided into two groups, as follows: Group 1 comprised pPPROM cases diagnosed between 12+0 and 21+6 weeks of gestation, and Group 2 comprised pPPROM cases diagnosed between 22+0 and 23+6 gestational weeks. In both groups, demographic characteristics and obstetric factors, ultrasonographic findings such as amniotic fluid index (AFI) and fetal heartbeat (FHB), gestational age at admission, duration of the latent period, birth age, C-reactive protein (CRP), leukocyte count, and medical treatments were compared. Additionally, the rates of cesarean or hysterotomy, transfusion, maternal sepsis, termination, live birth, birth weight, and neonatal intensive care unit (NICU) admission were analyzed. As secondary outcomes, obstetric and neonatal outcomes of fetuses with a live birth over 500 g and fetuses followed in the NICU were subgrouped and compared in both groups.

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS, IBM Corp., Armonk, NY, US) software, version 28. The distribution of numerical variables was subjected to a Kolmogorov-Smirnov test. As the data did not demonstrate a normal distribution, all numerical data are presented with median (minimum-maximum) values. Furthermore, percentages (numbers) were employed in the context of categorical variables. The two groups were compared using the chi-square test for categorical variables and the Mann-Whitney U test for numerical variables. Odds ratios (OR) with 95% confidence intervals (CI) were calculated for significant categorical variables. The variables that were found to be significant in the univariate analysis were then evaluated in a multivariate regression analysis. The results were considered statistically significant at the $p< 0.05$.

## RESULTS

By the eligibility criteria, a total of 181 (75.1%) cases of pPPROM were identified, with 45 (24.8%) falling within Group 2. There was no difference in age, BMI, or obstetric parameters such as gravida and parity in both groups ($p>0.05$, Table 1).

**Table 1: Demographic and obstetric characteristics of the groups**

| | Group 1 | Group 2 | |
|---|---|---|---|
| Variables | n=136 (75.18%) | n=45 (24.82%) | p value |
| | Median (min-max) | Median (min-max) | |
| Age (years) | 32 (17-46) | 30 (18-41) | 0.278 |
| Body Mass Index (kg/m$^2$) | 26 (21-36) | 27 (22-33) | 0.527 |
| Gravida (n) | 2 (1-9) | 2 (1-5) | 0.178 |
| Parity (n) | 1(0-5) | 1 (0-4) | 0.636 |
| Previous miscarriages, (n) | 0(0-)6 | 0 (0-3) | 0.328 |
| Number of children | 1(0-5) | 1 (0-4) | 0.780 |
| Stillbirth, (n) | 0 (0-2) | 0 (0-1) | 0.732 |
| Ectopic pregnancies, (n) | 0 (0-1) | 0 (0-0) | 0.315 |
| Cesarean birth, (n) | 0 (0-3) | 0 (0-3) | 0.241 |
| Duration of antibiotics (days) | 5 (2-30) | 7 (3-37) | **<0.001** |
| C-reactive protein (mg/l) | 32 (1-254) | 6.5 (1-302) | 0.411 |
| Leukocyte count, (x10$^9$/L) | 10.67 (5.10- 25.0) | 10.12 (4.71-21.60) | **0.023** |
| Gestational age at diagnosis (days) | 123 (84-152) | 165 (154-166) | **<0.001** |
| Ultrasonographic gestational age (days) | 127 (81-165) | 166 (136-180) | **<0.001** |
| Latent period (days) | 2 (2-197) | 10 (2-93) | **<0.001** |
| Birth Age (days) | 131 (86-278) | 175 (157-250) | **<0.001** |

Although the CRP values of the groups were similar at admission ($p=0.411$), the leukocyte count was significantly higher in Group 1 ($p=0.023$), but the duration of antibiotic use was significantly longer in Group 2 ($p<0.001$, Table 1). The median duration of the latent period was 2 days (2-197) in Group 1 and 10 days (2-93) in Group 2 (Table 1). The median birth age of Group 2 was 175 days (157-250), while that of Group 1 was 131 days (86-278), as shown in Table 1. The birth ages of these two groups are illustrated in the box plots of Figure 1.

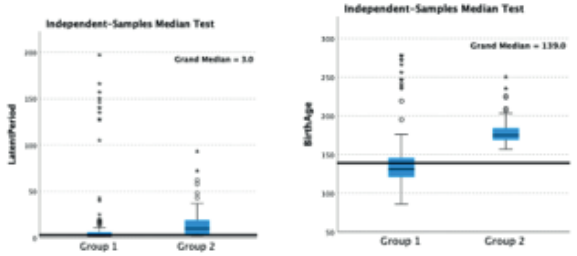


**Figure 1: The duration of the latent period (day) and birth age (day) according to the groups in all fetuses.**

The significant variables in Table 1, including antibiotic duration, leukocyte count, gestational age, birth age, and latent period were evaluated in a multivariate regression analysis and the results indicated a statistically significant difference at the p < 0.001 level in this model (R=0.806, R2=0.649, and aR=0.639).

A comparison of outcomes of pregnancies in the two groups revealed that 98 cases (72.1%) in Group 1 had been terminated, in contrast to 7 cases (15.6%) in Group 2 (p < 0.001). In addition, 10 cases in Group 1 had resulted in intrauterine fetal death (IUFD), in comparison to 2 cases in Group 2. Furthermore, 8 cases in Group 1 resulted in spontaneous abortion, in contrast to 1 case in Group 2. The live birth rate was 77.8% in Group 2 and 14.7% in Group 1 (p < 0.001). All terminations were conducted via drug-induced abortion, except two cases in Group 1, where the pregnancy was terminated by hysterotomy due to unresponsiveness to medical treatment.

The incidence of postpartum hemorrhage was higher in Group 2 (1 (0.7%) vs. 3 (6.7%), p=0.048, Table 2).

