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İlk olarak, çocuk acil servisinde kuduz profilaksisi yapılan hastaların değerlendirilmesine dair çalışmada, saha deneyimlerinin pratik yansımalarını bulacaksınız. Ardından, Türkiye sağlık sektöründe iş kazalarına ilişkin TÜİK ve SGK verileri temelinde hazırlanmış güncel değerlendirme, mesleki risklerin boyutlarını gözler önüne sermektedir.

Sayımızda ayrıca, uyarılmamış nöbet sonrası çocuklarda nöbet tekrarının risk faktörlerini ele alan araştırma, klinik açıdan önemli çıkarımlar sunarken; FMF hastalarında tedaviye uyumu inceleyen Orta Anadolu verileri, kronik hastalık yönetimine dair gerçek yaşam bulgularını ortaya koymaktadır.

Güncel konulardan biri olan mikrobiyota ve diyabet ilişkisini mekanistik yaklaşımlar eşliğinde değerlendiren derlememiz, translasyonel araştırmalar açısından değerli bir katkı niteliğindedir. Ayrıca, üriner inkontinans ile başvuran bir çocukta nadir görülen spinal ependimom olgusu, klinisyenlere tanı sürecinde dikkat edilmesi gereken noktaları hatırlatmaktadır.

Her zaman olduğu gibi hedefimiz; bilimsel üretimi desteklemek, klinik uygulamalara katkı sağlamak ve araştırmacılar için tartışma zemini oluşturmaktır. Bu sayımıza katkıda bulunan yazarlarımıza, titiz değerlendirmeleri için hakemlerimize ve değerli okuyucularımıza teşekkür ediyor, keyifli ve ufuk açıcı okumalar diliyoruz.

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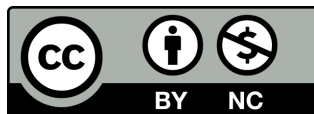
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HAKKINDA

Türk Tıp Dergisi, 2007 yılında Ankara Atatürk Eğitim ve Araştırma Hastanesi bünyesinde tıp dünyasıyla tanışmış ve kendine saygın bir yer edinmeyi başarmıştır. Dergimiz, Ankara Atatürk Eğitim ve Araştırma Hastanesi'nin taşınma sürecinde verdiği kısa aranın ardından, imtiyaz haklarının Ankara Yıldırım Beyazıt Üniversitesi Yenimahalle Eğitim ve Araştırma Hastanesi tarafından devir alınmasıyla kaldığı yerden ve daha yenilikçi vizyonuyla yayın hayatına devam etmektedir.

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Türk Tıp Dergisi / Turkish Medical Journal

Cilt / Volume: 10 | Sayı / Issue: 3 | Yıl / Year: 2025

İÇİNDEKİLER | CONTENTS

ARAŞTIRMA MAKALESİ | RESEARCH ARTICLE

87-91 ÇOCUK ACİL SERVİSİNDE KUDUZ PROFİLAKSİSİ YAPILAN HASTALARIN DEĞERLENDİRİLMESİ

Evaluation of Patients Receiving Rabies Prophylaxis in the Pediatric Emergency Department

Berrak Naz KIRGIL, Halise AKÇA, Ayşegül Neşe ÇITAK KURT

92-101 OCCUPATIONAL ACCIDENTS IN TURKEY'S HEALTH SECTOR: A CURRENT ASSESSMENT BASED ON TURKSTAT AND SGK DATA

Türkiye'de Sağlık Sektöründe İş Kazaları: TÜİK ve SGK Verileriyle Güncel Bir Değerlendirme

Harika ŞEN

102-107 RISK FACTORS FOR SEIZURE RECURRENCE IN CHILDREN FOLLOWING AN UNPROVOKED SEIZURE

Uyarılmamış Nöbet Sonrasında Çocuklarda Nöbet Tekrarı İçin Risk Faktörleri

Emregül IŞIK, Deniz YILMAZ, Yahya Kemal Yavuz GÜRER

108-114 TREATMENT ADHERENCE IN FAMILIAL MEDITERRANEAN FEVER PATIENTS: REAL-LIFE DATA FROM CENTRAL ANATOLIA

FMF Hastalarında Tedaviye Uyum: Orta Anadolu'dan Gerçek Yaşam Verileri

Özlem KARAKAŞ, Sualp Mete SEVİL, Dudu ÇELİK TAM

DERLEME | REVIEW

115-123 MİKROBİYOTA VE DİYABET: GÜNCEL BULGULAR VE MEKANİSTİK YAKLAŞIMLAR

Microbiota and Diabetes: Recent Findings and Mechanistic Approaches

Kübra ÖĞÜT

OLGU SUNUMU | CASE REPORT

124-128 A RARE DIAGNOSIS IN A CHILD PRESENTING WITH URINARY INCONTINENCE: SPINAL EPENDYMOMA

Üriner inkontinans ile başvuran çocukta nadir bir tanı: Spinal ependimom

Hatice Zeynep TERZİ, Muhammed Mustafa GÜNEYLİOĞLU, İnci Pınar BİLEN,

Tayfun PEHLİVAN, Duygu BAYKAL, Murat TUTANÇ

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Evaluation of Patients Receiving Rabies Prophylaxis in the Pediatric Emergency Department

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ÖZET

Amaç: Kuduz, insan ve memeli hayvanların çoğunda ensefalit tablosu meydana getiren viral, zoonotik bir hastalıktır. Bu çalışmada Çocuk Acil Polikliniği'ne başvuran ve kuduz şüphesi bulunan olguların demografik bilgileri ve aşılanma şemalarının araştırılması amaçlanmıştır. **Yöntem:** Çalışmada Ankara Yıldırım Beyazıt Üniversitesi Yenimahalle Eğitim ve Araştırma Hastanesi Çocuk Acil Polikliniği'ne 1 Ocak – 31 Temmuz 2018 tarihleri arasında kuduz virüsüyle temas riski nedeniyle başvuran hastaların medikal kayıtları geriye dönük olarak incelendi. Hastaların demografik bilgileri, ısırık yerleri, maruziyet kaynakları, tetanoz / kuduz aşısı ve immünglobulin yapılma oranları kayıt altına alındı.

Bulgular: Çalışmaya dahil edilen 244 hastanın yaş ortalaması $93,7 \pm 53,6$ ay ve %53'ü kız cinsiyeteydi. Hastaların yaralanma yerleri en sık üst ekstremiteler (%57,1), en az ise gövde (%5,2) bölgesindeydi. Maruziyet kaynağının %61,6'sı kedi, diğerleri köpekti. Aylara göre bakıldığında vaka sayısının Nisan ayından itibaren arttığı görüldü. Tetanoz aşısı 36 hastaya (%14,8) yapıldı, tetanoz immünglobulin ihtiyacı olmadı. Toplam 244 hastaya 790 adet kuduz aşısı yapılırken, kuduz immünglobulinini 86 (%35,2) hastaya yapıldı. Hastaların 124'ü (%50,8) aşısı takvimini tamamladı. **Tartışma:** Kuduz erken dönem yara bakımı, yara yeri enfeksiyon kontrolü ve aşılanma ile %100 önlenabilir bir hastalıktır. Sağlık personeli ve halkın kuduz profilaksisi hakkında bilgilendirilmesi önem arz etmektedir.

Anahtar Kelimeler: Acil servis, Aşılanma, Çocuk, Kuduz

ABSTRACT

Objective: Rabies is a viral and zoonotic disease that causes encephalitis in humans and most mammals. This study aimed to investigate the demographic characteristics and vaccination schedule of patients who were admitted to the Pediatric Emergency Outpatient Clinic with suspected rabies exposure. **Method:** In this retrospective study, medical records of patients admitted to the Pediatric Emergency Outpatient Clinic of Yıldırım Beyazıt University Yenimahalle Education and Research Hospital between January 1 and July 31, 2018, due to potential exposure to the rabies virus, were reviewed. Data on demographics, bite sites, sources of exposure, and administration of tetanus/rabies vaccines and immunoglobulin were collected. **Results:** The mean age of the 244 patients included in the study was 93.7 ± 53.6 months, and 53% were female. The upper extremity was the most common injury site (57.1%), while the trunk was the least common (5.2%). Cats accounted for 61.6% of the exposure cases, while the remainder involved dogs. An increase in the number of cases was observed starting in April. Tetanus vaccine was administered to 36 patients (14.8%), and none required tetanus immunoglobulin. A total of 790 rabies vaccine doses were administered to 244 patients, and rabies immunoglobulin was given to 86 patients (35.2%). A full vaccination schedule was completed in 124 patients (50.8%). **Discussion:** Rabies is a 100% preventable disease through early wound care, infection control, and appropriate vaccination. Raising awareness among healthcare professionals and the general public about rabies prophylaxis is essential.

Keywords: Child, Emergency department, Rabies, Vaccination

GİRİŞ

Kuduz, insan ve memeli hayvanların çoğunda görülen Rhabdoviridae virüsün neden olduğu zoonotik, akut, ilerleyici bir ensefalomyelit tablosudur. Yılda yaklaşık 60.000 insanın ölümüne neden olup, belirti ve semptomlar ortaya çıkmaya başladıktan sonra genellikle ölümcüldür (Liu & Cahill, 2020). Ağırlıklı olarak Afrika ve Asya'daki kırsal kesim etkilenmekte olup vakaların yaklaşık %40'ını 15 yaşın altındaki çocuklar oluşturmaktadır (O'Brien & Nolan, 2019). İnsanlık tarihinin en eski hastalıklarından biri olan kuduz sadece insanları değil hayvanları da etkilemektedir. Tüm sıcakkanlı hayvanlar kuduz virüsü ile enfekte olsalar da hayvanların kuduz virüsüne karşı hassasiyeti birbirinden farklıdır. Aynı zamanda temas sonrası bulaştırma riski açısından da türler arasında fark bulunmaktadır (Aydın & Aydın, 2024; T.C. Sağlık Bakanlığı, 2019). Ülkemizde 1997-2017 yılları arasında toplam 6465 hayvanda kuduz tespit edilmiş olup kuduzla yakalanma ihtimali olan hayvan türleri; köpek, kedi, koyun gibi evcil hayvanlar (%90) ile birlikte kurt, tilki, çakal gibi yabani hayvanlardır (%10). Son yirmi yılda kuduz olan hayvanların ilk sırasında %43,6 ile köpeklerin olduğu görülmektedir. Köpek teması kuduz riski bakımından orta risk grubunda olmasına rağmen kuduzun bulaşmasındaki en önemli araçlardır. Bu nedenle evcil hayvan aşılması hayati önem taşımaktadır. Kuduzda inkübasyon süresi çok değişken olduğundan, riskli temas sonrasında aradan geçen süreye bakılmaksızın temas kategorize edilerek uygun profilaksiye olabildiğince erken başlanmalıdır. Uygun yara bakımı ile erken ve önerilere uygun yapılan temas sonrası profilaksi ile kuduz tamamen önlenabilir bir hastalıktır (T.C. Sağlık Bakanlığı, 2019). Kuduz aşısı erişkinlerde deltoid bölgeye, küçük çocuklarda uyluğun anterolateral bölgesine kas içine uygulanır. Gluteal bölgeye aşı enjeksiyonu, yeterli antikor yanıtı oluşturmadığı için yapılmamalıdır. Profilaksi gerektirmeyen durumlarda da yara temizliği, antibiyotik tedavisi, tetanoz profilaksisi gibi ihtiyaç duyulan tedavi yaklaşımları ihmal edilmemelidir. Türkiye'de riskli hayvan temasında uygulanan profilaksi, T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü'nün Rehberi'ne göre uygulanmaktadır (Şekil 1).

Bu çalışmada, Çocuk Acil Polikliniği'ne başvuran ve kuduz şüphesi bulunan olguların demografik bilgileri ve aşılama şemalarının araştırılması amaçlanmıştır.

GEREÇ VE YÖNTEMLER

Çalışmada Ankara Yıldırım Beyazıt Üniversitesi Yenimahalle Eğitim ve Araştırma Hastanesi Çocuk Acil Polikliniği'ne 1 Ocak – 31 Temmuz 2018 tarihleri arasında kuduz virüsüyle temas riski nedeniyle başvuran hastaların medikal kayıtları geriye dönük olarak incelendi. Hastaların demografik bilgileri, yaralanma yerleri, maruziyet kaynakları, tetanoz / kuduz aşısı ve immünglobulin yapılma oranları kayıt altına alındı. Bu çalışma için Ankara Yıldırım Beyazıt Üniversitesi Yenimahalle Eğitim ve Araştırma Hastanesinden yazılı onam alınmıştır.

İstatiksel Analiz: Verilerin analizi için Statistical Package for Social Sciences for Windows 22.0 (SPSS Inc.; Chicago, IL, ABD) programı kullanılmıştır. Tanımlayıcı istatistikler; ortalama, standart sapma, sayı ve yüzde olarak sunulmuştur. Nominal değişkenlerin grup karşılaştırmalarında Ki-kare ve Fisher'in Kesinlik Testi kullanılmıştır. İstatistiksel anlamlılık düzeyi $p < 0.05$ olarak kabul edilmiştir.

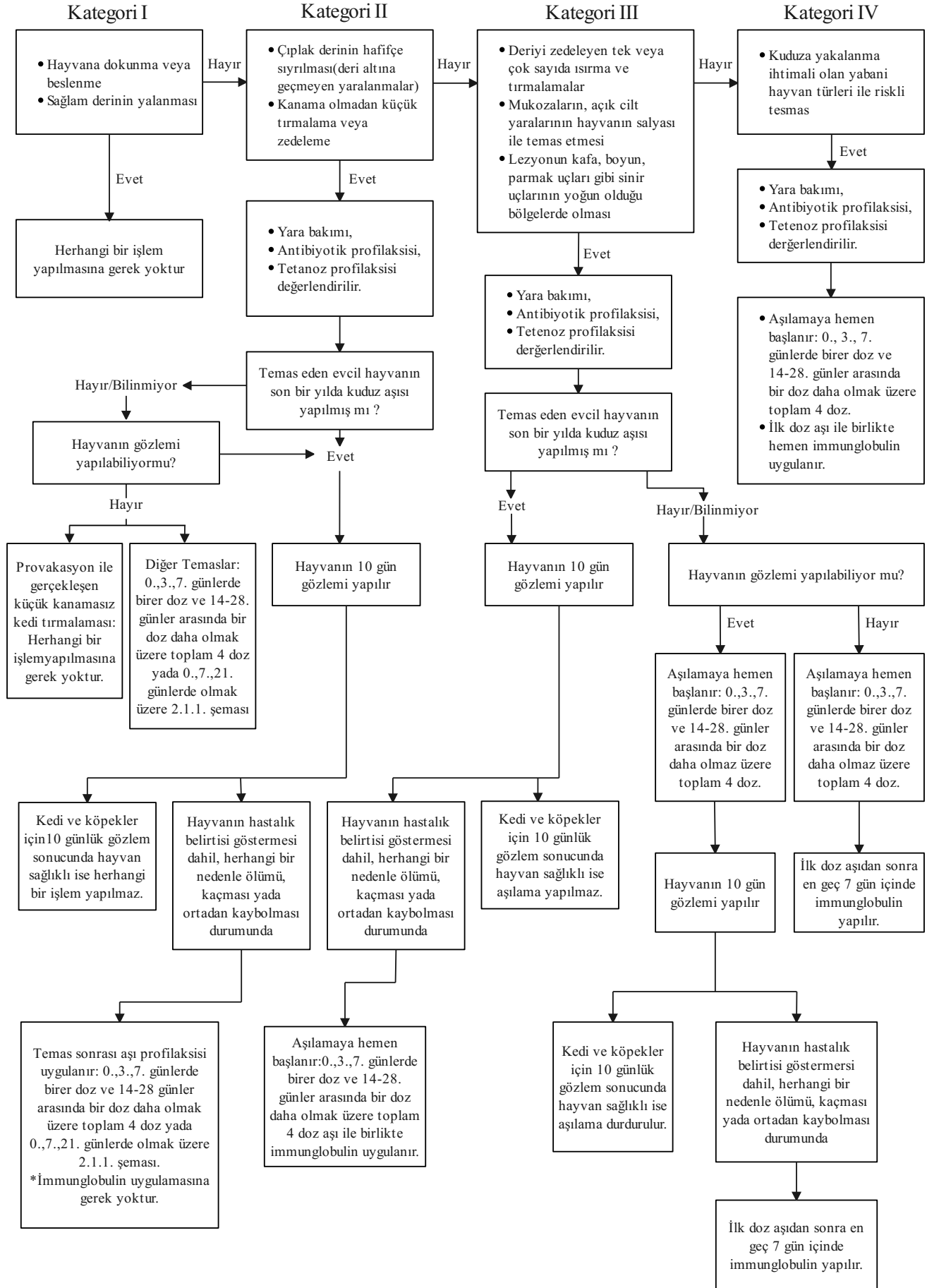
BULGULAR

Altı aylık sürede toplam 244 hasta kuduz virüsüyle temas riski nedeniyle hastanemize başvurdu. Hastaların %53'ü kız ve genel yaş ortalaması $93,7 \pm 53,6$ aydı. Kızların yaş ortalaması $86,3 \pm 46,9$ ay iken erkeklerin yaş ortalaması $102,2 \pm 56,9$ aydı ve aradaki fark istatistiksel olarak anlamlıydı. Hastaların vücudundaki yaralanma bölgeleri en sık üst ekstremitte (%57,1) en az ise gövde idi (%5,2). Tablo 1'de hastaların kuduz ile temas bölgeleri gösterilmiştir.

