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Türk Tıp Dergisi / Turkish Medical Journal

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EDİTÖRDEN / EDITORIAL,

Değerli Meslektaşlarımız ve Alanın Kıymetli Profesyonelleri,

Türk Tıp Dergisi'nin 2025 yılı ilk sayısı ile yine sizlerleyiz. Bu sayıda üç araştırma makalesi, iki olgu sunumu yer almakta. Araştırma makalemizden ilki oral kavite ve orofarenks skuamöz hücreli karsinomlarında HPV sıklığının ve immun kontrol noktası inhibitörleri ile ilişkisinin incelendiği bir araştırma. İkinci araştırma makalemiz olan çocuk ve gençlerde son yıllarda sıklığı giderek artan bir sorun olan kendine zarar verici davranışların yatan hasta popülasyonunda incelendiği bir çalışma. Bu çalışma ile cinsel istismara uğrama, intihar girişimi öyküsünün bulunması ve düşük ferritin düzeyleri ile kendine zarar verici davranışlar arasındaki güçlü ilişki ortaya konulmuş. Üçüncü araştırma makalemiz ile ise COVID-19 kısıtlama sürecinde egzersiz yapma, ekran kullanım süresi ve yeme alışkanlıklarının olumsuz etkilendiğini Ankara Pursaklar örnekleminde ortaya konulmuştur.

Olgu sunumlarında ilkinde asemptomatik COVID-19 enfeksiyonu sırasında ortaya çıkan şiddetli hipertransaminazemi bulunan bir hasta, ikincisinde ise dikkat eksikliği hiperaktivite bozukluğu belirtileri ile kendini gösteren ancak ağır nörodejenerasyona ilerleyen bir nöronal seroid lipofusinozis 5 olgusudur.

Dergimize ilginiz için siz tüm okurlarıma teşekkür ederiz. Sürece katkıda bulunan tüm yazarlar, hakemler, yardımcı editörler, editörler kurulu üyeleri, teknik ekibimize yürekten teşekkür ederiz.

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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.

AMAÇ VE KAPSAM

"Türk Tıp Dergisi" bağımsız, tarafsız, çift-kör gözden geçirme ilkeleri üzerine yayınlanmakta olan bir genel tıp dergisidir. "Türk Tıp Dergisi" 'nin öncelikli amacı tıp ve diş hekimliği alanlarında yapılan, bilimsel açıdan nitelikli ve literatüre yeni bir katkı sunacak olan klinik ve deneysel araştırmalar ile teorik çerçeveli makaleleri yayınlamak, klinik uygulamayı geliştirmek, ulusal ve uluslararası bilgi paylaşımına katkıda bulunmak ve eğitim ve araştırmanın sürekliliğini sağlamaktır.

"Türk Tıp Dergisi", genel tıp ve diş hekimliği alanlarını ilgilendiren tüm konulardaki orijinal, tıbbi, klinik öncesi ve klinik araştırmaları ve incelemeleri yayınlayan açık erişimli süreli yayın organıdır. Türk Tıp Dergisi birçok yazı türünü kabul eder. Orijinal makalelerin yanı sıra kısa rapor, derleme yazıları, olgu sunumları, editöre mektuplar, eğitim yazıları, literatür özetleri ve kongre/toplantı izlenimlerini de yayınlar.

"Türk Tıp Dergisi" her yılın Şubat, Mayıs, Ağustos, Kasım aylarında olmak üzere üç (3) ayda bir yılda dört (4) kez yayınlanır. Gerekli durumlarda özel ya da ek sayılar da yayınlanabilir. Derginin yayın dili Türkçe ve İngilizcedir. Türk Tıp Dergisi bilim etiği çerçevesinde çift-kör hakemlik süreçleri, uygun yayın süresinin sağlanması ve hızlı gözden geçirme ilkesi ile hareket etmektedir. Derginin hedef kitlesi tıp ve diş hekimliği alanlarında çalışan veya bu alanlara ilgi duyan araştırmacılardır.

"Türk Tıp Dergisi" açık erişim olup, kayıt, makale gönderme ve kabul edildiği takdirde makalenin yayınlanması ücretsizdir. Yayınlanmak üzere gönderilen makalelerin daha önce başka bir dergide yayınlanmamış olması gerekmektedir. İçerik, yayın sürecinin tamamlanmasını takiben derginin internet sayfasında ücretsiz erişime açık hale getirilir.

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Araştırma Makalesi / Research Article
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ORAL KAVİTE VE OROFARENKS SKUAMÖZ HÜCRELİ KARSİNOMLARINDA HPV SIKLIĞI, İMMUN KONTROL NOKTASI İNHİBİTÖRLERİ İLE İLİŞKİSİ

HPV Frequency in Oral Cavity and Oropharynx Squamous Cell Carcinomas and its Association with Immune Checkpoint Inhibitors

Hayriye TATLI DOĞAN[1], Mustafa TAHTACI[1]

Afiliasyon / Affiliation:
[1]Ankara Yıldırım Beyazıt Üniversitesi, Tıp Fakültesi, Ankara, Türkiye

Sorumlu Yazar / Correspondence:
Doç. Dr. Hayriye TATLI DOĞAN
Ankara Yıldırım Beyazıt Üniversitesi, Tıp Fakültesi, Patoloji AD Bilkent, Ankara, Türkiye
E-mail: hayriyetatlidogan@aybu.edu.tr