**Table 2: Complication rates and other obstetric outcomes of the groups**

| | | Group 1 | Group 2 | | | |
|---|---|---|---|---|---|---|
| | | n (%) 136 (75.18) | n (%) 45 (24.82) | p value | Odds Ratio | %95 CI |
| Assisted reproductive techniques | No | 131 (96.3) | 42 (93.3) | 0.256 | | |
| | In vitro fertilization | 3 (2.2) | 3 (6.7) | | | |
| | Intrauterine insemination | 2 (1.5) | 0 (0.0) | | | |
| Comorbid systemic disease | No | 124 (91.2) | 44 (97.8) | 0.137 | | |
| | Yes | 12 (8.8) | 1 (2.2) | | | |
| Presence of active amniotic flow | No | 23 (16.9) | 1 (2.2) | **0.012** | 8.956 | 1.174-68.339 |
| | Yes | 113 (83.1) | 44 (97.8) | | | |
| Amniotic fluid index | Oligohydramnios or anhydramnios | 118 (86.8) | 32 (71.1) | **0.16** | 2.663 | 1.181-6.007 |
| | Normal | 18 (13.2) | 13 (28.9) | | | |
| Termination of pregnancy | No | 38 (27.9) | 38 (84.4) | **<0.00 1** | 0.071 | 0.029-0.174 |
| | Yes | 98 (72.1) | 7 (15.6) | | | |
| Live birth over 500 g | No | 116 (85.3) | 10 (22.2) | **<0.00 1** | 20.30 0 | 8.699-47.400 |
| | Yes | 20 (14.7) | 35 (77.8) | | | |
| Cesarean section or hysterotomy | No | 123 (90.4) | 27 (60.0) | **<0.00 1** | 6.308 | 2.761-14.409 |
| | Yes | 13 (9.6) | 18 (40.0) | | | |
| Gender | Unspecified | 114 (83.8) | 4 (8.9) | **<0.00 1** | | |
| | Girl | 12 (8.8) | 18 (40.0) | | | |
| | Boy | 10 (7.4) | 23 (51.1) | | | |
| Chorioamnionitis | No | 133 (97.8) | 39 (86.7) | **0.03** | 6.821 | 1.630-28.533 |
| | Yes | 3 (2.2) | 6 (13.3) | | | |
| Maternal sepsis | No | 136 (100.0) | 44 (97.8) | .249 | | |
| | Yes | 0 (0.0) | 1 (2.2) | | | |
| Abruptio placentae | No | 2 (1.5) | 2 (4.4) | .239 | | |
| | Yes | 134 (98.5) | 43 (95.6) | | | |
| Placental rest | No | 132 (97.1) | 43 (95.6) | 0.625 | | |
| | Yes | 4 (2.9) | 2 (4.4) | | | |
| Endometritis | No | 134 (98.5) | 45 (100.0) | 1.000 | | |
| | Yes | 2 (1.5) | 0 (0.0) | | | |
| Blood transfusion | No | 130 (95.6) | 42 (93.3) | 0.546 | | |
| | Yes | 6 (4.4) | 3 (6.7) | | | |
| Postpartum hemorrhage | No | 135 (99.3) | 42 (93.3) | **0.048** | 9.643 | 0.977-95.176 |
| | Yes | 1 (0.7) | 3 (6.7) | | | |

Chorioamnionitis, diagnosed based on the presence of fever, malaise, infective vaginal discharge, and uterine tenderness, was observed significantly more frequent in Group 2 (3 (2.2%) vs 6 (13.3%), p=0.03). Maternal severe sepsis was observed in only one woman at 23+1 weeks in Group 2, resulting in intrauterine fetal death (IUFD). There were no maternal deaths or thromboembolic events in any of the casesistor.

Table 3: Neonatal outcomes of groups in fetuses born over 500 g

| | | Fetuses live born over 500 g | | |
|---|---|---|---|---|
| | | Group 1 | Group 2 | |
| | | n=20 | n=35 | p value |
| **Age**, years, Median (min-max) | | 31.5 (21-46) | 30 (21-41) | 0.508[a] |
| **Gestational age at diagnosis** (days), Median (min-max) | | 122 (84-153) | 165 (157-167) | **<0.001[a]** |
| **Latent period** (days), Median (min-max) | | 127 (2-197) | 18 (2-93) | **<0.004[a]** |
| **Birth Age** (days), Median (min-max) | | 238 (153-281) | 183 (162-250) | **0.019[a]** |
| **Birth weight** (gr), Median (min-max) | | 2265 (500-4330) | 930 (545-2410) | 0.074[a] |
| **Duration of antibiotics** (days), Median (min-max) | | 7 (2-30) | 7 (3-19) | 0.745[a] |
| **C-reactive protein**, (mg/L), Median (min-max) | | 15 (3-32) | 6.5 (1-305) | 0.416[a] |
| **Leukocyte count**, (x10³/L), Median (min-max) | | 12.11 (7.86-18.20) | 12.89 (7.93-18.46) | 0.414[a] |
| **Amniotic fluid index**,n (%) | Oligohydramnios or anhydramnios | 5 (25.0) | 22 (62.9) | **0.007[b]** |
| | Normal | 15 (75.0) | 13 (32.1) | |
| **Cesarean section**, n (%) | No | 9 (45.0) | 17 (48.6) | 0.799[b] |
| | Yes | 11 (55.0) | 18 (51.4) | |
| **Administration of corticosteroids**, n (%) | No | 9 (45.0) | 0 (0) | **<0.001[b]** |
| | Yes | 11 (55.0) | 35 (100) | |
| **Gender**, n (%) | Boy | 12 (60.0) | 15 (42.9) | 0.221[b] |
| | Girl | 8 (40.0) | 20 (57.1) | |
| **1st-min Apgar score**, Median (min-max) | | 8 (1-9) | 6 (1-9) | **<0.001[a]** |
| **5th-min Apgar score**, Median (min-max) | | 9 (2-10) | 7 (0-10) | **0.016[a]** |
| **Admission at Neonatal intensive care unit (NICU)**, n (%) | No (healthy fetüs) | 8 (40.0) | 1 (2.9) | **0.002[b]** |
| | Yes | 11 (55.0) | 30 (85.7) | |
| | Unresponsive to neonatal resuscitation (death) | 1 (5.0) | 4 (11.4) | |

[a]=Mann Withney U test , [b] = Chi-square test, Bold is statistically significant

Table 3 presents the neonatal outcomes of 55 fetuses (20 vs. 35) born weighing over 500 g and 41 fetuses (11 vs. 30) hospitalized in NICU. There was no significant difference in age, duration of antibiotics, C-reactive protein, leukocyte count, birth weight, cesarean birth rate, and gender of fetuses born over 500 g in both groups (p > 0.05). The detection rate of oligohydramnios or anhydramnios was significantly higher in Group 2 (p=0.007, OR:0.197, 95% CI 0.058-0.669). However, as illustrated in Figure 2