Tablo 1. Isırık bölgeleri

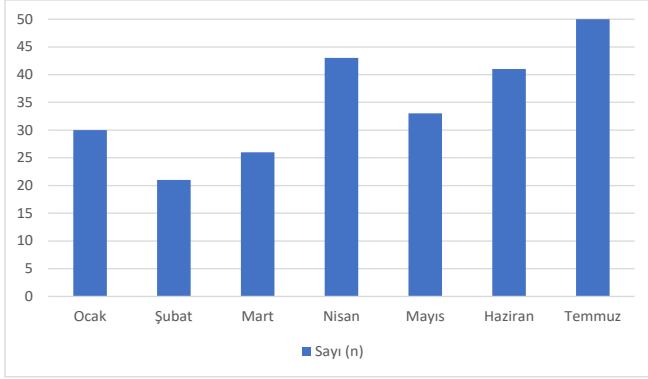
Temas Bölgeleri	Sayı (n)	Yüzde (%)
Üst Ekstremitte	139	57,1
Alt Ekstremitte	48	19,5
Yüz	22	9,1
Birden fazla bölge	22	9,1
Gövde	13	5,2

Çocuklarda Kuduz Profilaksisi



Şekil 1. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Kuduz Profilaksi Rehberi (T.C. Sağlık Bakanlığı, 2019)

Aylara göre bakıldığında vaka sayısının Nisan ayından itibaren arttığı görüldü, en fazla Temmuz ayında idi (Şekil 2). Maruziyet kaynağının %61,6'sı kedi, diğerleri köpekti.



Şekil 2. Aylara göre dağılım

Tetanoz aşısı 36 hastaya yapılırken tetanoz immünglobulini ihtiyacı olmadı. 244 hastaya toplam 790 adet kuduz aşısı yapılırken, kuduz immünglobulini 86 hastaya yapıldı. İmmünglobulin yapılma oranı hem kedi hem de köpek maruziyetlerinde benzer orandaydı. İmmünglobulin yapılanların 55'i (%64) aşı şemasını hastanemizde tamamlamıştı. Hastaların yalnızca 124'ü (%50,8) aşı takvimini tamamladı; diğerleri ya eksik bıraktı ya da başka merkezde devam etti. Tablo 2'de hastaların aşı uygulama durumu gösterilmiştir.

Tablo 2. Tetanoz ve Kuduz aşı/immünglobulin uygulama durumu

	Hasta sayısı (n=244)	Yüzde (%)
Kuduz aşısı	1 kez	39
	2 kez	28
	3 kez	53
	4-5 kez	124
Kuduz immünglobulini	86	35,2
Tetanoz aşısı	36	14,8
Tetanoz immünglobulini	0	0

TARTIŞMA

Kuduz ile riskli temas olguları acil servislerde çalışan hekimlerin sık karşılaştığı durumlardan biridir. Literatürde, hayvan teması sonrası kuduz profilaksisi için hastanelere başvuran tüm hastaların %41-49'unu çocuklar oluşturmaktadır (De Paula ve ark., 2018; Karadaş ve ark., 2018). Ülkemiz

verilerine göre, son beş yıl içerisinde kuduz kaynaklı ölümlerin ikisi çocuklarda, ikisi ise erişkin bireylerde meydana gelmiştir. Çalışmamızda en sık başvuru havaların ısınmaya başlayıp park etkinliklerinin arttığı ilkbahar mevsiminde olmuştur. Derinöz ve Akar (2017), Karadaş ve ark. (2018) yaptığı çalışmalarda da en sık ilkbahar ve yaz aylarında başvuru saptanmış olup çalışmamız ile uyumlu olduğu görülmüştür. Ülkemizde yapılan çalışmalarda erkek çocuklarda riskli temas sık bildirilse de bizim çalışmamızda temashıların %53'ü kızdı (Aydın ve Aydın., 2024; Kocabaş ve ark., 2018; Celiloğlu ve ark., 2021). Hayvan türüne ve temashıların yaşına göre yaralanan vücut bölgesi değişmektedir. Kedilerde sıklıkla el-üst ekstremiteler yaralanması olurken, köpeklerde bu durum provokasyon sonucu mücadele sırasında ısırılmaya bağlı alt ekstremiteler olarak değişebilir. Kocabaş ve ark. (2018) çalışmasında en sık etkilenen bölge üst ekstremiteler, temas eden hayvan %53 oran ile kedi iken, Kara ve Delice (2018) yaptığı çalışmada ise %65 köpek ısırığı saptanmış olup etkilenen bölge en sık alt ekstremiteler olarak bildirilmiştir. Çalışmamızda yaralanmaların çoğunun kedi aracılıklı ve üst ekstremitelerde olması nedeniyle çocukların bu hayvanları severken yaralandığı yorumunu yapabiliriz. Çalışmamızda hastaların %50,8'i kuduz aşılmasını tamamlamıştır. Kocabaş ve ark. (2018) çalışmasında tüm aşı dozlarının tamamlanma oranı %100 saptanmıştır. Çalışmamızdaki oranın az olmasının nedeninin yakın semtlerde başka hastaneler olması ve bu nedenle hastaların takibinin başka merkezlerde devam etmesi kaynaklı olduğunu düşünmekteyiz. T.C. Sağlık Bakanlığı'nın 2019 yılında yayınladığı Kuduz Profilaksi Rehberi doğrultusunda kuduz immünglobulin risk kategorisi IV ve hayvanın gözleminin yapılamadığı + aşılması yok/bilinmediği (kategori III) durumunda heterolog (at kaynaklı) ise 40 IU/kg, insan kaynaklı ise 20 IU/kg olarak yapılmalıdır (T.C. Sağlık Bakanlığı, 2019). Ülkemizde yapılan çalışmalara bakıldığında kuduz aşısı birlikte kuduz immünglobulin uygulama yüzdesi %6,8-56 olarak değişmektedir (Aydın & Aydın, 2024; Derinöz & Akar, 2017; Karadaş & ark., 2018; Kocabaş , 2018). Çalışmamızda kuduz immünglobulin uygulaması %35,2 oranında yapılmıştır. Temas sonrası hastalar tetanoz profilaksisi yönünden sorgulanması gerekmektedir.

Çalışmamızda tetanoz immünglobulini ihtiyacı olan hasta olmayıp, tetanoz aşısı uygulaması %14,8 hastaya yapılmıştır. Çocukluk çağı aşılama şemasında tetanoz aşısı bulunması sayesinde temas riskli vakaların çoğunda tetanoz aşısına gerek kalmamaktadır. Tetanoz immünglobulin yapılmaması risk kategorisi III ve IV olanların tetanoz aşılamalarının tam olması kaynaklı olduğunu düşünmekteyiz.

Sonuç olarak; Kuduz erken dönem yara bakımı, yara yeri enfeksiyon kontrolü ve aşılama ile %100 önlenabilir bir hastalıktır. Kuduz hastalığının önlenmesinde, başıboş hayvanlarla mücadele, maruz kalındıktan sonra aşı ve immünglobulin tedavisi, toplumun hastalık ve korunma konusunda eğitimi önem kazanmaktadır.

Çalışmanın kısıtlılıkları

Çalışmamızdaki en büyük kısıtlılık çalışmanın geriye

dönük olmasıdır. Bu nedenle hayvan ısırıkları T.C. Sağlık Bakanlığının Kuduz Profilaksisi Rehberine göre kategorize edilememiştir. Kayıtlardan temas eden hayvanın evcil ya da sähipsiz olması, hayvanın takip edilme imkanı, aşı şemasına hastanemizde devam etmeyen hastaların başka merkeze gidip gitmediğı ve gerçekten ne kadarının aşı şemasını tamamladığı bilgilerine ulaşılamamıştır.

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Çıkar Çatışması: Yazarlar, arasında herhangi bir çıkar çatışmasının olmadığını bildirmektedir.

Yazar Katkıları: Kavram, planlama, literatür taraması, veri toplama ve raporlama: BNK,HA,ANÇK Denetleme, revizyon ve son inceleme: HA, ANÇK.

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OCCUPATIONAL ACCIDENTS IN TURKEY'S HEALTH SECTOR: A CURRENT ASSESSMENT BASED ON TURKSTAT AND SGK DATA

Türkiye’de Sağlık Sektöründe İş Kazaları: TÜİK ve SGK Verileriyle Güncel Bir Değerlendirme

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ABSTRACT

Objective: This study aimed to analyze the trend of occupational accidents in the health sector in Türkiye between 2013 and 2023 using data from the Turkish Statistical Institute (TURKSTAT) and the Social Security Institution (SGK), and to develop recommendations for occupational health and safety measures specific to the sector. **Method:** Official statistics published by TURKSTAT and SGK were utilized in this study. Annual employment figures and reported occupational accidents within the scope of human health and social work activities (NACE Rev.2 - Q sector) were examined. The rate of occupational accidents per 1,000 employees was calculated and sectoral risk levels were comparatively analyzed. **Result:** The data revealed that, despite periodic fluctuations, the rate of occupational accidents in the health sector showed a general upward trend. It was determined that physical and psychosocial risks faced by healthcare workers increased significantly in the post-COVID-19 pandemic period. In certain years, the health sector exhibited higher accident rates than traditionally high-risk sectors such as construction and manufacturing. These findings indicate a discrepancy between the perceived safety of the health sector and the actual risks present. **Discussion:** Although the health sector is traditionally considered a low-risk field, the findings highlighted overlooked and underestimated hazards within the sector. Unreported incidents, excessive workload, and burnout were identified as serious threats to the occupational safety of healthcare workers. The study underscores the urgency of developing comprehensive, sustainable, and sector-specific occupational health and safety policies.

Keywords: Health Policy, Health Sector, Occupational Accident, Social Policy

ÖZET

Amaç: Bu çalışmanın amacı, Türkiye’de sağlık sektöründe meydana gelen iş kazalarının seyrini Türkiye İstatistik Kurumu (TÜİK) ve Sosyal Güvenlik Kurumu (SGK) verileri aracılığıyla 2013–2023 yılları arasında analiz etmek ve sektöre özgü iş sağlığı ve güvenliği önlemlerine ilişkin öneriler geliştirmektir. **Yöntem:** Araştırmada, TÜİK ve SGK tarafından yayımlanan resmi istatistikler kullanılmıştır. İnsan sağlığı ve sosyal hizmet faaliyetleri (NACE Rev.2 - Q sektörü) kapsamında yıllık çalışan sayıları ve iş kazası bildirimleri değerlendirilmiştir. 1000 çalışan başına düşen iş kazası oranı hesaplanarak sektörel risk düzeyleri karşılaştırmalı olarak analiz edilmiştir. **Bulgular:** Elde edilen veriler, sağlık sektöründe iş kazası oranlarının dönemsel dalgalanmalara rağmen genel olarak artış eğilimi gösterdiğini ortaya koymuştur. Özellikle COVID-19 pandemisi sonrası dönemde, sağlık çalışanlarının maruz kaldığı fiziksel ve psikososyal risklerin belirgin şekilde yükseldiği saptanmıştır. Bazı yıllarda sağlık sektörü, inşaat ve imalat gibi sektörlerden daha yüksek kaza oranlarına sahip olmuştur. Bu bulgular, sağlık alanındaki güvenlik algısının mevcut gerçeklikle örtüşmediğini göstermektedir. **Tartışma:** Sağlık sektörü, geleneksel olarak düşük riskli kabul edilmesine rağmen, veriler sektördeki görünmeyen ve ihmal edilen tehlikelerin altını çizmektedir. Raporlanmayan vakalar, yoğun iş yükü ve tükenmişlik sendromu gibi unsurlar sağlık çalışanlarının mesleki güvenliğini ciddi biçimde tehdit etmektedir. Çalışma, sektöre özgü, bütüncül ve sürdürülebilir iş sağlığı ve güvenliği politikalarının oluşturulmasının aciliyetini vurgulamaktadır.

Anahtar Kelimeler: İş Kazası, Sağlık Politikası, Sağlık Sektörü, Sosyal Politika

INTRODUCTION

Workplace accidents not only undermine the life of an employee to its core, but they also have profound socioeconomic effects that threaten the efficiency of institutions and the general well-being of society. Workplace accidents, which are largely preventable with appropriate risk management, training, and audit strategies, result in significant losses on a global scale every year if the necessary preventive measures are not taken (ILO, 2023; SGK, 2023). Healthcare is one of the sectors that pose serious risks in terms of occupational health and safety. Professionals employed in the healthcare sector face various occupational hazards during their duties. These risks range from blood-borne infections to radiation exposure, musculoskeletal disorders due to ergonomic deficiencies, physical fatigue due to intense workload and shift work, and increased psychological pressure. In addition, factors such as long-term contact with chemical substances, burnout, solitary working environments, and inadequate social support threaten both the physical and mental health of healthcare employees (WHO, 2022; ILO, 2021; Özkan & Demirci, 2023). It is essential for occupational healthcare that personnel working in healthcare institutions are aware of the potential hazards they may encounter during their duties. They should be able to anticipate when and under what conditions these hazards might arise and implement suitable preventive strategies. According to current legal regulations, the healthcare sector is classified as a high-risk occupational area (ILO, 2021; WHO, 2023). In these institutions, individuals from various occupational groups, including physicians, technicians, nurses, and support staff, work collectively, which can result in simultaneous exposure to biological, chemical, physical, and ergonomic hazards. In particular, respiratory infections, blood-borne pathogens, sharp-edged injuries, musculoskeletal strains, and allergic reactions are among the common and potentially hazardous types of occupational accidents affecting healthcare personnel (WHO, 2022; Çetin & Yıldız, 2022). This study aims to analyse the underlying causes of occupational accidents in the health sector using statistical data. The frequency, nature, and consequences of occupational risks faced by health

workers present a significant threat to both employee well-being and the continuity of health services. Based on the data obtained throughout the study, the goal is to develop policy recommendations that enhance occupational health and safety measures explicitly tailored for the health sector, ultimately contributing to the reduction of existing risks.

Conceptual Framework

The rapid changes in production methods since the Industrial Revolution have led to an increase in work-related accidents and occupational diseases. Today, workplaces contain numerous risk factors that threaten the physical and mental well-being of individuals (ILO, 2021; WHO, 2023). The World Health Organisation (WHO) (2023) defines an occupational accident as a situation that causes physical or psychological harm to the employee's health as a result of an unplanned and sudden event. Furthermore, according to the International Labour Organisation (ILO), an occupational accident is any adverse incident that occurs during the execution of an assignment, unexpectedly affecting the employee and causing direct harm (ILO, 2021). It is observed that the concept of an occupational accident is defined differently in the legislation that forms the basis of labour law in Türkiye. Although there is no clear definition of an occupational accident in Labour Law, Article 4857, it is conspicuous that evaluations are made in the context of employees' job security, working conditions, and employer responsibilities. It is noteworthy that an occupational accident is defined clearly and in detail in Article 13 of the Social Insurance and General Health Insurance Law, Article 5510. According to this article, an occupational accident is: While the insured is at work, Due to work carried out by the employer, While the insured is sent to another place outside the workplace on duty, During the time spent by a breastfeeding woman to breastfeed her child, While commuting to and from work in a vehicle provided by the employer, these are events that cause immediate or delayed physical or mental disability to the insured (Social Insurance and General Health Insurance Law No. 5510, 2006). On the other hand, Article 6331 of the Occupational Health and Safety Law, rather than directly defining an occupational accident, provides a systematic framework for

preventing occupational accidents by requiring the implementation of occupational health and safety measures. The purpose of the law is to define the obligations of employers and employees to ensure occupational health and safety in workplaces and to improve existing health and safety conditions. In this context, the employer is obliged to take all necessary measures to prevent occupational accidents (Occupational Health and Safety Law No. 6331, 2012). Occupational accidents remain a key focus of occupational health and safety policies in both developed and developing countries. Because, just as living on earth is a human right, being employed in a healthy and safe work environment is also seen as a human right (Parlar, 2008). Preventing occupational risks to which employees are exposed should be considered not only a legal and economic obligation, but also a moral responsibility. According to ILO, approximately 2.78 million people worldwide lose their lives each year due to work-related accidents or work-related diseases (ILO, 2019). The number of healthcare workers globally is estimated to exceed 59 million by 2024 (WHO, 2024). These workers are at significant biological risk, particularly due to the risk of contact with infected body fluids and contaminated sharps. According to the most recent assessments by the WHO, approximately 2 million healthcare workers experience at least one occupational injury each year that involves contact with blood-borne pathogens (WHO, 2023). The vast majority of these injuries occur from needlesticks and surgical instruments, and the lack of adequate precautions in low- and middle-income countries further increases this risk (CDC, 2022; ILO, 2021). Various models have been developed in the literature to explain the causes of occupational accidents. While Heinrich's "Domino Theory" suggests that accidents are caused by human error, Reason's "Swiss Cheese" model argues that systemic vulnerabilities can trigger accidents (Heinrich, 1959; Reason, 1990). In this context, the view that occupational accidents are the result of organisational and managerial weaknesses rather than individual errors is gaining popularity. The approach that is more widely accepted in the occupational health and safety literature today is system-oriented models, which suggest that accidents are caused by multi-level and

complex causes (Dekker, 2011; Hollnagel, 2014). Studies conducted in high-risk sectors, particularly those lacking managerial control, inadequate training, communication gaps, and discrepancies in corporate culture, reveal that these factors play a crucial role in the occurrence of accidents (Flin et al., 2000; Gantt & Rochlin, 2020). Nevertheless, in recent years, it has been emphasised that in environments where human-machine interaction has increased, psychosocial factors as well as technology-based risks affect accidents (Carayon et al., 2006). In studies evaluating occupational accidents in terms of gender, occupational accidents experienced by female workers are increasingly being addressed. The high representation rate of female workers, particularly in the healthcare sector, exposes them to a greater risk of both physical and psychosocial hazards (Gürhan et al., 2020). The fact that women are often included in services considered as "invisible labour" causes them to be insufficiently visible in occupational accident statistics (Kahraman, 2021). Furthermore, the fact that ergonomics and personal protective equipment are often designed based on the male body creates additional risks for women (Şahin & Uysal, 2017). The organisational climate, as well as the physical conditions of the work environment, deeply affect occupational accidents. Institutional occupational health and safety culture, managerial support, adequate training, and control mechanisms are among the key factors in preventing accidents (Demirbilek, 2018). Studies have revealed that there is an inverse relationship between the frequency and quality of occupational safety training and the number of occupational accidents (Özkan & Kılınç, 2020). Occupational accidents in the health sector mostly occur in environments where direct patient contact is made during the completion of the task, where rapid decision making is required and where there is high physical and psychological load. The main reasons for these risks can be listed as cutting/piercing tool injuries, falls, biological factors, slipping and hitting, musculoskeletal strains, chemical substance contact, violence and assault, burns, and accidents caused by carrying and lifting. These reasons, along with their degree of danger and prevention methods, are presented in detail in Table 1.