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ÖZET

Amaç: Human papilloma virüs (HPV) ilişkili orofaringeal skuamöz hücreli karsinomların (SHK) prevalansı, etnik ve coğrafi farklılıklar göstermektedir. HPV ilişkili orofaringeal SHK'ların prognozunun, HPV ilişkisi negatif olanlara göre daha iyi olduğu bilinmektedir. Orofaringeal SHK gelişiminde immun sistemden kaçış da önemli mekanizmalardan biridir. T hücrelerinden eksprese olan programlanmış hücre ölüm reseptörü 1 (PD-1) ile programlanmış hücre ölüm reseptör ligandının (PD-L1) etkileşimi T hücre baskılanmasına neden olmaktadır. Çalışmamızda oral kavite ve orofarenks SHK'lerinde prognoz ve tedavide önemi olan, lenfoid doku ile yakından ilişkili HPV sıklığını, PD-1/PD-L1 etkileşimini değerlendirmeyi amaçladık. **Yöntem:** Orofarenks ve oral kavite yerleşimli SHK tanısı almış 70 olguda biyopsi ve eksizyon materyallerine ait parafin bloklardan hazırlanan kesitlerde HPV varlığı, p16 antikoru ile immunohistokimyasal boyama yöntemi ve HPV in-situ hibridizasyon (ISH) yöntemi ile retrospektif olarak araştırıldı. Ayrıca tümör hücrelerindeki PD-L1 ekspresyonu ve tümör mikro çevresindeki lenfoid hücrelerde PD-1 ekspresyonunu immunohistokimyasal boyama yöntemi ile değerlendirildi. **Bulgular:** Çalışmaya dahil edilen olgulardan ikisi orofarenks ve biri dil laterali olmak üzere üç olguda tümörde HPV pozitifliği saptanmıştır. PD-L1 pozitifliği 45 (%64,3) olguda izlenmiştir. PD1 ekspresyonu, PD-L1 pozitif olguların %75,6'sında, PD-L1 negatif olanların %24'ünde orta veya şiddetli olup bu oran istatistiksel olarak anlamlı bulunmuştur. HPV pozitif olan 3 olgunun yalnızca birinde PD-L1 pozitifliği saptanmıştır. PD-L1 pozitif olanlarda genel sağ kalım açısından PD-L1 negatif olanlara göre anlamlı farklılık saptanmamıştır. **Tartışma:** Oral kavite ve orofarenks SHK'de HPV durumundan bağımsız olarak PD-1 ya da PD-L1 ekspresyonu gözlenebilmektedir. HPV pozitifliğinin sıklıkla iyi prognoz ile ilişkili olduğu bildirilmekle birlikte özellikle ülkemizdeki çalışmalar kısıtlıdır. Bu biyobelirteçlerin prognostik ve prediktif önemi daha kapsamlı çalışmalar ile desteklenmelidir.

Anahtar Kelimeler: HPV, Oral kavite, Orofarenks, PD-L1

ABSTRACT

Objectives: The prevalence of human papillomavirus (HPV) associated oropharyngeal squamous cell carcinomas (SqCCs) varies ethnically and geographically and has better prognostic features compared to HPV negative cases. Escaping from the immune system is one of the important mechanisms in the development of oropharyngeal SCC. The interaction of programmed cell death receptor 1 (PD-1) and its ligand (PD-L1) causes T cell suppression. In our study, we aimed to evaluate the frequency of HPV and its relation with PD-1/PD-L1, which is closely related to lymphoid tissue and important in prognosis and treatment in oral cavity and oropharynx SCCs. **Method:** We retrospectively investigated the presence of HPV in sections prepared from paraffin blocks of biopsy and excision materials by immunohistochemical staining method with p16 antibody and HPV in-situ hybridization (ISH) method in our series of 70 patients diagnosed with oral (SqHC). We also evaluated PD-L1 expression in tumor cells and PD-1 expression in lymphoid cells in the tumor microenvironment by immunohistochemically staining method. **Results:** HPV positivity was detected in three tumors, two in the oropharynx and one lateral to the tongue. PD-L1 positivity was observed in 45 (64.3%) cases. PD-1 expression was moderate or severe in 75.6% of PD-L1 positive cases and 24% of PD-L1 negative cases and this ratio was statistically significant. PD-L1 positivity was detected in only one of the 3 HPV positive cases. There was no significant difference in overall survival in PD-L1 positive patients compared to PD-L1 negative ones. **Discussion:** PD-1 or PD-L1 expression can be observed in oral cavity and oropharynx SCC regardless of HPV status. Although HPV positivity is frequently reported to be associated with good prognosis, studies are limited especially in our country. The prognostic and predictive importance of these biomarkers should be supported by more comprehensive studies.

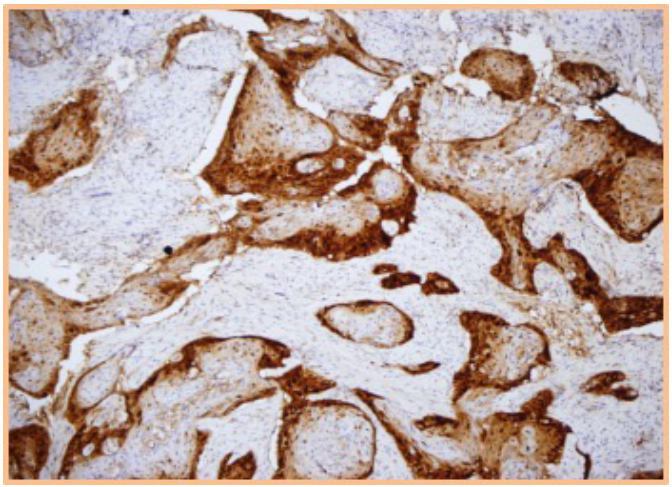
Keywords: HPV, Oral Cavity, Oropharynx, PD-L 1