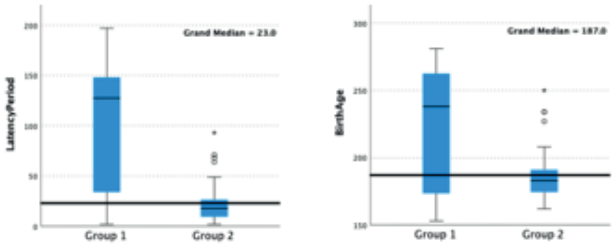


Figure 2: The duration of the latent period (day) and birth age (day) according to the groups of

, in fetuses with a birth weight of over 500 g, there was a significant difference between the groups in median latent period (127 (2-197) vs. 18 (2-93) days, p <0.004) and median birth age (238 (153-281) vs. 183 (162-250) days, p=0.019), with these durations being longer in Group 1, in contrast to all cases, as shown in Figure 1.The significant variables in Table 3, including Apgar 1, Apgar 5, gestational age, and latent period, were evaluated in a multivariate regression analysis and the results indicated a statistically significant difference at the p<0.001 level in this model (R=0.786, R2=0.619, and aR=0.588). Furthermore, the first and fifth-minute Apgar scores were observed to be superior in Group 1 in fetuses with a birth weight of over 500 g (p < 0.05). Consequently, the number of cases admitted to the neonatal intensive care unit (NICU) from fetuses born over 500 g was significantly higher in Group 2 (11 (55.0%) vs. 30 (85.7%), p=0.002). The 41 fetuses admitted to the NICU unit were evaluated in Table 4,

Table 4: Neonatal outcomes of groups in fetuses with Neonatal intensive care unit (NICU) admission

| | | Fetuses with NICU admission n=41 | | p value |
|---|---|---|---|---|
| | | Group 1 | Group 2 | |
| | | n=11 | n=30 | |
| **Mortality rate**, n (%) | No | 7 (63.6) | 21 (70.0) | 0.698[b] |
| | Yes (death) | 4 (36.4) | 9 (30.0) | |
| **Postnatal immediate intubation**, n (%) | No | 4 (36.4) | 15 (50.0) | 0.438[b] |
| | Yes | 7 (63.6) | 15 (50.0) | |
| **Day of hospitalization in the NICU**, Median (min-max) | | 7 (1-126) | 59 (1-143) | 0.095[a] |
| **Necrotizing enterocolitis**, n (%) | No | 11 (100.0) | 27 (90.0) | 0.555[b] |
| | Yes | 0 (0.0) | 3 (10.0) | |
| **Transition to total enteral nutrition**, n (%) | No | 4 (36.4) | 5 (16.6) | 0.051[b] |
| | Yes | 7 (63.6) | 25 (83.3) | |
| **Day of transition to total enteral nutrition**, Median (min-max) | | 6 (0-21) | 10 (0-30) | 0.127[a] |
| **Patent ductus arteriosus**, n (%) | No | 6 (54.5) | 14 (43.7) | 0.711[b] |
| | Yes | 5 (45.5) | 16 (53.3) | |
| | Unknown | 0 (0.0) | 1 (3.3) | |
| **Respiratory Distress Syndrome**, n (%) | No | 3 (27.3) | 4 (13.3) | 0.293[b] |
| | Yes | 8 (72.7) | 26 (86.7) | |
| **Number of surfactants given**, Median (min-max) | | 1 (0-2) | 1 (0-3) | 0.896[a] |
| **Bronchopulmonary dysplasia**, n (%) | No | 10 (90.9) | 23 (76.7) | 0.308[b] |
| | Yes | 1 (9.1) | 7 (23.3) | |
| **Periventricular/ intraventricular hemorrhage**, n (%) | No | 10 (90.9) | 23 (76.7) | 0.308[b] |
| | Yes | 1 (9.1) | 7 (23.3) | |
| **Grade of periventricular/ intraventricular hemorrhage**, Median (min-max) | | 0 (0-3) | 0 (0-4) | 0.308[a] |
| **Retinopathy of the prematüre**, n (%) | No | 4 (36.4) | 8 (26.7) | 0.727[b] |
| | Yes | 3 (27.3) | 12 (40.0) | |
| | Not required | 4 (36.4) | 10 (33.3) | |
| **Stage of retinopathy of the prematüre**, Median (min-max) | | 1 (1-2) | 1 (1-3) | 0.789[a] |
| **Pulmonary hypoplasia**, n (%) | No | 10 (90.9) | 28 (93.3) | 0.762[b] |
| | Yes | 1 (9.1) | 2 (6.7) | |
| **Intermittent extubation**, n (%) | No | 10 (90.9) | 16 (53.3) | 0.077[b] |
| | Intermittent oxygen | 0 (0.0) | 6 (20) | |
| | Intermittent extubation | 1 (9.1) | 8 (26.7) | |
| **Neonatal sepsis**, n (%) | No | 9 (81.8) | 28 (93.3) | 0.271[b] |
| | Yes | 2 (18.2) | 2 (6.7) | |

[a]=Mann Withney U test , [b] = Chi-square test, Bold is statistically significant

and no significant differences were observed between groups in mortality rate, day of hospitalization in the NICU, rate of necrotizing enterocolitis (NEC), patent ductus arteriosus (PDA), respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), periventricular/intraventricular hemorrhage (P/IVH), retinopathy of prematurity (ROP), and neonatal sepsis were all found to be statistically insignificant (p>0.05).
Consequently, the number of cases resulting in termination or loss of pregnancy in the groups was 121 (89%) and 23 (51.2%), respectively (p < 0.001). Of the 55 surviving fetuses presented in Table 3, 15 (75%) live fetuses remained in Group 1, and 22 (62.8%) live fetuses in Group 2 (p=0.36). In conclusion, only 37 of the fetuses survived, representing 11% of cases in Group 1 and 48.8% of cases in Group 2 (p < 0.001).

## DISCUSSION

This study compared maternal and neonatal outcomes of cases with pPPROM before and after 22nd week of gestation. The duration of the latent period, the gestational age at birth, the number of fetuses born over 500 g, and the rate of complications such as chorioamnionitis and postpartum hemorrhage were found to be higher in Group 2. In Group 1, the rate of termination of pregnancy (TOP) was higher, but in fetuses born over 500g, the duration of the latent period and the gestational age at birth were found to be higher. Furthermore, better neonatal outcomes with higher Apgar scores and lower rates of NICU admission were also observed in Group 1.