Occupational Accidents in Turkey's Health Sector

Table 1. Types of Occupational Accidents in the Health Sector (Compiled from SGK, WHO, EU-OSHA)

Occupational Accident Type	Detailed Description	Exposure Level	Prevention Method
Sharp/Needlestick Injuries	It occurs as a result of contact with instruments such as injection needles, scalpels or blood collection needles. It carries the risk of infection.	High	Proper disposal of single-use equipment, use of gloves, safe waste bins
Fall (Same Level / High)	It occurs due to situations such as slipping while carrying the patient or losing balance while climbing stairs.	Medium	Providing dry and clean floors, non-slip surfaces on stairs and ramps
Exposure to Biological Agents	There is a risk of contact with blood-borne diseases such as HIV and Hepatitis B/C.	High	Personal protective equipment (mask, gloves), infection control protocols
Slips, Trips and Falls	It occurs as a result of slipping on damp surfaces or hitting stretchers or equipment.	Medium	Constant checking of floors, warning signs, use of appropriate footwear
Electric Shock	Exposure to electrical current due to medical devices or installation malfunctions.	High	Regular maintenance and grounding, training in the use of electrical equipment
Musculoskeletal System Strains	Musculoskeletal injuries due to heavy patient handling, repetitive movements, or standing for long periods of time.	Medium	Use of ergonomic equipment, staff training, task rotation
Violence and Attack	Incidents such as physical attacks, pushing, slapping, kicking, etc. from patients or their relatives.	High	Anger management training for employees, presence of security guards, mobbing prevention policies
Chemical Substance Contact	Sterilization occurs as a result of incorrect contact with substances used in laboratory environments.	High	Chemical substance labeling, ventilation, material safety data sheets training
Burns (Thermal/ Chemical)	It is caused by contact with autoclaves, sterilizers, hot substances or chemicals.	Medium	Personal protective equipment, emergency response training, demarcation of hazardous areas
Accidents Caused by Carrying and Lifting	Lifting heavy equipment and maneuvering patients can cause waist, knee and shoulder strain.	Medium	Trained handling techniques, lifting equipment, rest breaks

*Created by the author by compiling data from SGK Statistical Yearbooks, European OSH Agency, and WHO.
HIV: Human Immunodeficiency Virus

The most common accidents include sharp-edged tool injuries, falls, exposure to biological agents and musculoskeletal strains. Sharp-edged tool injuries and biological risks in particular pose a high risk of infection transmission, while incidents such as electric shock can have fatal consequences. Despite the magnitude of the danger, it is noteworthy that many accidents can be prevented by taking simple precautions. For example, the complete use of safe waste bins, the provision of appropriate personal protective equipment, ensuring floor safety and regular training for employees are among the practices that can significantly reduce accidents. In addition, external risk factors of the medical environment, such as physical violence by patients and their relatives, are also considered within the definition of occupational accidents and threaten the safety of healthcare professionals. This data

reveals not only the frequency of accidents but also the multidimensional threats faced by the healthcare workforce.

METHODS

This study is based on a quantitative data analysis conducted to analyse the course of occupational accidents occurring in the health sector in Türkiye over the years. In the study, statistical data on occupational accidents between the years 2013-2023 were obtained from the Statistical Yearbooks published by the SGK and the relevant data sets of the TURKSTAT. These yearbooks, published by the SGK, include occupational accident, occupational disease and death data of insured employees within the scope of Article 4-1/a (formally insured workers under Article 4-1/a of the Social Insurance Law) of

Law No. 5510. The analysis is limited to data after 2013, particularly because the SGK transitioned its notification system to an electronic environment in 2013 and began publishing it in a manner that encompasses all notifications. While conducting analyses related to the healthcare sector, the annual number of employees and work accident notifications belonging to the “Human Health Services” sector, defined by code 86 according to the NACE Rev. 2 classification in the SGK Statistical Yearbooks, were taken into account. Additionally, The Accident Incidence Rate (AIR) was calculated to evaluate sectoral risk levels comparatively. $AIR = (\text{Number of Work Accidents} / \text{Total Number of Employees}) \times 100,000$ This rate represents the number of work accidents per 100,000 employees, as defined by the European Statistical Office (Eurostat). The study's findings were evaluated to make the risks faced by employees working in health services visible and to form the basis for the development of sector-specific preventive policies.

Data Limitations and Reliability Assessment

The data used in this study were obtained from official statistics published by the SGK and the TURKSTAT. Although these data sources contain the most

comprehensive and reliable records of occupational accidents and diseases in Türkiye, they also present certain methodological limitations. Firstly, the SGK data only includes insured employees under 4-1/a, and employees who are employed off the books or who are covered by different insurance are excluded from this analysis. This situation highlights the existence of hidden occupational accidents (underreported or unrecorded incidents) and unreported cases, particularly among healthcare workers in private hospitals and subcontractor companies. In addition, problems such as under-reporting and reporting bias due to the fact that notifications are made through employers or institutions are among the factors limiting data reliability. Another limitation is that occupational groups do not disaggregate the data. In the SGK yearbooks, the general health worker group is listed under the heading of “Human Health Services.” However, occupational distinctions, such as doctors, nurses, technicians, and cleaning personnel, are not presented in detail. This makes it challenging to conduct a detailed analysis of the risks to which different occupational groups in the sector are exposed.

FINDINGS

Table 2. Number of Insured Employees, Work Accidents, Occupational Diseases and Deaths in Turkey within the Scope of Article 4-1/a of Law No. 5510 (2013-2023)

Year	Number of Employees	Total Number of Work Accidents	Total Number of Occupational Diseases	Number of Deaths
2013	13.136.339	191.389	351	1.360
2014	13.967.837	221.366	494	1.626
2015	14.802.222	241.547	510	1.252
2016	15.355.158	286.068	597	1.405
2017	16.369.073	359.653	691	1.633
2018	16.054.759	430.985	1.044	1.541
2019	16.010.002	422.463	1.088	1.147
2020	17.358.140	384.262	908	1.236
2021	18.399.864	511.084	1.207	1.417
2022	19.814.531	588.823	953	1.525
2023	18.613.745	681.401	945	1.966

(SGK, 2023)

Occupational Accidents in Turkey's Health Sector

A significant increase is observed in both the number of employees and the reported cases of accidents and occupational diseases between 2013 and 2023. During this period, the total number of employees increased by approximately 42%, while the number of occupational accidents increased by a much higher rate of 256%. Particularly in the period after 2020, there has been a re-increase in accidents and deaths. This situation suggests that working

conditions are becoming increasingly hazardous and that current occupational health and safety measures are insufficient. Fluctuations in occupational diseases, on the other hand, indicate that awareness and diagnosis processes are still in development. The general picture reveals that occupational accidents remain a significant problem that requires serious and systematic solutions.

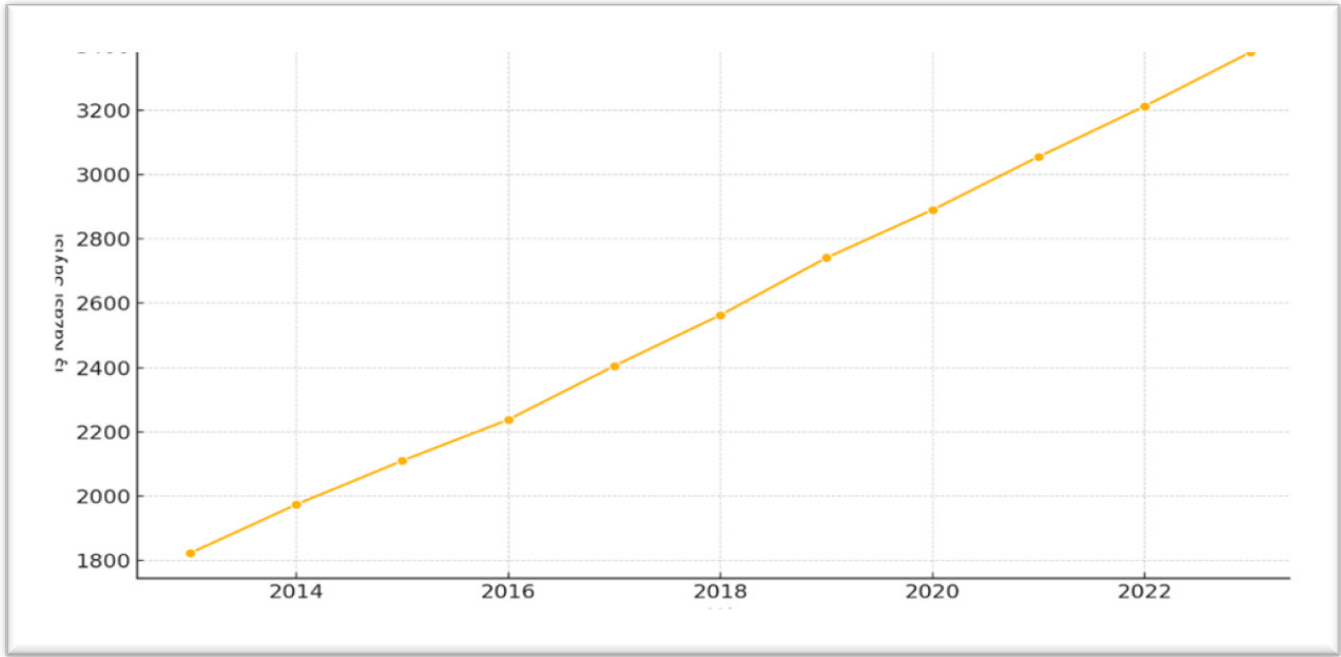


Figure 1. Number of Work Accidents in the Health Sector Between 2013 and 2023
TURKSTAT, 2024

The graph showing the distribution of the number of occupational accidents that occurred in the health sector by year between 2013 and 2023 reveals a remarkable upward trend. The number of occupational accidents, which was approximately 1,830 in 2013, increased to 3,390 by 2023. This increase is not only due to fluctuations in certain years, but also due to a linear increase that occurs regularly and steadily every year. The fact that an average of 150-180 additional occupational accidents occur every year shows that the sector is becoming increasingly risky. The primary factors contributing to this increase include rising demand for health services, personnel shortages, prolonged working hours, increased work intensity, post-pandemic pressures, and inadequate occupational safety measures. In addition, factors such as psychosocial risks that health workers are exposed to and patient-related violence may also indirectly increase occupational accidents. These

findings indicate that urgent and comprehensive measures must be implemented in the health sector to address occupational health and safety concerns. Developing policies that prioritise employee safety, conducting regular risk assessments, enhancing occupational safety training, and improving working conditions will be crucial steps in reversing this negative trend. Otherwise, this increasing trend may threaten both the health of healthcare workers and the sustainability of healthcare services. These findings reveal that the risk of occupational accidents in the health sector is relatively high, contrary to popular belief, and has increased over time. This apparently demonstrates the need to increase occupational health and safety measures for healthcare workers and develop sector-specific strategies.

Occupational Accidents in Turkey's Health Sector

Table 3. Occupational Accident Statistics of Healthcare Workers Between 2013 and 2021

Year	Number of Employees (Human Health Services)	AIR*	AFR**	FAFR**	Number of Employees (RCA)	AIR**	AFR** (RCA)	FAFR** (RCA)
2013	238 597	470,2	1,9	33,5	17 846	196,1	0,56	0
2014	260 498	769,7	3,2	3,8	20 156	272,8	0,78	0
2015	281 643	1 041,3	4,3	21,3	24 028	441,2	1,14	0
2016	284 363	1 565,9	6,5	24,6	26 996	618,6	1,70	37,04
2017	327 963	2 137,1	8,9	33,5	28 887	827,3	2,29	0
2018	491 631	2 115,6	8,8	12,2	33 206	1 069	3,30	30,11
2019	549 861	2 503,9	10,4	9,09	34 511	1 356	4,02	0
2020	812 270	2 317,9	9,6	14,7	47 659	851,8	2,45	20,9
2021	824 215	2 591,4	10,8	14,5	48 632	1 151,5	3,46	0
Average	—	1 723,6	7,1	18,5	—	753,8	2,1	9,7

AIR: Number of work accidents per 100,000 employees, AFR (Accident Frequency Rate): Number of work accidents per 1,000,000 working hours, FAFR (Fatal Accident Frequency Rate): Number of fatal accidents per 1,000,000 working hours, RCA: Residential Care Activities

When Table 3 is examined, an increasing trend is observed in the basic indicators regarding occupational accidents suffered by healthcare workers working in both human health services and inpatient care activities during the period 2013–2021. The significant increase in the AIR and AFR indicators in human health services, particularly since 2016, suggests the emergence of systemic vulnerabilities in terms of occupational health and safety within this sector. The AIR value, which was 470.2 in 2013, increased to 2,591.4 in 2021, representing a nearly 5.5-fold rise. Similarly, the AFR rate also showed a significant increase, increasing from 1.9 to 10.8 in the same period. When the FAFR is examined, a fluctuating trend is observed. The fact that it showed the same value (33.5) in 2013 and 2017 may be related to an increase in reporting in some years or

the worsening nature of the incidents. However, the downward trend after 2019 can be interpreted as indicating that fatal cases during the pandemic period were more closely related to infection and fell outside the definition of classical work accidents. This situation necessitates a discussion of the pandemic's impact on work accident statistics. In the field of RCA, the relatively low number of employees causes the overall accidents to appear statistically lower. However, the sudden increases in the FAFR values in 2016, 2018 and 2020 are striking. For example, the FAFR recorded at 37.04% in 2016 indicates critical structural deficiencies and inadequate protective mechanisms in the field of residential care. Such sudden jumps become more pronounced in small sectors, where individual incidents can have a significant impact on the overall rate.