GİRİŞ

Human papilloma virüs (HPV) baş-boyun skuamöz hücreli karsinomların (SHK) bir kısmının etyolojisinde yer almakta ve özellikle orofarenkste gelişim göstermektedir (Gillison ve ark., 2000). Amerika'da orofaringeal SHK'lerin %40-60'ı HPV ilişkili olup enfeksiyonun tetiklediği kronik inflamasyonun karsinogenezde etkili olduğu öne sürülmektedir (Marur ve ark., 2010). HPV ilişkili kanserler genellikle daha iyi prognozlu olup, daha genç yaşta ve yüksek sosyoekonomik düzeyli toplumlarda daha sık görülmektedir (Richards, 2010). Baş boyun SHK'lerinde de immun sistemden kaçış mekanizmalarından birisi immun kontrol noktası regülasyon bozukluklarıdır (Bauman & Ferris, 2014). Tümörü infiltre eden lenfositler sitotoksik T lenfosit ilişkili antijen 4 ve programlanmış hücre ölüm reseptörü (PD-1) eksprese ederler. Hücre yüzey glikoproteini olan programlanmış hücre ölüm ligandı (PD-L1) ise T hücre yüzeyindeki PD-1 reseptörleri ile etkileşerek T hücre inhibisyonu veya apopitozuna neden olur (Flies ve ark., 2011). PD-1 ve PD-L1 etkileşiminin inhibisyonunu hedef alan antikor temelli immunoterapiler küçük hücreli dışı akciğer kanseri, melanom, baş boyun SHK'leri gibi pek çok kanser türünde son zamanlarda olumlu sonuçlar veren tedaviler arasında yerini almıştır (Garon ve ark., 2015; Robert ve ark., 2015). Sitotoksik T lenfositlerde PD-1 ekspresyonunun HPV pozitif baş-boyun SHK'de HPV negatif olanlara göre daha fazla olduğu bildirilmektedir. Ancak oral SHK'de PD-L1 ekspresyonunun HPV varlığı ile ilişkisi net değildir (Badoual ve ark., 2013). Bu çalışmada oral SHK'de HPV sıklığının belirlenmesi, immun kontrol noktası inhibitörlerinin ekspresyonu ve birbirleri ile olan ilişkisi ele alınmıştır.

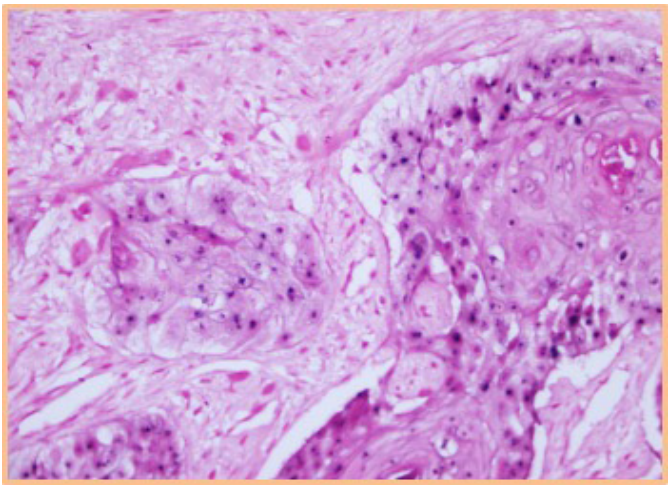
GEREÇ VE YÖNTEM

Çalışmamız için Ankara Bilkent Şehir Hastanesi Tıbbi Araştırmalar Bilimsel ve Etik Değerlendirme Kurulu'ndan TABED 1-24-781 numaralı Etik Kurul Onayı alınmıştır. 2013-2018 yılları arasında SHK tanısı alan ve arşivde materyali bulunan 15'i orofarenks, 55'i oral kavite lokalizasyonlu olmak üzere toplam 70 olguya ait parafin bloklardan doku mikrodizilim yöntemi ile yeni parafin blok oluşturulmuştur. Bu bloklardan hazırlanan kesitlere yüksek risk HPV'yi saptamaya yönelik immunhistokimyasal olarak P16 boyaması (Resim 1)



Resim 1. Tümör hücrelerinde immunohistokimyasal olarak p16 pozitifliği

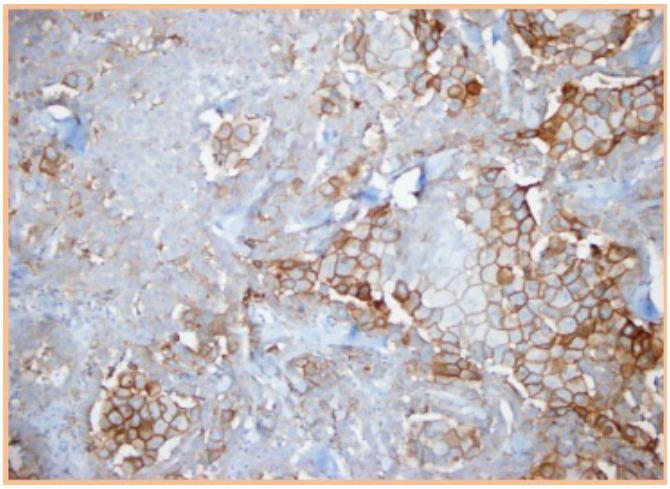
ve Inform HPV III, Family 16 probe16, 18, 31,33, 35, 39, 45, 51, 52, 56, 58, 66 kiti ile in situ hibridizasyon (ISH) çalışması yapılmıştır (Resim 2).