ACOG recommends that cases of pPPROM be offered immediate delivery and expectant care and that patients receive the most ap-

propriate counseling regarding how management decisions affect the health of the mother and fetus (1). In our early pregnancy service, we provided verbal and written counseling for pPPROM cases by offering both options prélabor managed all cases by considering both the patient's decisions and maternal and fetal factors. Consequently, 58% of all pPPROM cases resulted in TOP, and the number of cases who did not prefer TOP and required expectant management was significantly higher in Group 2 (27.9% vs 84.4%, p < 0.001). As a result, the latency period was longer in Group 2, chorioamnionitis was detected at a higher rate of 6.821 times (95% CI, 1.630-28.533) and postpartum hemorrhage was detected at a higher rate of 9.643 times (95% CI, 0.977-95.176) compared to the other group in this study (p<0.05).

In the study conducted by Sklar et al., which examined 350 cases of pPPROM, 48.1% of cases opted for TOP as the initial management strategy. Women who chose TOP had 4.1 times the odds of developing chorioamnionitis compared to women who chose expectant management (38.0% vs. 9.3%) and the odds of developing chorioamnionitis were 13.0 % (95% CI, 2.03-8.26), while the odds of postpartum hemorrhage were 2.44 times higher (95% CI, 1.13-5.26) (7). Approximately 40% to 50% of women who choose expectant management experience maternal morbidity such as infection, retained placenta, and/or hemorrhage (2,8), and in deliveries of pre-viable pregnancies compared to term pregnancies; this is approximately six times more likely to result in poor outcomes, including chorioamnionitis, blood transfusion, hysterectomy, and/or admission to the maternal intensive care unit (ICU) (9). In this study, no cases of hysterectomy, maternal ICU admission, or maternal death were observed, and no significant differences were identified between the groups in complications, including sepsis, blood transfusion, placental rest, and endometritis.
Several studies have demonstrated that neonatal survival rates in cases of pPPROM range from 0% to 56%, while severe neonatal morbidity rates range from 40% to 100% (3,8,10-13). In this study, the overall neonatal survival rates and the overall survival without serious neonatal morbidity were found to be 20.4% and 4.97%, respectively, in all pPPROM cases. In Group 2, where pPPROM was detected between the 22nd and 24th weeks of gestation, the overall neonatal survival rates were 6.563 times higher than in the other group. Similarly, in the study by Kibel et al. of 140 fetuses diagnosed with pPPROM at 20-24 weeks of gestation, it was found that gestational age at preterm PROM of 22 weeks or greater was significantly associated with overall survival and survival without severe neonatal morbidity. The adjusted odds ratio (aOR) for survival and survival without severe neonatal morbidity with latency periods was found to be 12.2 and 4.8, respectively (10). However, in the study conducted by Lorthe et al. with 427 fetuses (331 singletons and 96 twins) in cases of pPPROM) at 22-25 weeks gestation, 38.8% were survivors at discharge without severe morbidity, and 46.4% were survivors at 2 years without cerebral palsy (13). Although the NICU admission rate was significantly higher in Group 2 (55% vs. 85.7%) for viable fetuses weighing over 500 g (p=0.002), there was no difference in neonatal outcomes between the two groups. This included PDA, P-IVH, ROP, RDS, PBD, neonatal sepsis, and mortality rate (p<0.05).

A number of risk factors for PPROM have been identified (1). Among these are factors that may be amenable to modification, including smoking, a body mass index (BMI) of less than 18.5 kg/m$^2$, diabetes mellitus, and poor nutrition. Others are related to the maternal obstetric history, including previous preterm labor (PTB), prior cervical conization or a second-trimester short cervical length (CL), and second-trimester vaginal bleeding (14). To date, no preventive treatment for PPROM has been documented. However, a recent study suggests that low-dose aspirin prophylaxis might reduce the prevalence of PPROM in women screened at high risk for preeclampsia (15). A recent study by El-Achi et al. proposed the development of a predictive model for the first trimester, utilizing information currently collected at 11–14 weeks of gestation, though its screening performance was modest. The study found that maternal factors predictive of PPROM included nulliparity, pre-existing diabetes mellitus (DM), maternal age group and BMI category (16). However, further analysis revealed that the uterine artery pulsatility index (UAPI) and biochemical parameters at first-trimester screening (PAPP-A, free βHCG) were not statistically significant (16). The improved early prediction of women at high risk for PPROM is important for further investigation of potential preventive interventions. The prediction and prevention of pPPROM pregnancies are also significant in view of the maternal and fetal consequences. Further studies are required on this subject.

Due to the retrospective design of the study and the pregnancies that resulted in TOP, it was not possible to observe the actual effect of pPPROM in all pregnancies in a prospective manner. Nevertheless, the inclusion of NICU follow-up and results of viable fetuses as a subgroup in pPPROM cases represents a significant strength of this study. Furthermore, the maternal, obstetric, and neonatal outcomes of a considerable number of cases of pPPROM before and after the 22nd week of gestation were compared.

## CONCLUSION

A shorter latent period is observed in pPPROM cases before the 22nd week of gestation, which is attributed to a higher rate of TOP. Nevertheless, if a viable live birth weighing over 500 g occurs in this group, birth occurs at an older gestational age with a longer latent period, resulting in fewer NICU admissions with higher Apgar scores. In pPPROM cases between 22 and 24 weeks of gestation, a prolonged latent period was observed due to a lower rate of TOP and a higher rate of maternal complications, including chorioamnionitis and postpartum hemorrhage. Nevertheless, in this group, despite a higher rate of viable live births over 500 g, birth occurs at an earlier gestational age with a shorter latent period, resulting in more NICU admissions with lower Apgar scores. Nevertheless, there was no discernible difference in the neonatal outcomes of the fetuses admitted to the NICU in both groups.

Conflict of interest: The authors declare no conflict of interest.
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Ethical statement: This study was approved by the local ethics committee as a retrospective study of Etlik Zübeyde Hanım Maternity and Women's Health Teaching and Research Hospital, Ankara, Turkiye (14/05/2020, with approval number 07).