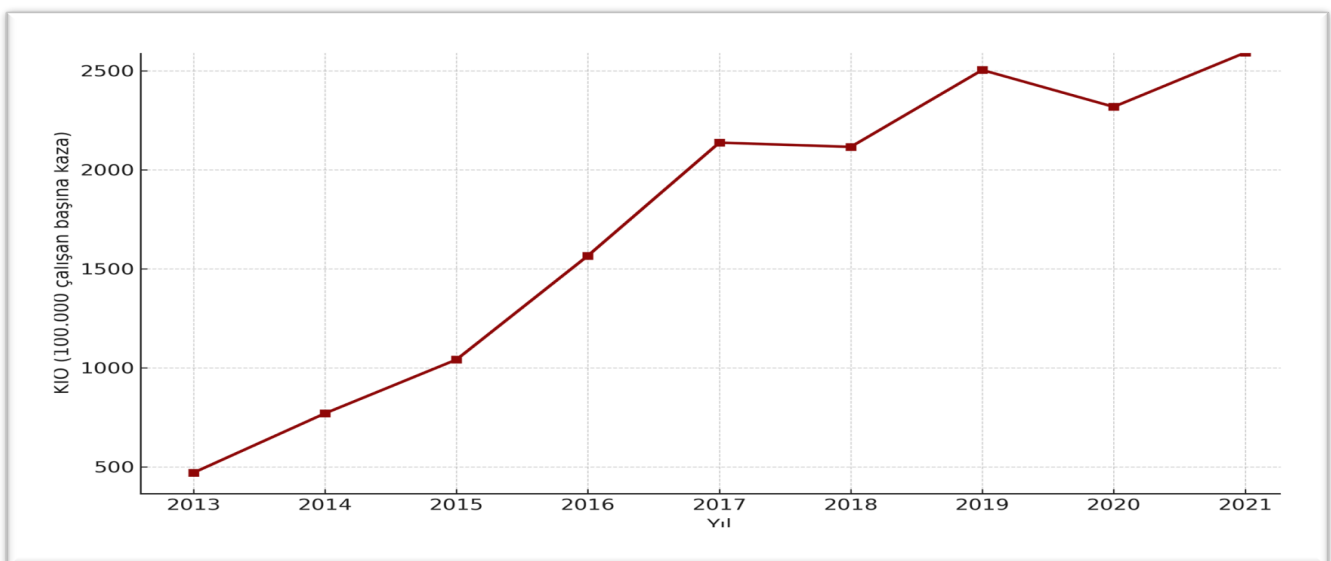


Figure 2. Change in Accident Incidence Rate (AIR) in the Health Sector by Year (2013–2021)

SGK Statistical Yearbooks, 2022.

Figure 2 illustrates the occupational accident rates (OAR) per 100,000 employees in the health sector in Türkiye between 2013 and 2021. The graph reveals a significant upward trend, particularly in the period after 2016. The occupational safety gaps faced by healthcare professionals have gained a systemic dimension. This situation may be related to increased patient load, staff shortage, long working hours, shift work patterns, physical fatigue, and psychosocial pressures that have intensified in the post-pandemic period. When general averages are taken into account, the fact that the AIR in human health services is 1,723.6, the AFR is 7.1, and the FAFR is 18.5 clearly indicates that the health sector is among the sectors with the highest risk of occupational accidents in Türkiye. On the other hand, the fact that the FAFR average in RCA is at a remarkable level of 9.7 reveals that this sub-sector is an area that should not be neglected. In line with these findings, it is necessary to acknowledge that occupational accidents are not only a statistical reality but also a structural, organisational, and political problem. Restructuring occupational health and safety policies specific to the healthcare sector, increasing personnel training, making reporting systems transparent, and systematically implementing protective measures are priority intervention areas to reduce similar risks in the future.

DISCUSSION

Although the health sector is generally perceived as a “low-risk” area in society, it is apparent that personnel working in this area are heavily exposed to biological, physical and psychosocial risk factors. Factors such as infection risk, sharp-edged injuries, violence, long working hours and emotional exhaustion make this sector quite vulnerable in terms of occupational accidents (ILO, 2023). It has been observed that occupational accidents in the healthcare sector in Türkiye have increased steadily over the years. The analysis based on TURKSTAT data for the period 2013–2023 reveals a notable trend in accident incidence and frequency rates, which is consistent with the increase in the number of employees and the rise in the number of reported work accidents. The increased risk level, particularly in the period following the COVID-19 pandemic, has

led to a questioning of the adequacy of current work safety practices in the healthcare sector. The most comprehensive statistical data on work accidents and occupational diseases in Türkiye are obtained through official records kept by the SGK. When the data for the period 2013–2023 is examined, it is seen that the total number of insured employees in the country increased by approximately 41.7% from 13,136,339 to 18,613,745 in 11 years. The number of reported work accidents in the same period increased by a remarkable 356% from 191,389 to 681,401. In 2020, the relative decrease in occupational accidents can be attributed to restrictions on working hours and workforce mobility imposed by the COVID-19 pandemic. Nevertheless, when this year is excluded, a general upward trend in occupational accidents is apparent, corresponding to the increase in the number of employees. On the other hand, occupational disease data does not follow a course directly related to the number of employees; a significant increase is particularly striking in 2018. Deaths due to occupational accidents or occupational diseases did not show significant fluctuations over the years; they varied between 1,147 and 1,966. In terms of AFR, the health sector can reach values similar to or higher than those of the manufacturing and construction sectors in some years (SGK, 2023). This situation necessitates the development of sector-specific occupational safety strategies. Targeted, unit-based risk management approaches should be implemented, particularly for healthcare workers working in high-risk units, such as emergency services, intensive care units, and pandemic clinics. In addition, the fact that accidents in the health sector mostly occur in the form of minor injuries or invisible psychosocial effects can also cause serious deficiencies in the reporting of these incidents. This situation also brings to the agenda the existence of hidden occupational accidents that are not reflected in statistics but have a direct impact on work efficiency and employee health. Chiefly during the pandemic period, healthcare workers working on the front lines have become more vulnerable to these risks, and the number of incidents resulting in occupational accidents has increased. This comprehensive classification reveals that risk prevention policies in healthcare institutions should be planned with a multidimensional approach.

Effective training programs, regular inspections, the complete provision of personal protective equipment, and support mechanisms for employee mental health play a critical role in preventing these accidents. A deeper understanding of the causes of occupational accidents in the healthcare sector not only protects employee health but also enhances service quality and strengthens the sustainability of the healthcare system. In conclusion, it is evident that occupational accidents in the health sector constitute a challenge that must be addressed not only at the individual level but also through institutional and societal interventions. Correct identification, reporting and management of such risks are of great importance for a sustainable health system.

CONCLUSION

The increasing trend of occupational accidents in the healthcare sector in Türkiye highlights the need for this area to be addressed not only at the individual level but also at the structural and public policy levels. Healthcare workers have been exposed to increased physical, biological, and psychosocial risk factors during the post-pandemic period. This situation has a profound impact on the sustainability of healthcare services. In this context, health policies aimed at preventing occupational accidents should be supported not only at the legislative level, but also with strategies based on field-specific, dynamic, evidence-based and unit-based risk analyses. The development and implementation of sector-specific institutional safety protocols are of great importance, particularly for workers in high-risk areas, such as emergency services, intensive care units, and operating rooms. Future studies may incorporate qualitative interviews with healthcare professionals to uncover underreported incidents and enhance statistical findings. It can be argued that occupational health should be integrated into a comprehensive health policy that encompasses not

only physical safety but also mental well-being and resilience. Invisible harms such as burnout, post-traumatic stress, and patient violence should be included in the definition of occupational accidents, and the scope of the concept should be expanded within the framework of changing conditions. On the other hand, these findings also provide significant messages in terms of social policy. The weight of women in the health sector, combined with discussions on ergonomic risks and invisible labour, necessitates the development of gender-sensitive occupational health policies. Revising data collection systems to eliminate the invisibility of women workers, designing personal protective equipment in accordance with gender, and making care work visible are also of vital importance in terms of social justice. In addition, the burden of occupational accidents on the social security system is not only an economic issue, but also a humanitarian and ethical issue. Problems such as unreported accidents and subcontracted services deepen the social dimension of occupational accidents. Making reporting processes transparent and developing a protective social policy framework for healthcare professionals should be among the priority goals. In conclusion, occupational accidents in the healthcare sector are not only a technical occupational health issue; they are also a matter of public health, social equality and human dignity. This reality should be evaluated with a holistic approach by policymakers, healthcare managers and social actors.

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RISK FACTORS FOR SEIZURE RECURRENCE IN CHILDREN FOLLOWING AN UNPROVOKED SIZURE

Uyarılmamış Nöbet Sonrasında Çocuklarda Nöbet Tekrarı İçin Risk Faktörleri

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ABSTRACT

Objective: The aim of this study was to identify the risk factors for seizure recurrence in children who have experienced an unprovoked seizure and have normal sleep electroencephalogram (EEG). **Method:** The study population included 80 children who presented with first unprovoked seizure and had normal sleep EEG in the first week of the seizure. Demographic data and characteristics of the seizure were recorded from patient files. Patients were evaluated for seizure recurrence at the first year of the initial seizure and classified into two groups: Group 1 (no seizure recurrence) and Group 2 (seizure recurred). **Results:** The study population comprised 80 patients. The mean age at presentation was 82.3 ± 56.1 months. The first seizure type was generalized in 77.5% of the patients, with a mean seizure duration of 5 minutes. Group 2, consisted of 35 patients (44%) who had seizure recurrence during the first year. Seizure recurrence was within the first 6 months in 29 (83%) of the patients. There was no significant difference in terms of age, gender, consanguinity, birth history, mental development, presence of seizure or epilepsy in the family, seizure type, seizure duration, seizure occurring at sleep or awake time, and the number of seizures in the first 24 hours and cranial imaging findings between group 1 and group 2. **Discussion:** Following a first unprovoked seizure, we could not find any risk factor for recurrence of the seizure in the children who have normal EEG evaluation. We suggest larger series and extended follow-up will be helpful to identify the risk factors for recurrence in this population.

Keywords: Electroencephalogram, Epilepsy, Seizure

ÖZET

Amaç: Bu çalışmanın amacı, uyarılmamış nöbeti olan ve uyku elektroensefalogram (EEG) incelemesi normal olan çocuklarda nöbet tekrarı açısından risk faktörlerinin belirlenmesi **Yöntem:** Çalışma grubuna ilk uyarılmamış nöbet ile başvuran ve nöbetin ilk haftasında uyku EEG si normal olan 80 çocuk dahil edildi. Demografik bilgi ve nöbet özellikleri hasta dosyalarından kaydedildi. Hastalar, ilk nöbetin 1. yılında nöbet tekrarı açısından değerlendirildi ve iki grupta sınıflandırıldı: Grup 1 (nöbeti tekrarlamayan) ve Grup 2 (nöbet tekrarı olan). **Bulgular:** Çalışma grubu 80 hastadan oluştu. Ortalama yaş $82,3 \pm 56,1$ ay idi. İlk nöbet tipi hastaların %77,5'inde jeneralize idi. Ortalama nöbet süresi 5 dk idi. Grup 2, ilk yılda nöbet tekrarı olan 35 hastadan (%44) oluşmakta idi. Nöbet tekrarı, 29 (%83) hastada ilk 6 ay içerisinde idi. Yaş, cinsiyet, akrabalık, doğum öyküsü, mental gelişim, ailede nöbet veya epilepsi öyküsü, nöbet tipi, nöbet süresi, nöbetin uykuda ya da uyanık olması, ilk 24 saatte nöbet sayısı ve kranial görüntüleme bulguları açısından grup 1 ve grup 2 arasında anlamlı fark bulunmadı. **Tartışma:** İlk unprovoked nöbeti takiben, EEG incelemesi normal olan çocuklarda nöbet tekrarı açısından herhangi bir risk faktörü bulamadık. Daha geniş seriler ve daha uzun izlem süresinin bu grupta nöbet tekrarı için risk faktörlerini belirlemede faydalı olacağını düşünüyoruz.

Anahtar Kelimeler: Electroencephalogram, Epilepsi, Uyarılmamış nöbet

INTRODUCTION

Seizure is a transient clinical condition which is caused by abnormal, excessive, and synchronized discharge of a group of neurons. This discharge results in abnormal motor movements, sensory disturbances, automatisms, and changes in the level of consciousness (Falco-Walter et al., 2018; Fisher et al., 2005; Stafstrom & Rho, 2017; Shinnar et al., 1996). A seizure is considered unprovoked when no causative factor can be identified in the absence of infections, trauma, or metabolic or toxic disturbances that could affect the brain. To consider a diagnosis of epilepsy, there must be at least one seizure and at least a 60% risk of recurrence in 10 years' time (Falco-Walter et al., 2018). EEG abnormality is an important risk factor for the recurrence of seizures (Chen et al., 2024; Takami & Nakagawa, 2021). In this study, we investigated the children who have experienced an unprovoked seizure and have normal EEG and evaluated the risk factors which can have a potential effect on the recurrence of seizures other than EEG. Follow-up of these children and investigation of the risk factors will be helpful to discriminate the population who will develop epilepsy earlier.

METHOD

The study was done as a pediatric thesis in 2009 in a single center at Ankara Dr. Sami Ulus Child Health and Diseases Education and Research Hospital, retrospectively. It involved 80 children who were followed up in the pediatric neurology unit with a first unprovoked seizure and who had normal sleep EEG evaluation in the first week of the seizure. Seizure type was defined based on International League Against Epilepsy (ILAE) criteria; having more than one seizure in the first 24 hours is accepted as one seizure (Fisher et al., 2005). Sleep EEG were recorded during the first week following the seizure and analyzed in standard protocols. Patients with febrile seizures, symptomatic seizures (metabolic, infectious), who have epilepsy diagnose or started on antiepileptics were excluded. Demographic data (age, gender, consanguinity, birth history (birth weight, type of delivery, postnatal hospitalization), mental development, family history of seizure and

epilepsy), seizure characteristics (type, duration, timing of the first seizure; at sleep or at awake time, occurrence of more than one seizure in the first 24 hours, time interval between the first seizure and second seizure in the seizure recurrence group), neuroimaging (computerized tomography (CT)/magnetic resonance (MRI)) findings, and neurological examination results were retrieved from patient files. Patients were classified into two groups according to seizure recurrence within 1 year, group 1 (who had no seizure recurrence) and group 2 (who had seizure recurrence).

Statistical Analysis:

Statistical analysis was performed using SPSS 2009, Shapiro–Wilk test was used to evaluate the distribution of the variables. Student t test or Mann-Whitney U test were used to analyze continuous variables. Pearson's Chi-squared test or Fisher's exact test were used to analyze nominal variables. Univariate logistic regression analysis was used to calculate odds ratio (OR) and 95% confidence interval (CI) for the risk factors to predict seizure recurrence. Multivariate logistic regression analysis was performed for the results of $p < 0.25$. Stepwise Logistic Regression Analysis was performed to identify the most predictive factors for seizure recurrence and values of $p < 0.05$ was accepted statistically significant.

RESULTS

The study involved 80 patients, comprising 46 males (57.5%) and 34 females (42.5%). Group 1, consisted of 45 patients and group 2 consisted of 35 patients. The mean age at presentation was 82.3 ± 56.1 months (range: 9-192 months). Five patients (6.3%) were less than 1 year, 13 patients (16.3%) were between 1-2 years, 21 patients (26.3%) were between 3-6 years, and 41 patients (51.3%) were older than 6 years. There was consanguinity in 17.8% in Group 1 and 14.3% in Group 2 ($p = 0.67$, $OR = 0.77$). The mean birth weight was similar, 3148 ± 758 grams in Group 1 and 3288 ± 628 grams in Group 2. The ratio of delivery by cesarean section was 24.4% in Group 1 and 28.6% in Group 2 ($p = 0.67$, $OR = 1.24$). Postnatal hospitalization was 22.2% in Group 1 and 8.6% in Group 2 ($p = 0.10$, $OR = 0.33$). Mental development

Risk Factors For Seizure Recurrence

was reported abnormal in 8.9% of Group 1 and in 8.6% of Group 2 ($p=1.00$, $OR=0.96$, 95% CI: 0.2-4.6). Family history of epilepsy was 17.8% in Group 1 and 31.4% in Group 2 ($p=0.15$, $OR=2.12$, 95% CI: 0.7-6). Family history of febrile convulsions was 26.7% in Group 1 and 22.9% in Group 2 ($p=0.69$, $OR=0.81$). Seizure type was generalized in 62 patients (77.5 %), focal in 10 patients (12.5 %), combined generalized and focal in 4 patients (5%) and not identified in 4 patients (5%). First seizure occurred at sleep in 40 patients (50%) and at awake time in 40 patients (50%). The mean duration of the seizure was 5 minutes and 12 patients (15%) had more than one seizure in the first 24 hours. During the first year, 45 patients (56.2%) had no seizure recurrence, classified as group 1, while 35 patients

(43.8%) had seizure recurrence, classified as group 2. The age at first seizure was 80.1 ± 52.8 months in Group 1 and 85.2 ± 60.7 months in Group 2 ($p=0.78$). The male/ female ratio was 1.36 in Group 1 and 1.33 in group 2, consisting of 26 males (57.8%) and 19 females (42.2%) in group 1 and 20 males (57.1%) and 15 females (42.9%) in Group 2 ($p=0.95$). The first year seizure recurrence was 43.7%. The second seizure occurred within the first six months in 29 (83%) of the patients. Seizure recurrence occurred in 21 patients (60%) within the first three months, in 8 patients (22.9%) between four and six months, and in 6 patients (17.1%) between seven and twelve months after the first seizure. Comparison of the age at the first seizure, gender and characteristics of the first seizure in group 1 and 2 is shown in Table 1.