Resim 2. Kromojenik in-situ hibridizasyon yöntemi ile HPV pozitifliği

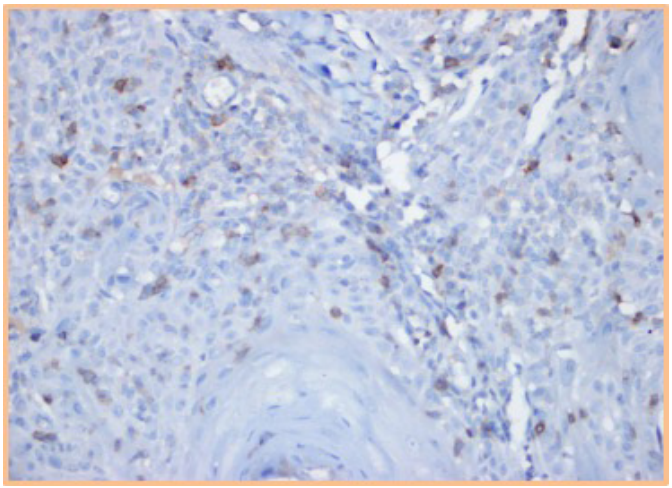
PD-1 ve PD-L1 ekspresyonunun değerlendirilmesine yönelik ise yine parafin bloklardan hazırlanan kesitlere PD-1 (Clone NAT 105) ve PD-L1 (Clone SP263) antikorları ile Ventana otomatik boyama platformunda immunhistokimyasal çalışma yapılmıştır. PD-L1 ekspresyonu tümör hücrelerinde, PD-1 ekspresyonu tümör komşuluğundaki lenfositlerde değerlendirilmiştir. PD-L1 ile tümör hüc-

relerinde >5% boyanma pozitif olarak (Resim 3)



Resim 3. Skuamöz hücreli karsinomda PD-L1 ekspresyonu

ve tümör mikroçevresinde PD-1 eksprese eden lenfosit yoğunluğu ise hafif, orta ve şiddetli olarak değerlendirilmiştir (Resim 4).



Resim 4. Tümör mikroçevresinde PD-1 eksprese eden orta yoğunlukta lenfoid hücreler

İSTATİSTİKSEL ANALİZ

IBM SPSS v21.0 (IBM Corp., Armonk, NY, USA) programı kullanıldı. Kategorik değişkenler için sıklık (n) ve yüzde (%) değerleri kullanıldı. Kategorik değişkenlere yönelik Pearson-$\chi 2$ ve Fisher's exact testleri kullanıldı. Sağ kalım analizi için Kaplan Meier metodu kullanıldı.

BULGULAR

Çalışmaya dahil edilen olguların 45'i erkek, 25'i kadın ve ortalama yaş 64,3 idi. Tümör 43 olguda dil, 8 olguda ağız tabanı, 4 olguda bukkal mukoza, 15 olguda orofarenks yerleşimliydi. HPV varlığını saptamaya yönelik p16 yaygın pozitifliği toplam 3 (%4,3) olguda tespit edilmiş olup bu olgularda yüksek risk HPV varlığı ISH yöntemi ile de kanıtlanmıştır. HPV pozitif olan olguların ikisinde tümör orofarenks, diğerinde ise dil laterali yerleşimliydi. Median 36 aylık takipte HPV pozitif olguların hepsi sağ idi. PD-L1 için %5 değeri sınır değer olarak kabul edildiğinde 45 (%64,3) olguda PD-L1 pozitif bulunmuştur. PD-1 ekspresyonu, PD-L1 pozitif olguların %75,6'sında, PD-L1 negatif olanların %24'ünde orta veya şiddetli olup bu oran istatistiksel olarak anlamlı bulunmuştur ($p<0,05$) (Tablo 1). HPV pozitif olan 3 olgunun yalnızca birinde PD-L1 pozitifliği saptanmıştır. PD-L1 pozitif olan olgularda tümör boyutu ve genel sağ kalım açısından PD-L1 negatif olanlara göre anlamlı farklılık saptanmamıştır ($P>0,05$).

Tablo 1. Tümör hücrelerinde PD-L1 ekspresyonu ile lenfoid hücrelerde PD-1 ekspresyonu ilişkisi

PD-1 eksprese eden lenfosit yoğunluğu	PD-L1 Negatif	PD-L1 Pozitif	Total
Hafif	19 %76	11 %24,4	30 %42,9
Orta-belirgin	6 %24	34 %75,6	40 %57,1
Total	25 %35,7	45 %64,3	70 %100

TARTIŞMA

HPV pozitif baş-boyun kaynaklı SHK'ler sıklıkla dil kökü, derin kriptler ve tonsil yerleşimli olup HPV negatif olanlara oranla mikroçevrede daha yoğun lenfosit infiltrasyonu göstermektedirler (Westra, 2009). Son zamanlarda PD-1: PD-L1 yolağının da HPV pozitif baş-boyun kanserleri ile ilişkisi bildirilmiştir (Gildener-Leapman ve ark., 2013; Lyford-Pike ve ark., 2013). Ancak bu ilişkinin nedeni tam olarak açıklanamamaktadır. Orofaringeal ve oral kavite SHK'de PD-L1 ekspresyonu %50-90 gibi yüksek oranlarda saptanabilmektedir. Ancak HPV durumu ile immün kontrol noktası