### Author Contributions

YAR: Project Development, Data Collection or Management, Data Analysis, Manuscript Writing/Editing
FBF: Project Development, Data Collection and Management, Data Analysis, Manuscript Writing/Editing
AA, SST: Project Development, Data Collection and Management, Manuscript Writing/Editing
AKÖ: Data Collection and Management, Project Development
SYE, SÖ: Data Management, Data Analysis, Manuscript Writing/Editing
SE, YEÜ: Supervision, Manuscript Writing/Editing
All authors read and approved of the final manuscript.

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# YAYIN KURALLARI

## GENEL BİLGİLER

Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi; Ankara Eğitim ve Araştırma Hastanesi' nin süreli bilimsel yayın organıdır. Nisan, ağustos ve aralık aylarında olmak üzere yılda üç sayı olarak yayımlanır. Tıbbın her dalı ile ilgili olabilecek retrospektif, prospektif veya deneysel araştırma, (davetli) derleme, olgu sunumu, editoryal yorum / tartışma, editöre mektup, tıbbi ve cerrahi tedavi teknikleri, tıbbi kitap değerlendirmeleri ve tıp gündemini belirleyen güncel konuları yayımlayan, ulusal ve uluslararası tüm tıp camiasına ulaşmayı hedefleyen bilimsel bir dergidir.

## AMAÇ VE KAPSAM

Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi; Ankara Eğitim ve Araştırma Hastanesi' nin süreli bilimsel yayın organı olup 1966 yılında yayın hayatına başlamıştır. Nisan, ağustos ve aralık aylarında olmak üzere yılda üç sayı olarak yayımlanır.
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Dergiye gönderilen makale biçimsel esaslara uygun ise editör ve en az iki danışmanın incelemesinden geçip gerek görüldüğü takdirde, istenen değişiklikler yazarlarca yapıldıktan sonra yayımlanır.
Amacımız, bilime katkı yapmaya çalışan değerli araştırmacılarımızın yoğun emeklerinin eseri olan çalışmalarının karar verme ve yayımlanma sürecini en kısa sürede sonuçlandırmaktır. Dergimizin bilimsel kalitesini yükseltmek için yazar, hakem ve okuyucularımızın değerli görüş, öneri, bildirim ve yapıcı eleştirilerine açık olduğumuzu, bunlara gereken hassasiyeti gösterdiğimizi bildiririz.

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Addressi: .....
Phone: ..... Fax: .....
e-mail: .....

9. .....
Signature: .....
Addressi: .....
Phone: ..... Fax: .....
e-mail: .....

10. .....
Signature: .....
Addressi: .....
Phone: ..... Fax: .....
e-mail: .....

11. .....
Signature: .....
Addressi: .....
Phone: ..... Fax: .....
e-mail: .....

12. .....
Signature: .....
Addressi: .....
Phone: ..... Fax: .....
e-mail: .....

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Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi intihale sıfır tolerans politikası izlemektedir. Bu politikanın bir sonucu olarak Dergiye gönderilen tüm çalışmalar yazarları tarafından lisanslı bir uygulama (iThenticate ya da Turnitin) ile taranmalı ve benzerlik raporu makale dosyaları ile birlikte sisteme yüklenmelidir. Kabul edilebilir benzerlik oranı %20' nin altıdır. Belirlenen oranın üzerinde benzerliğe sahip yazılar değerlendirmeye alınmadan reddedilir.

## EPİDEMİYOLOJİK VE İSTATİSTİKSEL DEĞERLENDİRME

İstatistiksel inceleme yapılan tüm retrospektif, prospektif ve deneysel araştırma makaleleri dergiye gönderilmeden önce biyoistatistik incelemelerin geçerliliği ve gücü açısından değerlendirilmeli ve uygun plan, analiz ve raporlama ile belirtilmelidir. Editörler, gerekli gördükleri takdirde istatistiksel incelemeye ait ham verileri isteme haklarını saklı tutarlar

## YAZIM DİLİ YÖNÜNDEN DEĞERLENDİRME

Derginin yayın dili Türkçe ve İngilizce' dir. Türkçe çalışmalarda Türk Dil Kurumu'nun Türkçe sözlüğü veya "https://sozluk.gov.tr/" adresinde yer alan çevrimiçi sözlük esas alınmalıdır. Varsa ilgili branş derneklerinin kendi terim sözlükleri de kullanılabilir. İngilizce çalışmalar ve İngilizce özetler, dergiye gönderilmeden önce İngilizce dil uzmanı ve/veya ana dili İngilizce olan (native speaker) bir kişi tarafından değerlendirilmelidir. Çalışmayı, İngilizce yönünden değerlendiren kişi yazarlardan biri değil ise bu kişinin ismi makalenin sonunda bulunan "Teşekkür (Acknowledgement)" bölümünde belirtilmelidir. Dergimize yayımlanmak üzere gönderilen ve değerlendirme sonucunda yayıma kabul edilen çalışmalardaki yazım ve dilbilgisi hatalarının yazarlar tarafından düzeltilmesi gerekmekle beraber, gerek görüldüğü taktirde, çalışmanın bilimsel içeriğine dokunmadan, redaksiyon komitesi tarafından ayrıca düzeltilebilir. Yazarlar bu düzeltmeleri kabul etmiş sayılırlar.