Table 1. Age at the first seizure, gender and characteristics of the seizure in Group 1 and Group 2

	Group 1 (n=45)	Group 2 (n=35)	p	OR (95 %CI)
	n (%)	n (%)		
Age at first seizure (mo.)	80.1 $\pm$ 52.8	85.2 $\pm$ 60.7	0.78	1
≥ 24 months	40 (88.9%)	27 (77.1%)	-	1.00
< 24 months	5 (11.1%)	8 (22.9%)	0.158	2.37 (0.7-8.02)
Gender				
Male	26 (57.8%)	20 (57.1%)	-	1.00
Female	19 (42.2%)	15 (42.9%)	0.955	1.03(0.42-2.51)
Seizure type				
Generalized	37 (82.2%)	25 (71.4%)	-	1.00
Focal	6 (13.3%)	4 (11.4%)	0.985	0.99 (0.25-3.86)
Combined	1 (2.2%)	3 (8.6%)	0.208	4.44(0.44-45.15)
Unidentified	1 (2.2%)	3 (8.6%)	0.208	4.44 (0.44-45.15)
Time of seizure				
Awake	26 (57.8%)	14 (40.0%)	-	1.00
At sleep	19 (42.2%)	21 (60.0%)	0.115	2.05 (0.84-5.04)
Seizure duration(min)				
< 5 min	10 (22.2%)	13 (37.1%)	-	1.00
5-20 min	31 (68.8%)	18 (51.5%)	0.213	0.51 (0.18-1.46)
> 20 min	4 (8.8%)	4 (11.4%)	0.909	0.91 (0.18-4.64)
Seizure recurrence in the first 24 hours				
No recurrence	38 (84.4%)	30 (85.7%)	-	1.00
Recurrence	7 (15.6%)	5 (14.3%)	0.875	0.90 (0.26-3.14)

OR: Odds ratio, CI: confidence interval, min: minute

Consanguinity, birth weight, normal or cesarean delivery, postnatal hospitalization, mental development, family history of epilepsy or febrile convulsion had no effect on seizure recurrence ($p>0.05$, $OR = 1$). There was no significant difference

in age, gender, seizure occurrence at sleep or at awake time, seizure type, duration, and recurrence of seizure in the first 24 hours ($p>0.05$). The most common seizure type in both groups was generalized seizures (82.2% and 71.4%), followed by focal

seizures in Group 1 and Group 2, 13.3% and 11.4%, respectively. Duration of the first seizure was similar in both groups, most lasting less than 20 minutes. The majority of seizures (84.4% and 85.7%) in both groups did not recur in the first 24 hours and the ratio of more than one seizure in the first 24 hours was similar in both groups, with 15.6% and 14.3% of seizures in Group 1 and Group 2, respectively ($p=0.875$). Combination of various parameters, being younger than 24 months at the first seizure, first seizure occurring at sleep, postnatal hospitalization and family history of epilepsy were investigated as risk factors of seizure recurrence, but there was not any significant difference between the groups ($p>0.05$). Cranial imaging was performed in 67 patients at the initial seizure, including cranial CT in 9 patients and MRI in 58 patients. Glial tumors were identified in two patients on MRI from Group 1 which required surgical intervention. Other pathologies were arachnoid cyst, neuroepithelial cyst, Chiari type 1 malformation, mesial temporal sclerosis, cystic encephalomalacia and hyperintensities in the occipital and parietal regions, enlargement of the subarachnoid space and other nonspecific findings in 12 patients, six patients from group 1 and six patients from Group 2. Abnormalities on MRI or CT were not significant for the recurrence of the seizure ($p=0.68$). Focal neurological signs on physical examination were observed in 3 patients which had no effect on recurrence of the seizure ($p=0.57$).

DISCUSSION

(ILAE) defines epilepsy, a disorder of the brain predisposing the patient to develop epileptic seizures, and there should be at least one seizure for the diagnosis of epilepsy (Fisher et al., 2014). In a child presenting with an unprovoked convulsion, we face some questions like: what caused the seizure?, will it recur? what expects my child in the future? Seizure recurrence risk is important for the child, family, and the doctors dealing with the child to take preventive measures at the appropriate time. Epilepsy develops in approximately 30% of children who experience afebrile seizures. The risk of epilepsy is approximately 20% lower if the child's development is appropriate for the age

and neurological examination, EEG, and cranial MRI findings are normal (Mohamad,2020). In a prospective study of 467 children who were followed after a first unprovoked seizure without antiepileptic treatment, 60% of children had seizure recurrence and most recurrences were in the first 2 years (Takami & Nakagawa,2021). In a meta-analysis regarding 815 children who presented with a first unprovoked seizure, seizure recurrence was reported ranging from 34.3% to 63.7% (Garcia Pierce et al., 2017). In our study, we observed seizure recurrence in 35 patients (44%) at the first year of the initial seizure, and most of the recurrence (83%) was in the 6 months, which was appropriate with the literature (Chen et al., 2024; Jiménez-Villegas et al., 2021; Takami & Nakagawa,2021). In some studies, seizures occurring at sleep were reported to have increased risk of recurrence (Berg & Shinnar,1991; Ramos Lizana et al., 2000; Shinnar et al., 1996). But, in our study, seizures at sleep or awake time did not have any impact on recurrence of the seizure. In the children who had cranial imaging for seizures, identifying a pathology requiring emergency medical or surgical intervention is 1% (Shinnar et al., 2001). In focal seizures and children with abnormal EEG, abnormal imaging findings are frequently reported (Berg et al., 2000). In our study, cranial MRI revealed some pathologies in 9% of the patients; two patients were diagnosed with glial tumors, underscoring the significance of cranial MRI for children with unprovoked seizures. Abnormal EEG, neuroimaging findings, nocturnal seizures, abnormal MRI, prior brain insult, and focal seizures were reported as significant factors for seizure recurrence in children (Berg,2008; Chen et al., 2024; Takami & Nakagawa,2021) Abnormal EEG was reported as the most significant factor for seizure recurrence (Berg, 2007; Chen et al., 2024; Debicki, 2017; Kanemura et al., 2015). In this study, we studied the population with normal EEG results, thereby excluding the influence of EEG abnormalities on seizure recurrence. However, we could not find any parameter which had any effect on the first-year seizure recurrence. The small size of the study population and the focus solely on the first-year seizure recurrence rate were limitations of our study.

Conclusion: Following a first unprovoked seizure, it is important to distinguish the patients with a high risk of seizure recurrence. We suggest that extended follow-up in larger series will be helpful to find the risk factors for seizure recurrence and detect epilepsy earlier in the pediatric population.

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TREATMENT ADHERENCE IN FAMILIAL MEDITERRANEAN FEVER PATIENTS: REAL-LIFE DATA FROM CENTRAL ANATOLIA

FMF Hastalarında Tedaviye Uyum: Orta Anadolu'dan Gerçek Yaşam Verileri

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ABSTRACT

Objective: Familial Mediterranean Fever (FMF) is a hereditary autoinflammatory disorder characterized by recurrent febrile episodes and serosal inflammation. Colchicine remains the cornerstone of FMF treatment, and adherence to therapy is critical to prevent disease flares and long-term complications such as amyloidosis. However, studies on treatment adherence in FMF are limited and report varying rates. This study aimed to evaluate treatment adherence in FMF patients and its association with clinical variables using real-life data from Central Anatolia. **Methods:** This retrospective cross-sectional study included FMF patients aged 18 years and older who were followed at a tertiary rheumatology outpatient clinic and met the Tel-Hashomer diagnostic criteria. Demographic and clinical data were collected through structured interviews and medical record reviews. Treatment adherence was assessed via self-report. Associations between adherence and variables such as attack frequency, disease duration, drug adverse events, and follow-up visits were analyzed using Mann-Whitney U, Chi-square, and Spearman correlation tests as appropriate. **Results:** 70 patients (64.3% female, median age 33.5 years) were included. The majority (89.2%) reported regular adherence to treatment. Colchicine was the most commonly used drug, with a median dose of 1.5 mg/day. A weak, non-significant positive correlation was found between colchicine dose and the number of attacks in the last 6 months ($p = 0.229$, $p = 0.071$). There was no statistically significant association between treatment adherence and attack frequency ($p = 0.622$), disease duration ($p = 0.134$), follow-up frequency ($p = 0.779$), side effects ($p = 0.582$), proteinuria ($p = 1.000$), or marital status ($p = 0.105$). **Discussion:** Despite high levels of reported adherence to colchicine among FMF patients, this did not consistently correlate with improved clinical outcomes. These findings highlight the complex nature of treatment adherence and underscore the need for individualized support strategies and objective adherence assessment tools in FMF management.

Keywords: Attack frequency, Colchicin, Familial mediterranean fever, Treatment adherence

ÖZET

Amaç: Ailevi Akdeniz Ateşi (AAA), tekrarlayan ateş atakları ve serozal inflamasyon ile karakterize, kalıtsal bir otoinflatuar hastalıktır. Kolşisin, AAA tedavisinin temelini oluşturur ve tedaviye uyum, atakları önlemek ve amiloidoz gibi uzun vadeli komplikasyonları engellemek açısından kritik öneme sahiptir. Ancak, AAA hastalarında tedaviye uyum oranlarıyla ilgili veriler sınırlıdır ve literatürde değişken sonuçlar bildirilmiştir. Bu çalışmada, Orta Anadolu bölgesinden elde edilen gerçek yaşam verileri kullanılarak, AAA hastalarında tedaviye uyum ve bunun klinik değişkenlerle ilişkisi değerlendirilmiştir. **Yöntem:** Bu retrospektif kesitsel çalışma, Tel-Hashomer tanı kriterlerini karşılayan ve bir üçüncü basamak romatoloji polikliniğinde takip edilen 18 yaş ve üzeri AAA hastalarını içermektedir. Demografik ve klinik veriler yapılandırılmış görüşmeler ve tıbbi kayıt incelemeleri yoluyla toplanmıştır. Tedaviye uyum, hastaların kendi beyanına dayalı olarak değerlendirilmiştir. Uyum ile atak sıklığı, hastalık süresi, ilaç yan etkileri ve takip sıklığı gibi değişkenler arasındaki ilişkiler Mann-Whitney U, Ki-kare ve Spearman korelasyon testleri ile analiz edilmiştir. **Bulgular:** Çalışmaya 70 hasta (kadın oranı %64,3; medyan yaş: 33,5 yıl) dahil edilmiştir. Hastaların büyük çoğunluğu (%89,2), tedaviye düzenli olarak uyum sağladığını bildirmiştir. En sık kullanılan ilaç kolşisin olup, medyan günlük doz 1,5 mg'dır. Kolşisin dozu ile son 6 aydaki atak sayısı arasında zayıf, istatistiksel olarak anlamlı olmayan pozitif bir korelasyon saptanmıştır ($p = 0,229$; $p = 0,071$). Tedaviye uyum ile atak sıklığı ($p = 0,622$), hastalık süresi ($p = 0,134$), takip sıklığı ($p = 0,779$), yan etkiler ($p = 0,582$), proteinüri ($p = 1,000$) veya medeni durum ($p = 0,105$) arasında anlamlı bir ilişki bulunmamıştır. **Tartışma:** AAA hastalarının büyük çoğunluğu kolşisin tedavisine yüksek oranda uyum gösterdiğini belirtse de, bu durum klinik sonuçlarda belirgin bir iyileşme ile ilişkilendirilmemiştir. Bulgular, kronik hastalıklarda tedaviye uyumun karmaşık doğasını vurgulamakta ve AAA yönetiminde bireyselleştirilmiş destek stratejilerine ve objektif uyum değerlendirme araçlarına duyulan ihtiyacı ortaya koymaktadır.

Anahtar Kelimeler: Ailevi akdeniz ateşi, Atak sıklığı, Kolşisin, Tedaviye uyum

INTRODUCTION

Familial Mediterranean Fever (FMF) is a hereditary, monogenic autoinflammatory disease characterized by recurrent episodes of fever and/or serosal inflammation, and it is the most common autoinflammatory disorder worldwide (Tufan & Lachmann, 2020). The disease is particularly prevalent among Turks, Armenians, and Arabs, with a reported prevalence of 0.093% in Turkey (Ozen et al., 1998). Most patients experience their first attack during early childhood, with approximately 65% of cases having their initial episode before the age of 10 and 90% before the age of 20 (Majeed et al., 1999). The main goals of FMF treatment are to improve quality of life (QoL), reduce the frequency, severity, and duration of attacks, and minimize chronic/subclinical inflammation in order to prevent long-term complications—most notably AA amyloidosis. There is considerable interindividual variability in the frequency, type, and severity of attacks. Therefore, treatment should be individualized based on monitoring of clinical episodes and inflammatory markers (Knieper et al., 2017). Inflammation in FMF patients can be effectively controlled with treatments targeting interleukin (IL)-1 β , such as colchicine, the recombinant human IL-1 receptor antagonist anakinra, the fully human IgG1 monoclonal antibody directed against IL-1 β canakinumab, or the fully human dimeric fusion protein rilonacept (Jesenak et al., 2018; Sönmez, Batu, & Özen, 2016). Colchicine remains the cornerstone of FMF treatment. However, up to 5% of patients fail to respond to colchicine despite receiving the maximum tolerable dose. One of the most important factors contributing to colchicine resistance is poor treatment compliance (Padeh, Gerstein, & Berkun, 2012). Treatment resistance can not only lead to disease-related complications but also negatively impact patients' quality of life. In the literature, treatment adherence in FMF and other rheumatic diseases has been evaluated using various tools such as the Compliance Questionnaire-Rheumatology (CQR), the Morisky Medication Adherence Scale, electronic medication monitoring devices, and pharmacy refill records. Although these

methods are considered objective, their widespread use is limited due to disadvantages such as recall and social desirability bias, cultural adaptation difficulties, high cost, technical challenges, and the inability to confirm actual medication intake. Studies investigating treatment adherence in FMF are limited and have shown variable results. In one study evaluating adherence to colchicine treatment, adherence rates were reported as 73% in adults and 96% in children (Padeh, Gerstein, & Berkun, 2012). In another study conducted in Turkey involving 96 FMF patients, 35.5% of the patients reported that they did not use colchicine regularly (Karaaslan et al., 2015). This study aims to evaluate treatment adherence in FMF patients and, by presenting real-life data from Central Anatolia where the disease is highly prevalent, to contribute to the limited body of adherence research in Turkey and to a better understanding of its impact on disease course.

METHODS

Study Design and Patient Selection

This study was designed as a retrospective cross-sectional analysis. Patients aged 18 years and older who were diagnosed with FMF based on the Tel-Hashomer criteria and followed at the rheumatology outpatient clinic of Ankara City Hospital were included. To be eligible, participants were required to be under regular follow-up and treatment for at least 6 months. Exclusion criteria included patients with additional autoimmune diseases (e.g., overlap syndromes, Sjögren's syndrome, systemic sclerosis, inflammatory myositis), individuals under 18 years of age, and those not fulfilling the Tel-Hashomer diagnostic criteria. A total of 123 patients were initially assessed, of whom 43 were excluded due to irregular follow-up or incomplete medical records. Consequently, 70 patients were included in the final analysis. Ethical approval for the study was obtained from the Ankara City Hospital Ethics Committee (Date: 30.07.2025, Approval No: 1-25-1544), and the study was conducted in accordance with the ethical standards of the Declaration of Helsinki (1964) and its later amendments.

Data Collection

Demographic and clinical data were obtained through structured interviews and review of medical records. Collected variables included age, sex, disease duration, family history of FMF, number of attacks in the last 6 months, treatment type, colchicine dosage, side effects, proteinuria status, marital status, and annual follow-up visit frequency. Treatment adherence was determined based on patients' self-report of regular medication use.

Statistical Analysis

Statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as medians and ranges due to non-normal distribution. To evaluate the association between treatment adherence and attack frequency, the Mann-Whitney U test was applied. This test was also used to compare disease duration and the number of annual follow-up visits between patients with and without regular treatment adherence. The relationship between colchicine dosage and attack count was assessed using Spearman's correlation coefficient. Associations between categorical variables such as treatment adherence and side effects, proteinuria status, and marital status were evaluated using Pearson's Chi-square test or Fisher's Exact test where appropriate.

RESULTS

Demographic Characteristics

A total of 70 patients were included in the study, with a median age of 33.5 years (range: 19–77). Of these patients, 45 (64.3%) were female and 25 (35.7%) were male. The median disease duration was 10 years (range: 0–30). At least one comorbidity was present in 27 patients (40.3%) (Table 1). Among 37 patients who were aware of their family history, 27 (72.9%) reported a positive family history of FMF.

Table 1. Demographic Characteristics of FMF Patients

Median age (years) (min-max)	33.5 (19-77)
Gender, n, %	
Female	45 (64.3%)
Male	25 (35.7%)
Disease duration, median years (min-max)	10 (0-30)
At least one comorbidity, n, %	27 (40.3%)
Hypertension	6 (22.2%)
Diabetes Mellitus	5 (18.5%)
Treatment, n, %	
Colchicine	67 (95.71%)
Anakinra	1 (1.42%)
Canakinumab	1 (1.42%)
No current treatment	1 (1.42%)

FMF: Familial Mediterranean Fever

Disease Characteristics and Quality of Life

The median disease duration was 10 years (range: 0–30). The median age at FMF symptom onset was 23 years (range: 3–71). A majority of patients (97.1%) were receiving active treatment. Colchicine was the most commonly used medication, reported by 67 patients (95.71%), followed by anakinra and canakinumab in 1 patient each (1.42%). The median daily colchicine dose was 1.5 mg (range: 1–2). The median number of attacks within the past 6 months was 1 (range: 0–12). Although a weak positive correlation was found between colchicine dose and the number of attacks, this relationship was not statistically significant ($\rho = 0.229$, $p = 0.071$) (Figure 1).