inhibitörlerini ele alan oldukça kısıtlı çalışma bulunmaktadır. Lyford- Pike ve ark. ile Upko ve ark. HPV pozitif oral kanserlerde HPV negatiflere oranla daha yüksek PD-L1 ekspresyonu olduğunu ve ayrıca tümör mikroçevresinde PD-1 eksprese eden T lenfositlerin HPV pozitif olgularda daha yoğun olduğunu bildirmişlerdir (Lyford-Pike ve ark., 2013; Ukpo ve ark., 2013). Pike ve ark. ayrıca PD-1: PD-L1 etkileşiminin HPV pozitif hücrelerin immün kaçışı ve hayatta kalması için bağışıklık ayrıcalıklı bir alan oluşturduğunu göstermiştir (Lyford-Pike ve ark., 2013). Kim ve ark. 133 olguluk çalışmasında orofaringeal SHK'da HPV varlığını %67, PD-L1 ekspresyonunu %68 olarak bildirmiş, HPV pozitifliği ile PD-L1 ekspresyonu arasında ilişki tespit edememiştir. PD-L1 ekspresyonu ile genel sağ kalım arasında da ilişki bulunamamıştır (Kim ve ark., 2016). Bizim çalışmamızda PD-L1 pozitifliği %64 olarak saptanmakla birlikte HPV pozitifliği %4,3 olup batılı toplumlara oranla daha düşük bulunmuştur. Çalışmamızın kısıtlayıcı bir yönü HPV pozitif tümörlerin çok az olması nedeni ile HPV durumunun PD-L1 ekspresyonu ile ilişkisinin net olarak değerlendirilememesidir. PD-L1'in prognostik ve prediktif biyobelirleyici olabilmesine yönelik daha geniş prospektif çalışmalara ihtiyaç vardır. PD-L1 pozitifliğini değerlendirmek için daha standart boyama ve skorlama metotları geliştirilmelidir.

SONUÇ

PD-L1 ekspresyonu HPV durumundan bağımsız olarak oral kavite ve orofarenks SHK'lerinin çoğunda bulunabilir. Dünya Sağlık Örgütü verilerine göre prognostik önemi nedeni ile orofarenks tümörlerinde HPV test edilmelidir. PD-L1 ya da PD-1 ekspresyonu ise immunoterapiden fayda görecek hasta seçiminde yardımcı olabilir. İmmun kontrol noktası inhibitörlere yanıtı öngörmeye yardımcı olan biyobelirleyiciler ve beraberinde HPV durumu oral kanserli hastaların klinik yönetiminde ve uygun tedavinin belirlenmesinde yol gösterici olacaktır.

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Finansal Destek: Bulunmamaktadır.
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KAYNAKLAR

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NON-SUICIDAL SELF-INJURY IN CHILD AND ADOLESCENT PSYCHIATRIC INPATIENTS: CLINICAL CORRELATES AND HEMATOLOGICAL FINDINGS

Çocuk ve Ergen Psikiyatri Kliniğinde Yatan Hastalarda Kendine Zarar Verme: Klinik Korelasyonlar ve Hematolojik Bulgular

Merve OKUYUCU[1], Selma TURAL HESAPÇIOĞLU[2,3], Mehmet Fatih CEYLAN[2,3], Cafer Doğan HACIOSMANOĞLU[3], Seda KANOĞLU YÜKSEKKAYA[4]

Afiliasyon / Affiliation:
[1]Ministry of Health Doğubayazıt Dr. Yasar Eryilmaz State Hospital, Department of Child and Adolescent Psychiatry, Ağrı, Türkiye.

[2]Ankara Yıldırım Beyazıt University Faculty of Medicine, Department of Child and Adolescent Psychiatry, Ankara, Türkiye.

[3]Ministry of Health Ankara Yıldırım Beyazıt University Yenimahalle Education and Research Hospital, Department of Child and Adolescent Psychiatry, Ankara, Türkiye.

[4]Binali Yıldırım Unıversity Mengücek Gazi Training And Research Hospital, Department of Child and Adolescent Psychiatry, Erzincan, Türkiye.

Sorumlu Yazar / Correspondence:
Specialist Doctor Merve OKUYUCU
Ministry of Health Doğubayazıt Dr. Yasar Eryilmaz State Hospital, Department of Child and Adolescent Psychiatry, Ağrı, Türkiye
E-mail: merveokuyucu06@gmail.com

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ABSTRACT

Objective: Non-suicidal self-injury (NSSI) is a prevalent concern in child and adolescent psychiatry, often serving as a maladaptive coping mechanism. Despite its frequent occurrence in psychiatric inpatient settings, limited research has examined its clinical and biological correlates, particularly hematological parameters. This study investigates the prevalence of NSSI, its psychiatric and sociodemographic associations, and hematological parameters in a psychiatric inpatient population. **Method:** This study included psychiatric inpatients aged 10–18 years. Psychiatric evaluations were conducted using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL-DSM-5). Participants were classified into NSSI and non-NSSI groups.. **Results:** NSSI was observed among hospitalized adolescents, with self-cutting as the most frequent method. The primary motivations were distress (63.9%) and coping with difficulties (13.9%). Adolescents with NSSI had higher rates of sexual abuse exposure ($p = 0.0001$) and suicide attempts ($p < 0.0001$). depressive disorder was the most common diagnosis ($p = 0.03$), with 70.2% of NSSI individuals having at least one comorbid psychiatric disorder. Hematological analyses showed significantly lower ferritin levels in the NSSI group ($p = 0.01$), while other markers did not differ. Logistic regression identified sexual abuse exposure, suicidal behavior, and low ferritin levels as predictors of NSSI. **Discussion:** NSSI is highly prevalent among psychiatric inpatients and is strongly associated with sexual abuse history, psychiatric comorbidities, and low ferritin levels. Screening for abuse history, suicidality, and iron metabolism disturbances may enhance risk assessment. Future research should explore the mechanistic role of iron metabolism in NSSI.