## MAKALE DEĞERLENDİRME SÜRECİ

Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi'ne gönderilen çalışmalardan yayımlanabilir olduğu düşünülenler sıkı bir double-blind peer review sürecinden geçirilmektedir.
Dergiye yayımlanması dileğiyle gönderilen her çalışma, yazım kurallarına uygunluk açısından bir ön incelemeye tabi tutulmaktadır. Ön incelemeden geçen çalışmalara konusuna uygun olarak bir alan editörü belirlenir ve çalışma bu editöre yönlendirilir.
İlgili Alan editörü çalışmaya en az iki hakem atayarak çalışmanın bilimsel değerlendirme sürecini başlatır. Hakem seçimi çalışmanın konusuna göre yapılır.
Çalışmada yer alan yazarlarının kimlikleri, çalıştıkları kurumlar ve çalışmanın yapıldığı kurum/kurumlar hakemlerden gizli tutulmaktadır. Hakemler, dolduracakları "makale değerlendirme formu" ile alan editörlerine, çalışmanın bilimsel değeri, metodolojisi, istatistiksel değerlendirmelerin yerindeliği, verilerin tartışılmasının yeterliliği ve varılan sonuçların verilerle uyumlu olup olmadığı gibi konularda kendi bilimsel görüşlerini iletirler. İstatistik açısından daha detaylı incelenmesi gerektiği düşünülen çalışmalar istatistik uzmanlarına gönderilir. İlgili Alan editörü hakem değerlendirme formlarını da kapsayan genel bir değerlendirme ile kanaatini Dergi Editörler Kurulu'na sunar.
Hakem yorumları, değerlendirmeleri, eleştiri ve öneriler elektronik olarak çalışmanın sorumlu yazarına iletilir. Çalışmaların hakeme gönderilmesinde olduğu gibi bu süreçte de hakem kimlikleri yazara iletilmez ve gizli tutulur. Hakemler tarafından istenen düzeltmelerin yapılması için yazarlara geri gönderilen çalışmalarda Derginin daha önceden ilan ettiği süre içinde gerekli düzeltmelerin yapılarak, yeniden değerlendirmeye sunulması beklenir.
İstenen düzeltmelerin yapılması için geri gönderilen çalışmaların takip sorumluluğu yazarlara aittir. Hakem önerileri doğrultusunda düzeltilip derginin belirlediği süre içinde sisteme yüklenmeyen çalışmalar reddedilecektir.

## YAYIN PLATFORMU

Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi, elektronik ortamda TÜBİTAK-DERGİPARK online bilimsel dergi yayıncılık platformu üzerinden yayımlanmaktadır.
Derginin web adresi: https://dergipark.org.tr/tr/pub/aeahtd
Dergiye çalışma gönderimi ve süreç takibi DERGİPARK sistemi üzerinden yürütülmektedir. Çalışma gönderebilmek için öncelikle DERGİPARK platformuna üye olunmalıdır.
Derginin yayın kurallarına https://dergipark.org.tr/tr/pub/aeahtd/writing-rules adresinden elektronik olarak ulaşılabilir.
Çalışmanın DERGİPARK' a yüklenmesini takiben, Derginin e-posta adresine de makalenin DERGİPARK ID numarası ve başlığını da içeren bir bilgilendirme e-postası gönderilmesi gerekmektedir.
İletişim için e posta adresi: ankarahastanesidergisi@gmail.com

## YAYIN HAKKI


Yazarlar, "Yayın Hakları Formu" nu doldurup, çalışma ile birlikte göndermelidirler. Yayın Hakları Formu olmadan gönderilen çalışmalar değerlendirmeye alınmayacaktır.

## YAZI ÇEŞİTLERİ

Dergiye yayımlanmak üzere gönderilecek yazı çeşitleri şu şekildedir.

**EDİTÖRDEN:**
Dergide yayımlanarak bilimsel çevrelere ulaştırılmasına gerek görülen editör, editör yardımcıları ya da davetli yazar (lar) tarafından kaleme alınan kısa yazılardır.

**MAKALE YORUMU:**
Yayımlanan orijinal araştırma makaleleri ile ilgili olarak araştırmanın yazarlarından olmayan, araştırma konusunun uzmanı farklı bir bilim insanı tarafından yapılan değerlendirmedir.

**ÖZGÜN ÇALIŞMA:**

Prospektif ya da retrospektif her türlü deneysel ve klinik çalışmalar yayımlanabilmektedir.
Özgün çalışmalar aşağıdaki bölümlerden oluşmalıdır:
**Özet** (**Abstract**): Türkçe ve İngilizce olarak ayrı ayrı en fazla 300 kelime içermelidir. Amaç (aim), gereç ve yöntem (material and method), bulgular (results), sonuç (conclusion) bölümlerinden oluşmalıdır.
**Anahtar Kelime**ler (**Keywords**): Türkçe ve İngilizce olmak üzere en az 3, en fazla 5 kelimeden oluşmalı, Medical Subject Headings (MeSH)' e uygun olarak verilmelidir.
Giriş (Introduction): çalışmanın kısa ve anlaşılır şekilde amacının açıklandığı kısımdır.
Gereç ve Yöntem (Material and Method): Çalışmada kullanılan gereç, yöntem, istatistik değerlendirme vb nin detaylı şekilde açıklandığı kısımdır. Etik kurul onayı

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alınması gereken çalışmalar için etik kurul onayının alındığı kurum, tarih ve sayısı açık bir şekilde bu kısımda belirtilmelidir. Etik kurul onayı / bilgilendirilmiş onam formu olmayan yazılar değerlendirmeye alınmadan reddedilecektir.
Bulgular (Results): Çalışmada elde edilen bulguların detaylı şekilde açıklandığı kısımdır
Tartışma (Discussion): Elde edilen bulguların güncel literatür eşliğinde tartışıldığı kısımdır.
Sonuç (Conclusion): Elde edilen bulgular ve tartışma sonunda yazarların vardığı sonucun açıklandığı kısımdır.
Teşekkür (**Acknowledgements**): Çalışmaya katkıda bulunmakla beraber yazarlar içinde yer almayan kişilerle çalışmada katkısı olan kurum ve kuruluşların açıklandığı ve kendilerine teşekkür edilen kısımdır. Çalışmada herhangi bir kişi, kurum ya da kuruluştan maddi destek sağlanmış ise bu bölümde belirtilmelidir. Çalışmada herhangi bir çıkar çatışması olup olmadığı da bu bölümde açıklanmalıdır.
Kaynaklar (References): Makale içinde geçiş sırasına göre tüm kaynakların verildiği kısımdır.

**DERLEME:**

Dergi sadece davetli derleme kabul etmektedir. Editörler kurulu tarafından belirlenen tıbbi bir konuda en son tıbbi gelişmeleri de kapsayacak şekilde davet edilen yazar ya da yazarlar tarafından hazırlanır. Yazar / yazarların ilgili konu ile ilgili basılmış yayınlarının olması özellikle tercih nedenidir. Derleme makalelerinin yapısı aşağıdaki bölümlerden oluşmalıdır:
**Özet** (**Abstract**): Türkçe ve İngilizce olarak ayrı ayrı en fazla 250 kelime içermelidir. Derleme makalelerin özetlerinde bölüm olması zorunlu değildir.
**Anahtar Kelime**ler (**Keywords**): Türkçe ve İngilizce olmak üzere en az 3, en fazla 5 kelimeden oluşmalı, MeSH İndeksine uygun olarak verilmelidir.
Temel bölümler ardışık olarak numaralandırılmalıdır. Alt bölümler 1.1, 1.2 gibi alt başlıklarla belirtilmelidir. Derlemelerin başlıkları içerdikleri konuyu açıklayıcı olmalıdır.
Kaynaklar (References): Makale içinde geçiş sırasına göre tüm kaynakların verildiği kısımdır.