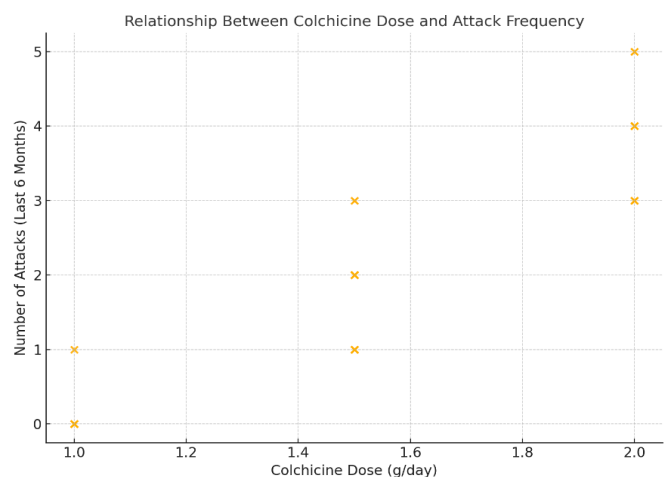


Figure 1. The relationship between colchicine dose and number of attacks in the last 6 months

Colchicine-related adverse events were reported by 9.9% of patients. The most common adverse event was diarrhea, observed in 85.8% of those reporting adverse events. One patient experienced

liver function abnormalities after colchicine use. Among patients receiving IL-1 antagonists, only one developed an allergic reaction following anakinra administration. A total of 89.2% of patients reported regular adherence to their treatment regimens. Among those receiving colchicine, 87.1% also reported consistent follow-up visits. The median frequency of outpatient follow-up visits in the past year was 2 (range: 1–8). There was no statistically significant difference in annual follow-up frequency between those with and without regular treatment adherence ($p = 0.779$). No significant association was found between experiencing drug-related side effects and adherence to regular treatment ($p = 0.582$). Similarly, no statistically significant difference was found between treatment adherence and disease duration ($p = 0.134$). When assessing the relationship between treatment adherence and attack frequency, no statistically significant difference was observed between regularly treated and non-regularly treated patients regarding the number of attacks in the past 6 months ($p = 0.622$) (Figure 2).

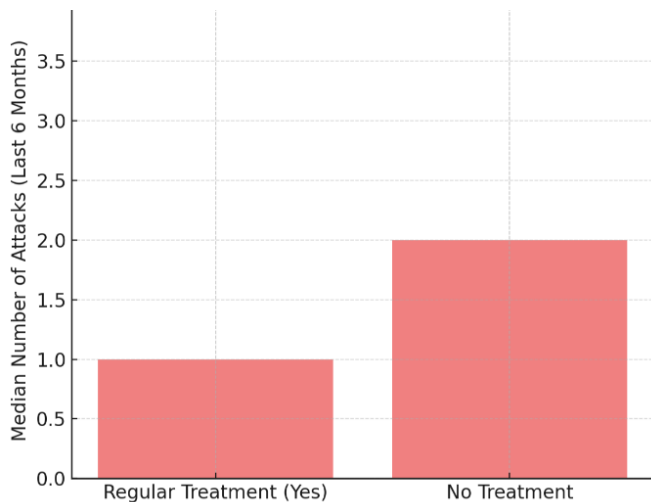


Figure 2. Comparison of Median Attack Frequency by Treatment Adherence

Proteinuria was observed in 11.1% of patients. There was no significant relationship between the presence of proteinuria and regular treatment adherence ($p = 1.000$). Regarding the impact of marital status on treatment adherence, no significant difference was found in treatment compliance between married and single patients ($p = 0.105$).

DISCUSSION

In this study, treatment adherence and related clinical factors were investigated in patients with FMF, and the majority of patients (89.2%) reported that they adhered to their treatment regimen regularly. However, no statistically significant relationship was found between regular treatment adherence and the number of attacks in the past 6 months ($p = 0.622$), disease duration ($p = 0.134$), or the frequency of annual outpatient visits ($p = 0.779$). Additionally, no significant association was observed between treatment adherence and variables such as the presence of drug-related side effects ($p = 0.582$), presence of proteinuria ($p = 1.000$), or marital status ($p = 0.105$). Although the majority of patients in our study reported regular adherence to colchicine therapy, this adherence did not result in significant improvements in clinical outcomes such as attack frequency or disease duration. This discrepancy may be explained by several interacting factors. First, adherence was assessed solely via patient self-report, a method prone to recall and social desirability bias. Recent European Alliance of Associations for Rheumatology (EULAR) guidelines (Özen et al., 2024) emphasize the importance of using objective methods for adherence assessment, including pharmacy refill records and validated adherence questionnaires, to ensure accurate monitoring. Treatment adherence was assessed by patient self-report. Although self-report is practical and commonly used in real-life clinical settings, it may be subject to recall and social desirability bias. The main advantage of using self-report is feasibility and accessibility in routine practice, while its limitations include potential overestimation of adherence compared to objective methods such as electronic monitoring or pharmacy refill data. Familial Mediterranean Fever is a hereditary monogenic autoinflammatory disease characterized by recurrent fever attacks accompanied by sterile peritonitis, pleuritis, arthritis, and/or erysipelas-like erythema (Masters et al., 2009). Although the attacks are self-limiting, patients are at risk of developing secondary amyloidosis, which can lead to renal failure and premature death due to chronic

inflammation and reduced quality of life (Ozen et al., 2016). The primary goals of FMF treatment are to prevent attacks and reduce chronic inflammation and its consequences. Regular monitoring of disease activity, complications, and inflammatory burden is essential for a comprehensive approach to FMF management (Bilici Salman et al., 2022). Colchicine is the mainstay of FMF treatment and has been proven effective in preventing attacks and secondary amyloidosis (Ozen, Kone-Paut, & Gül, 2017). Reported adherence rates to colchicine therapy vary between 58% and 73% in the literature (Corsia et al., 2017). In our study, this rate was found to be 87.1%. The recommended colchicine dose in adults is generally 1.0–1.5 mg/day (Demirkaya et al., 2016), and the median dose used by our patients was 1.5 mg/day, consistent with literature data. At recommended doses, oral colchicine is generally safe and well tolerated. Gastrointestinal side effects such as diarrhea, cramps, and abdominal pain may occur even at therapeutic doses (COLCRYSTM, 2009). In our patient group, the rate of side effects was 9.9%, with diarrhea being the most common (85.8%). According to the EULAR, FMF patients should ideally be evaluated every six months or more frequently by a rheumatologist (Özen et al., 2016). In our study, the median annual number of follow-up visits was two, which aligns with these recommendations. Previous studies have reported poor adherence to follow-up visits among FMF patients (Bilici Salman et al., 2022, Babaoglu et al., 2019); however, our findings indicate a relatively high rate of regular treatment adherence (89.2%). Although the treatment adherence rate in our FMF cohort was higher than expected, no significant association was found between regular adherence and clinical parameters such as attack frequency, disease duration, or follow-up visit frequency. This suggests that treatment adherence may be influenced by multifactorial aspects including individual awareness, patient education, and access to healthcare, in addition to clinical indicators. Multidisciplinary approaches aimed at improving adherence are crucial for both preventing complications and enhancing quality of life. These findings support the development of individualized follow-up strategies in FMF management.

Limitations: This study has several limitations. Firstly, its cross-sectional design precludes causal inferences between treatment adherence and clinical outcomes. Secondly, adherence was based solely on patient self-report, which may be subject to recall and social desirability bias. The absence of objective adherence measures (e.g., pharmacy records, electronic monitoring) may have led to overestimation. Additionally, genetic variability (e.g., MEFV mutations), treatment duration, and dose optimization were not analyzed—factors that could significantly influence response to therapy. Finally, the single-center setting, small sample size, and generally low attack rates may have reduced statistical power and limited generalizability. Despite these constraints, this study contributes meaningful real-world data and highlights the need for future prospective, multicenter research incorporating objective and individualized metrics.

Conclusion: In our study, although the majority of patients reported regular adherence to colchicine therapy, this was not found to be significantly associated with improvements in clinical parameters. This finding suggests that the relationship between treatment adherence and clinical outcomes is multifactorial and cannot be explained solely by the frequency of medication use.

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MİKROBİYOTA VE DİYABET: GÜNCEL BULGULAR VE MEKANİSTİK YAKLAŞIMLAR *Microbiota and Diabetes: Recent Findings and Mechanistic Approaches*

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ÖZET

Bağırsak mikrobiyotası, diyabet gibi metabolik hastalıkların patogeneğinde kritik bir rol oynamaktadır. Bu derlemede, mikrobiyota kompozisyonundaki değişimlerin tip 2 diyabet (T2DM) ile olan ilişkisi güncel literatür eşliğinde incelenmiştir. Mikrobiyal disbiyozun insülin direnci, glikoz metabolizması ve inflamatuvar süreçler üzerindeki etkileri vurgulanmıştır. Ayrıca, diyet ve probiyotikler gibi mikrobiyota modülatörlerinin diyabet yönetimindeki potansiyeli tartışılmıştır. Sonuç olarak, mikrobiyota temelli tedavi stratejilerinin diyabetin önlenmesi ve tedavisinde umut vaat ettiği görülmektedir.

Anahtar Kelimeler: Bağırsak mikrobiyotası, Disbiyoz, Diyet, Probiyotikler, Tip 2 diyabet

ABSTRACT

The gut microbiota plays a pivotal role in the pathogenesis of metabolic diseases such as diabetes. This review examines the relationship between microbiota composition and type 2 diabetes mellitus (T2DM) based on current literature. The effects of microbial dysbiosis on insulin resistance, glucose metabolism, and inflammatory pathways are highlighted. Additionally, the potential of microbiota modulators (e.g., diet and probiotics) in diabetes management is discussed. Evidence suggests that microbiota-targeted therapies hold promise for diabetes prevention and treatment.

Keywords: Diet, Dysbiosis, Gut microbiota, Probiotics, Type 2 diabetes

GİRİŞ

Bireyin genetik yapısı, yaşam tarzı ve çevresel faktörlere bağlı olarak şekillenen dinamik bir ekosistem olan mikrobiyota, son yıllarda sağlık ve hastalık süreçleri üzerindeki etkileriyle bilimsel araştırmaların odağında yer almaktadır (Lynch ve Pedersen, 2016). Sindirim, bağışıklık ve metabolik süreçlerdeki düzenleyici rolleri nedeniyle bağırsak mikrobiyotasındaki değişikliklerin, çeşitli hastalıklarla ilişkilendirildiği gösterilmiştir (Shreiner ve ark., 2015). Ayrıca mikrobiyota kompozisyonundaki değişimlerin, glikoz metabolizmasını ve insülin duyarlılığını doğrudan etkileyebileceği düşünülmektedir (Qin ve ark., 2012). Bağırsak mikrobiyotası, moleküler düzeyde bağırsak, karaciğer, beyin ve diğer organları etkiler (Martin ve ark., 2017). Ayrıca, metabolizma üzerinde önemli etkiler göstererek bariyer işlevi görmekte; emilim, sindirim, bağırsak motilitesi ve mukozal bağışıklığın düzenlenmesine katkıda bulunmaktadır (Pelzer ve ark., 2017; Sommer ve Bäckhed, 2016). Sağlıklı bireylerde geniş bir çeşitliliğe sahip mikroorganizmaların oluşturduğu mikrobiyota, doğumdan hemen sonra doğal yollarla yerleşmeye başlar (Berçem, 2024). Mikrobiyotanın yapısı, genetik özellikler, doğum şekli, yaş, beslenme alışkanlıkları ve yaşanan bölge gibi faktörlere bağlı olarak değişkenlik gösterebilir. Diyet, bağırsak mikrobiyotası kompozisyonunu belirleyen en önemli çevresel faktörlerden biridir (Berçem, 2024). Mikrobiyotanın gelişimine veya bozulmasına etki eden faktörler Tablo 1’de özetlenmiştir.

Tablo 1. Bağırsak Mikrobiyotasını Etkileyen Faktörler

İntrinsik faktörler	Çevresel faktörler	İlaçlar
Mide asiditesi azalması	Diyet	Antibiyotik
Oksijen miktarı		PPI
Motilite		Prokinetik ajanlar
Gastrointestinal sekresyonlar		Laksatifler
Antimikrobiyal peptidler		Opioidler
İmmünite		NSAİİ

NSAİİ: Non-steroid anti-inflamatuvar ilaçlar, **PPI:** proton pompa inhibitörleri

Diyabet, kronik hiperglisemiyle seyreden ve birçok sistemi etkileyen bir metabolik bozukluktur

(TEMED, 2020). Tip 2 diyabet, yetişkinlerde en sık görülen diyabet türü olup tüm diyabet vakalarının yaklaşık %90’ını oluşturmaktadır (TEMED, 2020). Patogeneğinde insülin direnci, insülin salgısında azalma ve inkretin hormon yetersizliği önemli rol oynar. Daha çok erişkin yaşta ortaya çıkar ve genetik yatkınlık belirgin bir etkidir. Bu hastalar genellikle fazla kilolu veya obezdir. Hastalık genellikle sinsi bir başlangıç gösterir ve ilerlemesi Tip 1 diyabete göre daha yavaştır. Tip 2 diyabette mutlak bir insülin eksikliği bulunmadığından diyabetik ketoasidoz riski düşük olmakla birlikte, uzun süreli hiperglisemi ya da insülin rezervinin tükenmesi durumunda ketoasidoz gelişebilmektedir. Diyabet, bulaşıcı olmayan hastalıklar arasında önemli bir konumda bulunmakta olup, günümüzde en ciddi halk sağlığı problemlerinden biri olarak değerlendirilmektedir. Uluslararası Diyabet Federasyonu’nun (IDF) araştırmalarına göre, diyabetin önümüzdeki yıllarda daha da yaygınlaşacağı öngörülmektedir (IDF, 2019). Türkiye Diyabet, Obezite ve Hipertansiyon Epidemiyolojisi Araştırması’nın (TURDEP II), erişkin Türk nüfusunda diyabet prevalansının %13,7’ye yükseldiğini ortaya koymuştur (Satman ve ark., 2013). IDF’nin raporlarına göre, %11,1 prevalans oranı ile Türkiye, Avrupa bölgesinde en yüksek diyabet oranına sahip ülke konumundadır ve yaklaşık 6,6 milyon diyabetli erişkin ile Almanya ve Rusya’dan sonra üçüncü sırada yer almaktadır (IDF, 2019). Ayrıca, 2045 yılı itibarıyla Türkiye’nin dünyada en fazla diyabetli bireyin yaşadığı ilk 10 ülke arasında bulunacağı tahmin edilmektedir. Bağırsakta bulunan yararlı mikroorganizmaların dengesinin bozulması ve zararlı mikroorganizmaların baskın hale gelmesi, pek çok akut ve kronik hastalıkla ilişkilendirilmiştir (Duvallat ve ark., 2017). Bu hastalıklar Tablo 2’de gösterilmiştir.

Tablo 2. Disbiyozise Eşlik Eden Hastalıklar

Hastalıklar
Atopi ve astım
Çölyak hastalığı
Kolon kanseri
Tip 1 DM
Tip 2 DM
HIV enfeksiyonu
İnflamatuvar Bağırsak hastalığı
İrritabl Bağırsak sendromu

Tablo 2 devamı.

Gastroenterit
Nekrotizan enterokolit
Obezite
Romatoid artrit

HIV: Human Immunodeficiency Virus, **Tip 1DM:** Tip 1 Diyabet,

Tip 2 DM: Tip 2 Diyabet

Bu çalışmada primer hedefimiz, mikrobiyota ile Tip 2 Diyabetes Mellitus (T2DM) arasındaki ilişkiyi ele alarak bağırsak mikrobiyotasındaki değişimlerin diyabet gelişimi üzerindeki etkilerini güncel literatür eşliğinde incelemektir (Karakan, 2023). Ayrıca diyet

ve yaşam tarzı değişikliklerinin bu süreç üzerindeki potansiyel katkıları değerlendirilecektir. Böylelikle, mikrobiyal kompozisyonun modülasyonuna dayalı yenilikçi tedavi stratejileri için bilimsel bir temel oluşturulması hedeflenmektedir.

Diyet ve Bağırsak Mikrobiyotası

Diyetteki değişiklikler, mikrobiyota içeriği ve mikroorganizmaların sayısında değişikliklere neden olur (Human Microbiome Project C, 2012; Lander ve ark., 2001). Bu değişiklikler Tablo 3'te belirtilmiştir.