Keywords: Comorbidity, Ferritin, Self-Injurious Behavior, Sexual Abuse.

ÖZET

Amaç: İntihar girişimi içermeyen kendine zarar verme davranışı (KZVD), çocuk ve ergen psikiyatrisinde yaygın bir sorundur ve sıklıkla uyumsuz bir başa çıkma mekanizması olarak görülmektedir. Psikiyatri yataklı servislerinde sık gözlemlenmesine rağmen, klinik ve biyolojik belirleyicileri, özellikle hematolojik parametrelerle ilişkisi yeterince araştırılmamıştır. Bu çalışma, psikiyatri yatış hastalarında KZVD prevalansını, ilişkili psikiyatrik sosyodemografik faktörleri ve hematolojik parametreleri incelemeyi amaçlamaktadır. **Yöntem:** Bu çalışmaya, Çocuk ve Ergen Psikiyatrisi Yataklı Servisi'nde yatan 10–18 yaş arası hastalar dahil edilmiştir. Psikiyatrik değerlendirme, Çocuklar İçin Duygudurum Bozuklukları ve Şizofreni Tarama Programı kullanılarak yapılmıştır. Katılımcılar, KZVD öyküsü olanlar ve olmayanlar olarak iki gruba ayrılmıştır. **Bulgular:** Hastaneye yatırılan ergenlerde en yaygın yöntemi kendini kesme olarak bulunmuştur. Ana motivasyonlar huzursuzluk (%63,9) ve zorluklarla baş etme (%13,9) idi. KZVD grubu, cinsel istismara maruz kalma ($p = 0,0001$) ve intihar girişimi ($p < 0,0001$) açısından anlamlı derecede daha yüksek oranlara sahipti. En yaygın psikiyatrik tanı depresif bozukluk idi ($p = 0,03$) ve KZVD grubundakilerin %70,2'sinin en az bir eş tanısı mevcuttu. Hematolojik analizler, KZVD grubunda ferritin seviyelerinin anlamlı derecede düşük olduğunu gösterdi ($p = 0,01$), ancak diğer hematolojik parametrelerde fark saptanmadı. Lojistik regresyon analizinde, cinsel istismar öyküsü, intihar girişimi öyküsü ve düşük ferritin düzeyleri KZVD için anlamlı yordayıcılar olarak belirlendi. **Tartışma:** KZVD, psikiyatri yatış hastalarında yaygın olarak görülmekte olup, cinsel istismara uğrama, intihar girişimi öyküsü ve düşük ferritin düzeyleri ile güçlü ilişkiler göstermektedir. İstismar öyküsü, intihar davranışı ve demir metabolizması bozukluklarının taranması risk değerlendirmesini geliştirebilir. Gelecekteki çalışmalar demir metabolizmasının KZVD üzerindeki olası mekanistik rolünü daha ayrıntılı olarak araştırmalıdır.

Anahtar Kelimeler: Cinsel istismar, Ferritin düzeyleri, İntihara yönelik olmayan kendine zarar verme, Psikiyatrik komorbiditeler.

INTRODUCTION

Non-suicidal self-injury (NSSI) is defined as the deliberate and often repetitive damage to one's own body without suicidal intent or posing a life-threatening risk (American Psychiatric Association, 2013; Herpertz, 1995; Klonsky, 2007a). It is primarily used as a coping mechanism to alleviate emotional distress, often by shifting focus from psychological stress to physical sensations (Klonsky, 2011; Nock, 2009; Taliaferro et al., 2019; Wilkinson et al., 2011). Other motivations include self-punishment, seeking attention, or attempting to communicate distress (Klonsky, 2011; Nock, 2009; Wilkinson & Goodyer, 2011). Several theoretical models have been proposed to explain NSSI in adolescents, most of which highlight its function in emotional regulation. The prevalence of NSSI among children and adolescents varies widely, with estimates ranging from 6% to 22% (Lim et al., 2019; Taylor et al., 2018). Systematic reviews suggest that adolescent lifetime prevalence rates range from 7.5% to 46.5% (Jacobson & Gould, 2007; Rojas-Velasquez et al., 2021). The prevalence increases in child and adolescent psychiatric inpatient units, reaching up to 50% (Kaess et al., 2013). The onset of NSSI typically occurs between the ages of 12 and 14, though the behavior may persist into adulthood (Cipriano et al., 2017; Daukantaitė et al., 2021; Kiekens et al., 2023). Cutting, scratching, and hitting are among the most frequently reported methods of self-injury in adolescents (Brown & Plener, 2017; Klonsky, 2011). NSSI is frequently comorbid with psychiatric disorders, including Major Depressive Disorder (MDD), Post-Traumatic Stress Disorder (PTSD), conduct disorders, and substance use disorders (Brown & Plener, 2017; Jacobson & Gould, 2007; Muehlenkamp & Gutierrez, 2007). Among these, MDD is the most commonly diagnosed condition in adolescents engaging in NSSI, with prevalence rates ranging from 41.6% to 58% (Jacobson & Gould, 2007; Nock et al., 2006). Furthermore, a well-established association exists between NSSI and suicide attempts, with specific risk factors—such as a prolonged history of self-injury, engagement in multiple methods, and a reduced experience of physical pain—contributing to an increased likelihood of suicidal behavior (Chesin et al., 2017; Mars et al., 2019; Nock et al., 2006). Beyond psychiatric comorbidities, adverse childhood experiences have been strongly linked to NSSI (Jacobson & Gould, 2007; Maniglio, 2011). A systematic review of 71 studies identified emotional abuse as a significant risk factor, with childhood sexual abuse also being frequently associated with engagement in self-injurious behaviors (Liu et al., 2018). Recent research has begun to explore potential biological markers distinguishing individuals who engage in NSSI from those who do not. While studies in adolescent populations remain limited, preliminary findings suggest alterations in hematological parameters, such as elevated monocyte-to-lymphocyte ratio (MLR) and platelet-to-lymphocyte ratio (PLR), among adolescents with NSSI (Zheng et al., 2022). Furthermore, anemia and deficiencies in key micronutrients have been implicated in the pathophysiology of mood disorders and suicidal behavior. A study investigating late-life depression (LLD) found that serum ferritin, folate, vitamin B12, red blood cell count, hemoglobin, hematocrit, mean platelet volume, and plateletcrit levels were significantly lower in LLD patients compared to healthy older adults (Li et al., 2024). Moreover, reduced serum folate and vitamin B12 levels were negatively associated with suicide attempts, suggesting a potential role for these biomarkers in assessing suicide risk (Li et al., 2024). Although direct evidence linking these findings to NSSI remains scarce, these results highlight the need for further research into the biological underpinnings of self-injurious behaviors in different age groups. Understanding the risk factors and clinical characteristics of NSSI is essential for developing targeted prevention and intervention strategies (Wilkinson & Goodyer, 2011). However, studies investigating the prevalence, psychiatric comorbidities, and underlying mechanisms of NSSI among hospitalized children and adolescents remain scarce. This study aims to address this gap by examining the prevalence of NSSI, associated psychiatric disorders, sociodemographic characteristics, hematological parameters, methods of self-injury, and underlying motivations in a child and adolescent psychiatry inpatient population.