**OLGU SUNUMU:**

Nadir görülen, tanı ve tedavide farklılık ya da yenilik gösteren olguların sunulduğu makalelerdir. Yeterli sayıda fotoğraflarla ve şemalarla desteklenmiş olmalıdır. Olgu sunumlarının yapısı aşağıdaki gibi olmalıdır:
**Özet** (**Abstract**): Türkçe ve İngilizce olarak ayrı ayrı en fazla 150 kelime içermelidir. Bölümsüz olmalıdır.
**Anahtar Kelime**ler (**Keywords**): Türkçe ve İngilizce olmak üzere en az 3, en fazla 5 kelimeden oluşmalı, MeSH İndeksine uygun olarak verilmelidir.

Giriş (Introduction): Olgunun sunum gerekçesinin kısaca belirtildiği, tanı, tedavi, laboratuvar verilerinin detaylı olarak açıklandığı kısımdır.
Tartışma (Discussion): Olgunun tartışıldığı kısımdır.
Kaynaklar (References): En fazla 12 tane olmalıdır.
Olgu sunumunda sunulan hastalardan (18 yaşından küçükler için yasal vasisinden) "bilgilendirilmiş onam formu (informed consent)" alınmalı ve çalışma içeriğinde belirtilmelidir.

**EDİTÖRE MEKTUP:**

Son bir yıl içinde dergide yayımlanan makaleler ile ilgili olarak, okuyucuların değişik görüş, tecrübe ve sorularını içeren en fazla 500 kelimelik yazılardır. Başlık ve özet bölümleri yoktur. Kaynak sayısı 5 ile sınırlıdır. Hangi makaleye (sayı, tarih verilerek) ithaf olunduğu belirtilmeli ve sonunda yazarın ismi, kurumu, adresi bulunmalıdır. Mektuba cevap, editör veya makalenin yazar(lar)ı tarafından, yine dergide yayımlanarak verilir.

**TIBBİ EĞİTİM:**

Güncel tıbbi konularda okuyucuya mesaj veren son klinik ve laboratuvar uygulamaların da desteklediği bilimsel makalelerdir. Yapısı aşağıdaki gibi olmalıdır:
**Özet** (**Abstract**): Türkçe ve İngilizce olarak ayrı ayrı en fazla 150 kelime içermelidir.
Temel bölümler ardışık olarak numaralandırılmalıdır. Alt bölümler 1.1, 1.2 gibi alt başlıklarla belirtilmelidir.
Kaynaklar (References)

**TIBBİ KİTAP DEĞERLENDİRMELERİ:**

Güncel değeri olan ulusal veya uluslararası kabul görmüş kitapların değerlendirmeleridir.

**YAZIM KURALLARI**

Yazım kurallarına uygun olmayan çalışmalar değerlendirmeye alınmayacaktır. Derginin yazım kurallarına uygun taslak formlara https://dergipark.org.tr/tr/pub/aeahtd/writing-rules adresinden ya da Derginin basılı halinin son kısmından ulaşılabilir. Dergiye yayınlanması için gönderilen çalışmalarda aşağıdaki biçimsel esaslara uyulmalıdır.
Çalışma, PC uyumlu bilgisayarlarda Microsoft Word Programı ile "Times New Roman" yazı formatında, 11 punto büyüklüğünde ve 1,5 satır aralığı verilerek yazılmalıdır. Özgün araştırma çalışmalarının toplam uzunluğu 5000 kelimeyi geçmemelidir.
Çalışmalar, Derginin internet sitesinde "formlar" kısmında, basılı halinde son sayfalarında yer alan "çalışma gönderimi için son kontrol listesi" ne göre kontrol edildikten sonra sisteme yüklenmelidir.

**Editöre Sunum Sayfası:**
Çalışmadan ayrı bir sayfa olarak "editöre sunum" başlığı ile gönderilmelidir. Gönderilen çalışmanın kategorisi, daha önce başka bir dergiye gönderilmemiş olduğu, varsa çalışmayı maddi olarak destekleyen kişi ve kuruluşlar ve bu kuruluşların yazarlarla olan ilişkileri, çalışma İngilizce ise İngilizce yönünden kontrolünün, araştırma makalesi ise biyoistatiksel kontrolünün yapıldığı belirtilmelidir. Örnek sayfaya Derginin internet sitesinde "formlar" kısmından ya da Derginin basılı halinin son sayfalarından ulaşılabilir.

**Başlık Sayfası:**
Çalışmadan ayrı bir sayfa olarak "başlık sayfası" başlığı ile gönderilmelidir. Makalenin başlığı (Türkçe ve İngilizce), tüm yazarların ad- soyadları, kurumları, ORCID numaraları, telefon numaraları, e-posta ve yazışma adresleri belirtilmelidir. Başlık sayfasında sorumlu (başlıca) yazar belirtilmelidir. Çalışma daha önce herhangi bir bilimsel toplantıda sunulmuş ise tebliğ yeri ve tarihi belirtilmelidir. Örnek sayfaya Derginin internet sitesinde "formlar" kısmından ya da Derginin basılı halinin son sayfalarından ulaşılabilir.

**Özetler:**
Yazı çeşitleri bölümünde belirtilen şekilde Türkçe ve İngilizce hazırlanarak, makale metni ile birlikte gönderilmelidir.

**Anahtar Kelimeler:**
En az 3, en fazla 5 adet, Türkçe ve İngilizce yazılmalıdır. Anahtar kelimeler 'Medical Subject Headings (MeSH)' e uygun olarak verilmelidir (www.nlm.nih.gov/mesh/MBrowser.html).Anahtar kelimeler özet sayfasının en alt kısmında yer almalıdır.

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**Kısaltmalar:**
Kelimenin ilk geçtiği yerde parantez içinde verilir ve tüm metin boyunca aynı kısaltmalar kullanılır. Uluslararası kabul görmüş kısaltmalar için "Bilimsel Yazım Kuralları" kaynağına başvurulabilir.
**Özet** kısmında kısaltma kullanılamaz.
Herkes tarafından genel kabul görmüş ve kısaltma hali ile kullanılan kelimeler (DNA, RNA vb.) açık hali verilmeden de kullanılabilir.