Tablo 3. Diyet ve Bağırsak Mikrobiyotası

Diyet bileşenleri	Mikrobiyota üzerindeki etkileri
Yüksek Lifli Gıdalar	Bağırsak mikrobiyotası tarafından fermente edilerek asetat, propiyonat ve bütirat gibi kısa zincirli yağ asitlerine dönüştürülür. Bu asitler, bağırsak hareketlerini düzenler, iştahı baskılar ve kan şekeri düşürür.
Bitkisel Bazlı Diyetler	Bağırsaktaki bakteri çeşitliliğini artırarak sağlıklı bir mikrobiyotanın korunmasına yardımcı olur. Özellikle bitkisel posa polisakkaritlerini parçalayan enzimlerden zengin Bacteroidetes bakterisinin oranını artırır.
Fermente Gıdalar (ev yapımı yoğurt, peynir, kefir)	Bu gibi probiyotikler, bağırsak mikrobiyotasını olumlu etkileyerek bütirat üretimini destekler.
Meyve, Sebze ve Baklagiller	Bağırsak mikroplarının çeşitliliğini artırarak sağlıklı metabolitlerin üretimini teşvik eder.

Araştırmalar, diyetin çeşitli bileşenlerinin inflamatuvar yolakları tetikleyebileceğini ortaya koymaktadır. Bu yolakları tetikleyen başlıca diyet bileşenleri arasında kırmızı et, yumurta, omega-6 uzun zincirli çoklu doymamış yağ asitleri (örneğin araşidonik asit), doymuş yağ asitleri, früktoz, süt yağları, bitkisel trans yağ asitleri ve tuz bulunmaktadır (Ochoa-Repáraz ve Kasper, 2016). Yağ oranı yüksek beslenme modelleri, oksidatif stresi artırmakta ve bunun sonucunda inflamasyon gelişmekte; bu süreç de insülin direnci ve diyabet riskini yükseltmektedir (Yao ve Rock, 2015). Diyetteki yağ ve şeker, bağırsakta patojen mikroorganizmaların büyümesine katkıda bulunur (Wasielowski ve ark., 2016). Yağ asitlerinin alımı, bazı laktobasil türlerinin (örneğin Streptokoklar, Laktokoklar, Klostridyalar) büyümesini teşvik etmektedir. Ayrıca, yüksek miktarda yağ ve şeker tüketiminin kronik inflamatuvar hastalıklarla bağlantılı olduğu bilinmektedir (Gregor ve Hotamisligil, 2011). Bu tür diyetler, mukus tabakasının azalmasına ve Helicobacter pylori ile Entamoeba histolytica'nın bağırsakta çoğalmasına neden olur. Mukus tabakasının incilmesi ve disbiyoz, yağ dokusu inflamasyonu, obezite ve

diyabet gelişimine yol açmaktadır (de Cossío ve ark., 2017). Kırmızı et ve emülsiyon içerikli besinler (örneğin tereyağı gibi yağ-su karışımları), bağırsak mukus tabakasının incelmeye sebep olur. Bağırsakta bulunan sekretuar IgA, patojenik enterobakterilere karşı koruma sağlarken mikrobiyal popülasyonu da etkiler. Ancak bu mekanizma, bazen tersine dönerek disbiyoz, yağ dokusu inflamasyonu, obezite ve diyabetle sonuçlanabilir (Liu ve ark., 2017). Adipoz dokudaki immün hücreleri hangi faktörlerin teiklediği tam olarak bilinmemekle birlikte, hayvan çalışmaları yağ içeriği zengin diyetlerin bağırsak geçirgenliğini ve oksidatif stresi artırdığını; bunun sonucunda obezitede görülen kronik düşük düzeyli inflamasyonun ortaya çıktığını ve glikoz intoleransı ile tip 2 diyabet riskinin yükseldiğini ortaya koymuştur (Tilg ve Moschen, 2015). Diyet, metabolik endotoksemi ve inflamatuvar toksinlerin azaltılmasında etkili olabilir. Bu nedenle, diyetin obezitenin önlenmesi ve kronik inflamasyonun azaltılmasında kritik bir rol üstlendiği düşünülmektedir. (Ochoa-Repáraz ve Kasper, 2016). Bazı klinik araştırmalar, obez ve zayıf bireylerde bağırsak mikrobiyotası çeşitliliğinin

farklılık gösterdiğini ortaya koymuştur (Altuntaş, 2017).

Mikrobiyota İlişkili Besinler

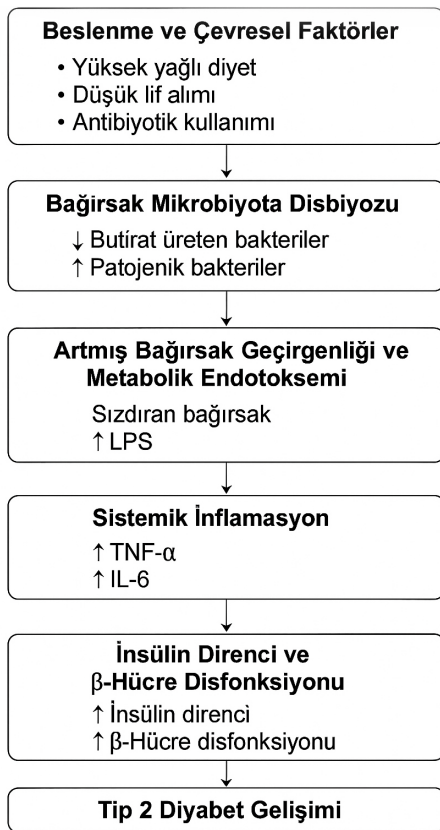
Mikrobiyotanın düzenlenmesinde probiyotikler en etkin bileşikler olarak kabul edilmektedir (Unno ve ark., 2015). Bu nedenle, diyetin mikrobiyota üzerindeki etkisi araştırılırken fermente besinlerle alınan mikroorganizmaların potansiyel etkileri büyük ilgi görmektedir. Yoğurt ve kefir gibi probiyotik bakteri içeren ürünlerin tüketimi üzerine yapılan çalışmalarda, *Bifidobacterium* ve Laktik asit bakteri popülasyonlarının yanı sıra β -galaktosidaz aktivitesinin ve kısa zincirli yağ asidi konsantrasyonlarının arttığı, *Enterobacteria* ve *Clostridia* popülasyonlarının ise azaldığı gösterilmiştir (Veiga ve ark., 2014). Bununla birlikte, fermente besinlerin mikrobiyota üzerindeki etkilerini daha iyi kavrayabilmek için yeni araştırmalara ihtiyaç vardır. Fermente besinlerin yanı sıra, prebiyotik özellik taşıyan karbonhidratlar, posa ve fitokimyasal içeriğe sahip bazı spesifik besinlerin mikrobiyota üzerindeki etkileri incelenmiştir. Bu kapsamda, en çok çalışılan besinler arasında tam tahıllar, badem ve fıstık gibi yağlı tohumlar, yaban mersini, böğürtlen, elma ve muz gibi meyveler ile çay ve kırmızı şarap gibi içecekler bulunmaktadır (Özdemir ve Büyüktuncer Demirel, 2017). Beslenme ile bağırsak mikrobiyotası arasında karşılıklı ve güçlü bir etkileşim olduğu düşünülmektedir (Schloissnig ve ark., 2013). Kişilerin bağırsak mikrobiyal yapılarındaki farklılıkların büyük ölçüde beslenme alışkanlıklarından kaynaklandığı belirtilmektedir. Beslenmenin, mikrobiyal çeşitlilik, genetik materyal, gen ekspresyonu ve enzim aktiviteleri üzerinde değişimler yaratarak mikrobiyota kompozisyonunu ve fonksiyonlarını dönüştürebildiği ortaya konmuştur (Zhang ve ark., 2021). Bu bağlamda, doğal prebiyotik kaynaklar içeren bitkisel besinlerin ve doğal probiyotikler barındıran fermente besinlerin tüketimiyle zenginleştirilmiş bir diyetin faydalı olabileceği öngörülmektedir.

Mikrobiyota Kompozisyonundaki Değişimler ve Diyabet

Bağırsak mikrobiyotası, çoğunluğu Firmicutes, Bacteroidetes, Proteobacteria ve Actinobacteria şubelerine ait olan, 9 filuma yayılmış 1000'den

fazla bakteri türünden oluşur (Wu ve ark., 2020). Yapılan pek çok çalışma, bağırsak mikrobiyotasının tip 2 diyabetin (T2DM) gelişiminde önemli bir rol oynadığını göstermektedir (Gurung ve ark., 2020). Mikrobiyota, glikoz metabolizması ve insülin duyarlılığının düzenlenmesinde etkili olabilir. Ayrıca, diyabet semptomlarının iyileştirilmesiyle mikrobiyota kompozisyonunda olumlu değişiklikler sağlanabilir ve bu durum prediabet sürecindeki glikoz toleransının ve açlık glikozunun düzelmesine katkı sunabilir (Li ve ark., 2020). T2DM hastalarında, Clostridia sınıfı ve Firmicutes şubesinin miktarının azaldığı, buna karşın Betaproteobacteria sınıfının artış gösterdiği ve plazma glikoz seviyeleriyle pozitif ilişkili olduğu saptanmıştır (Zhou ve ark., 2022). Bütirat üreten bakteriler (*Clostridiales* sp. SS3/4, *Faecalibacterium prausnitzii*, *Roseburia intestinalis*, *Eubacterium rectale* ve *Roseburia inulinivorans*) azalırken, fırsatçı patojen bakteriler (*Bacteroides caccae*, *Clostridium hathewayi*, *Clostridium symbiosum*, *Eggerthella lenta*, *Clostridium ramosum* ve *Escherichia coli*), mukus parçalayan bakteriler (*Akkermansia muciniphila*) ve sülfat indirgeyen bakteriler (*Desulfovibrio* sp. 3_1_syn3) artış göstermiştir (Qin ve ark., 2012). Bununla birlikte, bu farklılıkların esas olarak diyabetin kendisinden çok metformin tedavisiyle bağlantılı olduğu bildirilmiştir. Metformin tedavisi, *Escherichia* miktarını artırırken *Intestinibacter* seviyesini düşürerek gastrointestinal rahatsızlıklarla ilişkilendirilebilir. Daha ayrıntılı analizler, metforminin bağırsak lipid emilimini azalttığını, iltihabi yanıtı baskıladığını ve bütirat ile propiyonat üretimini artırdığını göstermiştir (Qin ve ark., 2012). Son dönemlerde araştırmacılar, prediabetik bireylerde veya henüz tedavi almamış T2DM hastalarında mikrobiyotanın rolünü incelemektedir. Allin ve ekibi, prediabetik dönemde bağırsak mikrobiyotasında anormal değişiklikler olduğunu, *Clostridium* ve *Akkermansia muciniphila* miktarının azaldığını; buna karşın *Dorea*, *Ruminococcus*, *Sutterella* ve *Streptococcus* seviyelerinin arttığını saptamıştır (Wu ve ark., 2020). İsveç'te yapılan bir başka çalışmada, bozulmuş glikoz toleransı (IGT) ve tedavi edilmemiş diyabet (T2D) gruplarının bağırsak mikrobiyota kompozisyonunun, normal glikoz toleransına (NGT) sahip bireylerden önemli ölçüde farklı olduğu, ancak bozulmuş açlık glikozu (IFG) grubunda belirgin bir

değişiklik gözlenmediği belirlenmiştir. Bu bulgular, bağırsak mikrobiyotasının sistemik insülin direncini düzenleyerek diyabet gelişiminde önemli bir etkiye sahip olduğunu göstermektedir (Wu ve ark., 2020). Prediyabet ve T2DM hastalarında, bütirat üreten bakterilerin (*Pseudoflavonifractor* spp., *Clostridium* spp., *Alistipes* spp., *Faecalibacterium* spp., *Oscillibacter* spp.) miktarı azalmış, bağırsak mikrobiyal disbiyozunun ise diyabetin patogeneğinde kritik rol oynadığı belirlenmiştir (Gurung ve ark., 2020). Mikrobiyota disbiyozunun tip 2 diyabet gelişimine katkı mekanizmaları (Şekil 1)'de özetlenmiştir.



Şekil 1. Mikrobiyota disbiyozunun tip 2 diyabet gelişimine katkı mekanizmaları.

Sonuç olarak, bağırsak mikrobiyotası, T2DM gibi metabolik hastalıkların bir biyobelirtici olarak değerlendirilmektedir.

Bağırsak Mikrobiyotası ve T2DM Arasındaki Nedensellik

Geniş çaplı bağırsak mikrobiyota çalışmaları, bağırsak florası ile T2DM arasındaki karmaşık ilişkiye dair önemli veriler sunmaktadır. Hollanda'da 952 gönüllü üzerinde yapılan bir çalışmada, bağırsak

mikrobiyotası ve T2DM arasındaki nedensel ilişki analiz edilmiştir. Araştırmada, katılımcıların tüm genom ve bağırsak metagenom verileri incelenmiş, dışkıdaki kısa zincirli yağ asitleri (SCFA) seviyeleri ölçülmüş ve klinik parametreler değerlendirilmiştir. Çift yönlü Mendelian Randomization (MR) analizleri, mikrobiyal özelliklerle kan glikoz düzeyleri arasındaki nedenselliği değerlendirmiştir. Konak genetiğinin yönlendirdiği bütirat artışının, oral glikoz tolerans testi sonrası insülin yanıtını iyileştirdiği belirlenmiştir (Sanna ve ark., 2019). Çinli T2DM hastalarında bağırsak mikrobiyotasının orta derecede düzensiz olduğu bulunmuştur. Özellikle, T2DM hastalarında *Clostridium hathewayi*, *Clostridium symbiosum* ve *Escherichia coli* gibi birden fazla patojenik bakteride artış görülmüştür (Qin ve ark., 2012). Başka bir çalışma, T2DM'li Avrupalı kadınlarda, normal glikoz toleransı olan bireylere kıyasla dört *Lactobacillus* türünün daha fazla ve beş *Clostridium* türünün daha az bolluğuna sahip olduğunu doğrulamıştır. (Karlsson ve ark., 2013) *Lactobacillus* türleri açlık glikozu ve HbA1c ile pozitif korelasyon gösterirken, *Clostridium* türleri açlık glikozu, HbA1c ve plazma trigliseritleri ile negatif korelasyon gösterdiği görülmüştür ve bu da bu bakteri taksonlarının T2DM gelişimi ile ilişkili olabileceğini göstermiştir (Karlsson ve ark., 2013). Benzer şekilde, yeni teşhis konmuş T2DM hastalarında *Lactobacillus* seviyeleri önemli ölçüde artarken, *Clostridium coccoides* ve *Clostridium leptum* seviyelerinin önemli ölçüde azaldığı görülmüştür (Chen ve ark., 2019). Normal glikoz regülasyonu olan bireylerle karşılaştırıldığında, prediyabeti olan Danimarkalı hastalarda bağırsak mikrobiyotasında, *Clostridium cinsi* ve *A. muciniphila*'nın bolluğunun azaldığı görülmüştür (Afri ve ark., 2018). Normal glikoz toleransı olan bireylerle karşılaştırıldığında, *Clostridia* sınıfı ve *Faecalibacterium prausnitzii*'den gelen metagenomik bağlantı gruplarının (MLG'ler) bolluğu daha düşük bulunmuş, buna karşın *E. coli*, *Streptococcus salivarius* ve *Eggerthella* sp.'den gelenler prediyabetiklerde daha yüksek olduğu bulunmuştur (Zhong ve ark., 2019). Bu bulgular, T2DM'nin farklı evrelerinin bağırsak mikrobiyotasının çeşitli özelliklerini gösterdiğini ve konak ile bağırsak mikrobiyotası arasında karmaşık etkileşimler olabileceğini göstermektedir. T2DM'li hastalarla yapılan çalışmalardan elde edilen önemli bulgular Tablo 4'te gösterilmiştir.

Tablo 4. T2DM’li hastalarla yapılan çalışmalardan elde edilen önemli bulgular.