METHODS

Subjects

This retrospective study evaluated patients who were hospitalized in the Child and Adolescent Psychiatry Department of Ankara Yıldırım Beyazıt University Yenimahalle Education and Resarch Hospital. Assessments were conducted under the supervision of experienced child and adolescent psychiatrists and/or professors. All participants were assessed for psychiatric disorders using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, based on DSM-5 criteria (K-SADS-PL-DSM-5) (American Psychiatric Association, 2013; Kaufman et al., 2016). Those with a history of NSSI were included in the case group, while those without a history of NSSI were included in the control group. Exclusion criteria for both groups included: 1) age younger than 10 years or older than 18 years. The study was conducted at the inpatient department of the Child and Adolescent Psychiatry Clinic of Ankara Yıldırım Beyazıt University Yenimahalle Education and Resarch Hospital. Approval was obtained from the Ethics Committee of Ankara Yıldırım Beyazıt University Yenimahalle Education and Resarch Hospital (protocol number: 47, approval date: 2019). The study adhered to the principles of the Declaration of Helsinki as revised in 2000, ensuring the welfare and rights of the participants.

Data collection tools

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL-DSM-5)

The K-SADS-PL-DSM-5 is a semi-structured diagnostic interview, revised by Kaufman et al. (2016), designed to assess psychopathology in children aged 6 to 18 years based on DSM-5 diagnostic criteria (Kaufman et al., 2016). Certified child psychiatrists administer the interview, incorporating information from both parents/caregivers and the child to ensure a comprehensive evaluation of each symptom across various psychiatric disorders. The Turkish adaptation of this scale was conducted and its validity was examined by Unal et al. (2019).

Socio-demographic data form

As part of routine clinical practice, clinicians administered a socio-demographic data collection form to all inpatients. This comprehensive form includes detailed information such as the patient's date of birth, school attendance, relationships with peers and teachers, socio-demographic characteristics of the patient and their family, parental marital status, personal and familial medical and psychiatric history, developmental milestones, history of NSSI and suicide attempts, as well as data on exposure to abuse (physical, psychological, sexual), neglect, bullying, and substance use.

Statistical analyses

The data obtained from participants were analyzed using SPSS (The Statistical Package for the Social Sciences) version 22.0. Descriptive statistics were presented as frequencies and percentages. The chi-square test was used to assess relationships between categorical variables, including gender, age, length of hospitalization, history of suicide attempts, psychiatric diagnoses, and exposure to sexual abuse. Since the data did not follow a normal distribution, the Mann-Whitney U test was applied for comparisons between independent groups. Logistic regression analysis was conducted to identify predictors of NSSI. A p-value of <0.05 was considered statistically significant.

RESULTS

The most frequently observed form of NSSI among patients was self-cutting, with distress being the most commonly reported reason. The methods and reasons for NSSI are presented in detail in Table 1.

Table 1. Methods and Reasons for NSSI

Method of Self-Injury	**n**	**%**
Cutting	68	63.0
Hitting oneself	12	11.1
Head banging	11	10.2
Biting nails to the point of bleeding	9	8.3
Hair pulling	4	3.7
Punching a wall	3	2.8
Pinching oneself	1	0.9
Reason for Self-Injury		
Distress	69	63.9
Coping with difficulties	15	13.9
To get what they want	11	10.2
Due to psychotic symptoms	8	7.4
To attract someone's attention	5	4.6

NSSI: Non-Suicidal Self-Injury.