**Şekil, Resim, Tablo ve Grafikler:**
Şekil, resim, tablo ve grafikler çalışmada işleniş sırasına uygun olarak numara verilip, kaynaklar kısmından sonra her biri ayrı sayfada olmak üzere gönderilmelidir.
Şekil, resim, tablo ve grafiklerin metin içinde geçtiği yerler ilgili cümlenin sonunda belirtilmelidir. Şekil ve resimler için altında, tablo ve grafikler için üstünde olacak şekilde açıklamaları eklenmelidir.
Çalışmanın Word dosyasına eklenecek şekil, resim, tablo ve grafik, 1 MB dan büyük ise, ayrı bir jpg dosyası olarak ta sisteme eklenebilir. Bu durumda, jpg dosyasına, çalışmanın Word şeklinin içinde geçen numaralara göre isim verilmelidir. Baskı kalitesinde standardın sağlanabilmesi için şekil, resim, tablo ya da grafiklerin en az 300 dpi çözünürlükte hazırlanarak sisteme eklenmesi gerekmektedir.
Şekil, resim, tablo ve grafiklerde kullanılan kısaltmalar ilgili görselin açıklamasında belirtilmelidir.
Şekil, resim ve grafikler, en fazla 16*20 cm, en az 8 cm büyüklükte olmalı ve büyütülerek ya da küçültülerek deforme edilmemiş olarak gönderilmelidir.
Daha önce başka bir yerde basılmış ya da yayımlanmış şekil, resim, tablo ve grafik kullanılmış ise yayın hakkı sahibinden yazılı izin alınmalıdır. Bu izin şekil, resim, tablo ve grafik açıklamasında belirtilmelidir.
Çalışma içerisinde ve eklerinde geçen uzunluk, yükseklik, hacim ölçümleri metrik ünitelerle (metre, kilogram ya da litre) ve bunların ast ve üst katları şeklinde verilmelidir. Sıcaklık ölçümleri derece santigrad (0 C), kan basıncı ölçümleri milimetre civa olarak (mmHg) belirtilmelidir. Laboratuvar değerleri International System of Units' e (SI) uygun olarak belirtilmelidir. SI karşılığı olmayan değerler metin içinde açıklanmak kaydıyla kullanılabilir.
Dört ve üzeri haneli sayılarda binlik basamaklar arasında boşluk bırakılmalıdır (Örnek: 1 000 000). Çift haneli sayılar, yazı içinde rakamla, tek haneli sayılar ise yazıyla verilmelidir. Ancak değerleri belirten ifadelerde tek haneler rakamla verilmelidir (Örnek: 1 cm). Yazı içinde ve tablolarda yüzdelik değerler virgülden sonra iki basamak, p değerleri virgülden sonra üç basamak olarak verilmelidir. Yazı, tablo ve şekillerde yer alan ondalık sayılar Türkçe yazılarda virgül ile İngilizce yazılarda nokta ile ayrılmalıdır.

**Kaynaklar:**
Ankara Eğitim ve Araştırma Hastanesi Tıp Dergisi, kaynak gösterim şekli olarak AMA standartlarını kabul etmektedir. AMA standartlarıyla ilgili detaylı bilgiye https://www.bcit.ca/files/library/pdf/bcit-ama_citation_guide.pdf adresinden ulaşılabilir.
Dergiye gönderilecek çalışmalarda kaynaklar makalede yer alış sırasına göre yazılmalı ve metinde cümle sonunda noktalama işaretlerinden hemen önce parantez içinde belirtilmelidir. (örnek: ..... (kaynak no).)
Çalışmaya katkı veren yazar sayısı 6 veya daha fazla ise ilk 6 isim yazılıp Türkçe kaynaklarda "ve ark.", İngilizce makalelerde "et al" eklenmelidir.
Yazarlar, kaynakların güncellik ve geçerliliğinden sorumludur.
Kongre bildirileri ve tezler ancak çok zorunlu ise kaynak olarak gösterilebilir.
Kişisel deneyimler ve basılmamış yayınlar ancak tartışma kısmında kullanılabilir, kaynak olarak gösterilemez.
İnternet adresleri tek başına kaynak olarak gösterilemez (https://dergipark.org.tr/tr/pub/aeahtd gibi).
Elektronik ortamda yayımlanmış makaleler ilgili makalenin web adresi ve alıntı yapıldığı tarih belirtilerek kaynak gösterilebilir. Elektronik ortamdaki kaynak kitaplar için de aynı kurallar geçerlidir.

Kaynakların yazımı için örnekler (Noktalama işaretlerine lütfen dikkat ediniz):

Makale için;
Yazar (lar) ın soyad (lar) ı ve isim (ler) inin baş harf (ler) i, makale ismi, dergi ismi, yıl, cilt, sayı, sayfa numarası belirtilmelidir. Varsa DOI ve /veya PMID numarası belirtilebilir (zorunlu değildir)
Altı ve daha fazla yazar varsa: Wells CR, Townsend JP, Pandey A, Moghadas SM, Krieger G, Singer B, et al. Optimal COVID-19 quarantine and testing strategies. Nat Commun. 2021;12(1):356. doi: 10.1038/s41467-020-20742-8. PMID: 33414470; PMCID: PMC7788536.
Altı ve daha az yazar varsa: Özcan NN, Özçam G, Koşar P, Özcan A, Başar H, Kaymak Ç. Correlation of computed tomography, magnetic resonance imaging and clinical outcome in acute carbon monoxide poisoning. Braz J Anesthesiol. 2016; 66(5): 529-32. doi: 10.1016/j. bjane.2014.05.006

Kitap için;
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Türkçe yayın: Sözen TH. Bruselloz. Topçu AW, Söyletir G, Doğanay M, editörler. İnfeksiyon Hastalıkları ve Mikrobiyoloji. Cilt 1. Sistemlere Göre İnfeksiyonlar.1. Baskı, İstanbul: Nobel Tıp Kitabevleri; 2002.s.636-42
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Musculoskeletal MRI Atlas. Available at: http://www.gla.med.va.gov/mriatlas/lndex.html. Erişim tarihi 25.09.2018. (Accessed September 25,2018.)

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