Hasta Grubu	Analiz Yöntemi	Özellikler	Ana Bulgular	Referanslar
T2DM	Tam-genom metagenomik shotgun analizi	Çinli, ortalama yaş 47.0±4.5 yıl	Acidaminococcella, Bacteroides pletolus ve Plasicolectobacterium sp. CHG, T2DM için potansiyel biyobelirteçler olabilir.	Wang T.Y. ve ark., 2020
T2DM	İki aşamalı metagenomik ilişki çalışması	Çinli, 13–86 yaş	T2DM hastalarında patojenik bakteriler artarken, sağlıklı kontrollerde bütirat üreten bakterilerin bolluğu yüksektir.	Qin ve ark., 2012
T2DM	Tam-genom metagenomik shotgun analizi	70 yaşında Avrupalı kadın	Avrupalı kadınlarda T2DM ile dört Lactobacillus türünün bolluğu artmış, beş Clostridium türünün bolluğu azalmıştır.	Karlsson ve ark., 2013
Yeni tanılı T2DM	16S rRNA sekanslama	Tayvanlı, ortalama yaş 51±12 yıl	Lactobacillus seviyeleri artmış, Clostridium coccoides ve Clostridium leptum seviyeleri azalmıştır.	Chen ve ark., 2019
RT2	16S rRNA sekanslama	Tayvanlı, ortalama yaş 64.37±2.194 yıl	RT2 hastalarında Bacteroides vulgaris ve Vellonella denticardii artmış, Metamarsia muciphilia ve Flexibacterium azalmıştır.	Shih ve ark., 2020
Prediyabet	16S rRNA sekanslama	Danimarkalı, 57–68 yaş	Danimarkalı prediyabet hastalarında Clostridium gyrys ve A. muciniphila bolluğu azalmıştır.	Allin ve ark., 2018
Prediyabet	Tam-genom metagenomik shotgun analizi	Çinli, ortalama yaş 61.75±0.93 yıl	Clostridia sınıfı ve Plescatbacterium praxendi azalmış, E. coli, Streptococcus salivarius ve Eggenhilis artmıştır.	Zhong ve ark., 2019
DN	16S rRNA sekanslama	Çinli, ortalama yaş 52.93±9.98 yıl	Escherichia-Spiraja ve Pleveralis, DN hastalarını T2DM olup renal hastalığı olmayanlardan ayırt edebilir.	Tao ve ark., 2019
DN	16S rRNA sekanslama	Çinli, ortalama yaş 60.95±6.69 yıl	Evre IV DN hastalarında Haemophilus ve Lachnospiraceae LOG-004, evre III DN hastalarına kıyasla daha yüksektir.	Du ve ark., 2021
DOI	16S rRNA sekanslama	Çinli, ortalama yaş 69.41±4.15 yıl	DOI hastalarında Bifidobacterium ve Trenefolates azalmış, Peptococcus ve Lauconostocaceae artmıştır.	Zhang ve ark., 2021a
DR	16S rRNA sekanslama	Çinli, ortalama yaş 60.28±10.5 yıl	Plasterallaceae, DR tanısı için non-invaziv bir biyobelirteç olarak kullanılabilir.	Huang ve ark., 2021

DN: Diyabetik Nefropati, **DOI:** Diyabetik Obezite İlişkili İnflamasyon, **DR:** Diyabetik Retinopati, **RT2:** Tedaviye dirençli Tip 2 Diyabet, **T2DM:** Tip 2 Diyabet

Bütirat ve T2DM İlişkisi

Bütirat, kısa zincirli bir yağ asididir (SCFA, short-chain fatty acid) ve bağırsak mikrobiyotası tarafından üretilir (Çağlar ve ark., 2017). Bütirat, genellikle lifli gıdaların (tam tahıllar, sebzeler, baklagiller gibi) sindirimi sırasında bağırsaktaki faydalı bakteriler (Faecalibacterium prausnitzii, Roseburia spp, Eubacterium rectale) tarafından üretilir. İnsülin duyarlılığını etkileyen bir metabolit olup, seviyesindeki azalmanın diyabetle ilişkili olduğu görülmüştür (Sanna ve ark., 2019). Yapılan bir çalışmada, bütirik asidin diyabet üzerindeki etkileri incelenmiştir. Araştırmada, sıçanlar çözünmeyen lif kaynağı olarak %5 buğday kepeği ve çözünür lif kaynağı olarak %2,5 guar gum içeren bazal diyetle beslenmiş, deney grubuna ise 250, 500 ve 750 mg/kg vücut ağırlığı/gün dozlarında bütirik

asit uygulanmıştır. Diyabetik durumda, kontrol grubuna göre su tüketimi, idrar miktarı, idrardaki şeker oranı ve açlık kan şekeri düzeylerinin yükseldiği; lifle beslenen diyabetik grupta ise bu değerlerin yaklaşık %20 oranında azaldığı tespit edilmiştir. Özellikle, 500 mg/kg vücut ağırlığı/gün dozundaki bütirik asit takviyesinin, diyabetik semptomlarda yaklaşık %40 oranında iyileşme sağladığı belirtilmiştir. Ayrıca diyabet döneminde idrar şekeri seviyesinin 7,2 g/gün’den 3,6 g/gün’e, açlık kan şekerinin ise 270 mg/dl’den 180 mg/dl’ye düştüğü gözlenmiştir. Sonuç olarak, bütirik asidin hücrel ve moleküler düzeyde diyabet komplikasyonlarının önlenmesinde fayda sağlayabileceği vurgulanmıştır (Çağlar ve ark., 2017).

Sonuç ve Öneriler

Mikrobiyota, insan sağlığı için hayati önem taşıyan, metabolik, bağışıklık ve nörolojik süreçlere katkıda bulunan bir ekosistem olarak kabul edilmektedir. Güncel bulgular diyabetin, bağırsak mikrobiyotasındaki çeşitliliği ve dengeyi bozduğu, bunun da insülin direnci, glikoz metabolizması bozuklukları ve inflamatuvar süreçlerle ilişkilendirildiği gösterilmiştir. Bu nedenle mikrobiyotanın zenginleştirilmesi ve korunması, diyabetin önlenmesi ve yönetiminde etkili bir araç olabilir. Bireylerin beslenme alışkanlıklarında olumlu değişiklikler yaparak hastalık riskini azaltabileceğini ve tedavi süreçlerini destekleyebileceğini göstermektedir. Sonuç olarak, diyabet tedavisinde mikrobiyotayı hedefleyen yeni stratejiler, beslenme ile birleşerek daha etkili sonuçlar

doğurabilir. Mikrobiyota ve beslenme arasındaki etkileşimlerin daha iyi anlaşılması, diyabetin önlenmesi ve tedavisinde önemli bir adım olacaktır. Bu yaklaşımların klinik etkinliğini doğrulamak için daha fazla randomize kontrollü çalışmaya ihtiyaç vardır.

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A RARE DIAGNOSIS IN A CHILD PRESENTING WITH URINARY INCONTINENCE: SPINAL EPENDYMOMA

Üriner inkontinans ile başvuran çocukta nadir bir tanı: Spinal ependimom

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ABSTRACT

Patients presenting with various symptoms to the pediatric emergency department may be diagnosed with a spinal mass. Spinal ependymoma is a central nervous system tumor that is quite rare in childhood. Early diagnosis is important in terms of reducing morbidity and mortality. The presenting symptoms should be well understood, and necessary tests for differential diagnosis should be conducted. In this case, a 9-year-old male patient who presented to our emergency department with complaints of urinary incontinence and walking difficulties and was diagnosed with spinal ependymoma will be discussed.

Keywords: Ataxia, Ependymoma, Spinal mass, Urinary incontinence

ÖZET

Çocuk acil servisine çeşitli semptomlarla başvuran hastalar spinal kitle tanısı alabilmektedir. Spinal ependimom, çocukluk çağında oldukça nadir görülen merkezi sinir sistemi tümörüdür. Erken tanı konulması morbidite ve mortalitenin azaltılması açısından önemlidir. Başvuru semptomları iyi bilinmeli ve ayırıcı tanıya yönelik gerekli tetkikler yapılmalıdır. Bu vakada, acil servisimize idrar kaçırma ve yürüme bozukluğu şikayetleri ile başvuran ve spinal ependimom tanısı alan 9 yaşındaki erkek hastadan bahsedilecektir.

Anahtar Kelimeler: Ataksi, Ependimom, Spinal kitle, Üriner inkontinans

INTRODUCTION

In children, spinal cord tumors constitute less than 10% of all pediatric central nervous system tumors, and approximately 30% of these are ependymomas (Hsu & Jallo, 2013). Patients with spinal masses most commonly present with symptoms such as weakness in the lower extremities, numbness, ataxia, and sphincter dysfunction (Bach et al., 1990). In cases where spinal cord tumor is suspected, neuroimaging methods should be performed for diagnosis. Here, we will discuss a 9-year-old male patient who presented to the emergency department with complaints of urinary incontinence, had a detailed history of gait disturbance, constipation, and pain in the sacral region, and was diagnosed with spinal ependymoma by neuroimaging.

CASE

A 9-year-old male patient presented to our pediatric emergency department with complaints of urinary incontinence and sacral region pain that started 3 days ago. The patient, unable to urinate voluntarily, was experiencing dribbling incontinence that was continuous and had inability to pass flatus or stool for the past three days. In his history, there was no trauma, poisoning, dysuria, discoloration of urine, headache, fever, recent infection, or vaccination history. Upon detailed questioning, it was learned that he had been limping for 3 months but had not consulted any center for this complaint. At the time of admission, the patient's general condition was good, vital signs were stable, and the Glasgow Coma Scale was 15. In the neurological examination, cranial nerves were intact, deep tendon reflexes were normal, and pathological reflexes were not detected. There were no signs of meningeal irritation. In the upper extremities, muscle strength was 5/5, while in the lower extremities, it was 3/5 bilaterally in the distal regions. In the sensory examination, loss of sensation was detected in the L3 - L5 dermatomes. In the examination of other systems, a palpable distended bladder was detected, and due to the presence of dribbling-type urinary incontinence, overflow urinary incontinence was considered. No pathology was detected in the examination of the sacral region. During the rectal

examination, there was fecal contamination, but the anal tone was weak. There were no significant features in the personal and family history. In the preliminary evaluation, differential diagnoses included myelitis, Guillain-Barré syndrome, and a spinal mass. To assess for urinary retention possibly related to neurogenic bladder dysfunction, bladder catheterization was performed, yielding 600 cc of urine output. This finding supported a neurological etiology. Laboratory investigations, including blood and urine tests, were unremarkable, reducing the likelihood of infectious or systemic inflammatory causes such as myelitis. Additionally, abdominal ultrasound was performed to rule out urological or structural abdominal pathologies and revealed no abnormalities. Given the persistence of neurological symptoms and suspicion of a spinal lesion, contrast-enhanced lumbosacral magnetic resonance imaging (MRI) was obtained. The MRI revealed an intradural, extra-axial mass extending from the L4 to S1 vertebral levels, occupying the spinal canal and demonstrating heterogeneous hypointense signals (Figure 1). Based on these imaging findings, the patient was diagnosed with a spinal cord tumor.

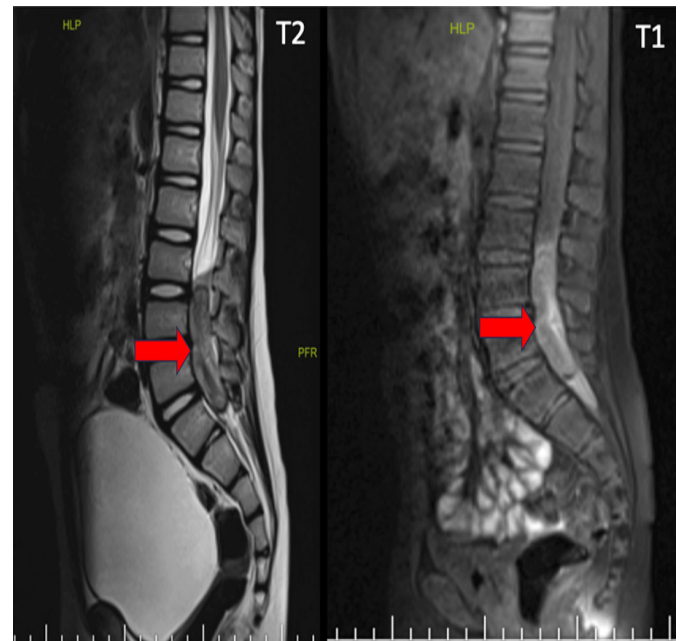


Figure 1. Lumbar magnetic resonance imaging a) T2 sequence showing an intradural extra-axial mass with heterogeneous hypointense signals in the spinal canal at the L4-L5-S1 level and a globular bladder appearance b) T1 sequence showing heterogeneous enhancement of the mass at the L4-L5-S1 level.

Dexamethasone at a dose of 0.5 mg/kg was administered to the patient with spinal cord compression in the emergency department. During follow-up, there was no hypotension or bradycardia. The patient was consulted with neurosurgery. A contrast-enhanced cranial MRI was performed for metastasis; no lesions compatible with metastasis were observed. The patient was operated on by neurosurgery, and the mass was totally resected. The patient discharged on the 7th day of follow-up with recommendations for physical therapy and during the first week, the patient continued to experience urinary incontinence and constipation. By the end of the first month, these symptoms had significantly improved. The pathology result was grade 2 papillary ependymoma. The pediatric oncology department did not recommend sequential treatment and decided to follow up with intermittent imaging. The patient's follow-up is being continued at our center. Informed consent has been obtained from the family for this case presentation.

DISCUSSION

This study presents the pediatric case with complaints of urinary incontinence, gait disturbance, constipation, and pain in the sacral region, and was diagnosed with spinal ependymoma. Although central nervous system tumors are frequently seen in pediatric age, spinal cord tumors are quite rare (~10%) (Farzan et al., 2022). Their frequency is higher in men compared to women (McGuire, Sainani, & Fisher, 2009). They are histologically benign character and slow-growing tumors (Martinez-Perez et al., 2012). Ependymal tumors are neuroepithelial malignancies of the central nervous system that can be seen in both children and adults (Korshunov et al., 2010). Spinal ependymomas are most common in adults between the ages of 20 and 40 (Pajtler et al., 2015). They stated that in children with spinal tumors, the most common symptoms are impairment of motor functions (74.2%), pain (40%), sensory findings (paresthesia, hypoesthesia, anesthesia) (16.6%), and urinary symptoms (11.4%) (inability to urinate/incontinence). Due to the non-specific early-stage symptoms, it is difficult to diagnose without high clinical suspicion (Farzan et al., 2022). Our case also presented to our emergency department with the

urinary incontinence. Early diagnosis of pediatric spinal tumors is important for preventing morbidity and ensuring effective treatment. Due to the spinal canal being narrower in children compared to adults, symptoms related to spinal masses appear at an earlier stage (Ekuma et al., 2017). In cases of spinal ependymoma, the most common symptoms are localized pain, spasticity in the lower extremities, sensory loss, and gait disturbances (Handbook of Clinical Neurology, 1997). Sofuoğlu et al., in their study of 46 pediatric spinal cord tumor cases, stated that the most commonly observed presenting symptoms were weakness and numbness in the lower extremities (Sofuoğlu & Abdallah, 2018). There is also a risk of spontaneous bleeding in spinal ependymomas. In cases with bleeding, sudden onset back pain may occur, and this can happen before neurological deficits appear (Ekuma et al., 2017). Our patient presented with motor weakness, sensory deficits, ataxia, and sphincter dysfunction. Spinal cord tumors can be intradural (45%) or extradural (55%), and those that are intradural are divided into intramedullary or extramedullary (Parsa et al., 2004). The mass in our case was situated intradural extramedullary. Ependymomas are graded histologically based on their characteristics, such as cell structure, mitotic activity, pleomorphism, necrosis, and vascular proliferation (Louis et al., 2016), and are classified into three grades. Myxopapillary ependymoma and subependymoma are benign and grade I lesions. Grade II lesions have weak anaplastic features; they have classic, cellular, papillary, clear cell, and tanycytic subtypes. Our patient was classified histopathologically as a grade 2 papillary ependymoma. Anaplastic ependymomas, on the other hand, are grade III and are the most aggressive type (Godfraind et al., 2012; Kresbach, Neyazi, & Schüller, 2022). In pediatric patients with central nervous system tumors, the 10-year survival rate is approximately 64% (Tihan et al., 2008). In addition to surgical resection and radiotherapy, corticosteroids such as dexamethasone are frequently used to reduce peritumoral edema and alleviate symptoms. Several studies have reported its short-term benefits in controlling neurological symptoms (Dixit & Kumthekar, 2020). In our case, dexamethasone was used and a response was obtained to the treatment. Gross total resection

forms the basis of spinal ependymoma treatment; in cases with a residual mass, radiotherapy can be added to the treatment. Benesch et al. reported that the overall survival rate was 100% with gross total resection treatment in 29 pediatric primary spinal ependymoma cases (Benesch et al., 2010). The extent of surgical resection in ependymomas has long been considered the only prognostic factor associated with survival (Merchant et al., 2009). Khalid et al. retrospectively evaluated survival in histologically confirmed spinal ependymomas in patients aged 17 and under; they found that tumor size and the extent of total resection were associated with survival (Khalid et al., 2018). Tihan et al., in their study of 96 pediatric central nervous system ependymomas, associated the patient's age, tumor location, extent of resection, and radiation therapy status with survival (Tihan et al., 2008). Rudà et al. stated that histopathological criteria alone cannot predict prognosis; more studies are needed for this (Rudà et al., 2018). Our patient was 9 years old and the intradural and extraaxial location of the tumor may have caused the clinical course to be milder.

CONCLUSION

Patients presenting to the pediatric emergency department with overflow urinary incontinence should be evaluated for signs of spinal cord compression. The rarity of spinal ependymoma cases in children makes it difficult to diagnose cases

and establish a standard treatment protocol. Our case is significant not only for contributing to the pediatric spinal ependymoma literature but also for demonstrating that cases can be diagnosed in the emergency department with a detailed history and physical examination. Spinal tumors, although rare in children, should be considered in the differential diagnosis of persistent or progressive neurological symptoms, back pain, gait disturbances, or urinary incontinence. Early spinal MRI is crucial for timely diagnosis and intervention.

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