A comparison between individuals with NSSI and the control group revealed significant differences in exposure to sexual abuse (p=0.0001) and history of suicide attempts (p<0.0001). Additionally, depression was identified as the most prevalent psychiatric disorder among individuals with NSSI (p=0.03). The socio-demographic characteristics and psychiatric diagnoses of individuals with and without NSSI were compared, and the findings are presented in Table 2. It shows that multiple diagnoses could be assigned to the same patient in Table 2.

Table 2. Comparison of Sociodemographic Characteristics Between Individuals With and Without NSSI

Variables		Without NSSI	With NSSI	X^2 or t	p
Gender	Girl	68 (49.6%)	72 (66.7%)	7.153	**0.007**
	Boy	69 (50.4%)	36 (33.3%)		
Age (years, mean ± SD)		14.5±2.4	14.5±2.0	-0.719	0.47
Hospitalization Duration (days, mean ± SD)		24.6±16.3	30.7±16.0	-3.535	**<0.0001**
Suicide Attempt		27 (19.7%)	50 (46.3%)	19.810	**<0.0001**
Psychiatric Diagnoses					
Depression		51 (37.2%)	55 (50.9%)	4.618	**0.03**
Bipolar Affective Disorder		32 (23.4%)	20 (18.5%)	0.846	0.35
Conduct Disorder		31 (22.6%)	33 (30.6%)	1.967	0.16
PTSD		11 (8%)	10 (9.3%)	0.117	0.73
Psychotic Disorders		19 (13.9%)	11 (10.2%)	0.763	0.38
ASD		11 (8%)	10 (9.3%)	0.117	0.73
Anxiety Disorders		19 (13.9%)	22 (20.4%)	1.832	0.17
Conversion Disorder		8 (5.8%)	6 (5.6%)	0.009	0.92
OCD		6 (4.4%)	3 (2.8%)	0.438	0.51
Eating Disorders		7 (5.1%)	3 (2.8%)	0.839	0.36
Substance Use Disorders		7 (5.1%)	13 (12.0%)	3.866	**0.04**
ADHD		35 (25.5%)	33 (30.6%)	0.755	0.38
ID		36 (26.3%)	35 (32.4%)	1.103	0.29
Tic Disorders		2 (1.5%)	1 (0.9%)	0.142	0.71
History of Sexual Abuse		12 (8.9%)	26 (24.3%)	10.709	**0.001**
Incest		3 (2.2%)	4 (3.8%)	0.507	0.477

NSSI: Non-Suicidal Self-Injury; PTSD: Post-Traumatic Stress Disorder; ASD: Autism Spectrum Disorder; OCD: Obsessive-Compulsive Disorder; ADHD: Attention-Deficit/Hyperactivity Disorder; ID: Intellectual Disability.

The distribution of patients is presented based on the number of comorbid psychiatric diagnoses, indicating that the majority had multiple diagnoses, with two diagnoses being the most common (40.8%). Further details are provided in Table 3.

Table 3. Distribution of Patients by the Number of Comorbid Psychiatric Diagnoses

Variables	n	%
Patients with one diagnosis	73	29,8
Patients with two diagnosis	100	40,8
Patients with three diagnosis	50	20,4
Patients with four diagnosis	19	7,8
Patients with five diagnosis	1	0,4
Patients with six diagnosis	2	0,8

Ferritin levels were found to be significantly lower in individuals with NSSI (p=0.01). Comparisons of iron, total iron-binding capacity, hemoglobin, ferritin, vitamin D, vitamin B12, and folic acid levels between adolescents with and without NSSI are presented in Table 4.

Table 4. Iron, Iron Binding Capacity, Hemoglobin, Ferritin, Vitamin D, Vitamin B12, and Folate Levels in Patients with and without NSSI

Parameters	Without NSSI	With NSSI	Z	p
Iron	90.8±47.7	82.6±44.9	-1.224	0.22
Iron Binding Capacity	278.2±72.8	297.6±92.5	-1.220	0.22
Hemoglobin	13.5±1.3	13.4±1.3	-0.529	0.59
Ferritin	50.6±43.3	37.9±31.1	-2.419	**0.01**
Vitamin B12	18.2±14.2	17.2±10.3	-0.362	0.72
Vitamin B12	319.3±155.9	327.1±153.9	-0.489	0.62
Folate	6.1±3.0	6.2±3.5	-0.340	0.73

NSSI: Non-suicidal Self-Injury

To identify predictors of NSSI, a logistic regression model was constructed, including variables such as gender, history of suicide attempts, depressive disorder, substance use-related disorders, exposure to sexual abuse, and ferritin levels. The analysis indicated that exposure to sexual abuse, history of suicidal behavior, and ferritin levels were significant predictors of NSSI. These findings are presented in Table 5.

Table 5. Logistic Regression Analysis for Variables Predicting NSSI

Variables	B	OR	Sig	CI
Exposure to Sexual Abuse	1.165	3.205	0.01	1.298-7.913
Suicidal Behavior	0.968	2.633	0.003	1.396-4.966
Ferritin Levels	-0.01	0.990	0.03	0.981-0.999

NSSI: Non-suicidal Self-Injury, OR: Odds ratio, CI: Confidence interval

DISCUSSION

Our findings are consistent with previous studies, indicating that NSSI is more prevalent among females, particularly during the transitional phase of adolescence (Baiden et al., 2017; Dougherty et al., 2009; Groschwitz et al., 2015; Muehlenkamp & Gutierrez, 2004). During the transitional phase of adolescence, females are more likely to encounter risk factors leading to depression, which may make them more susceptible to depressive symptoms compared to males. This increased vulnerability could subsequently elevate the prevalence of both depression and NSSI (Nolen-Hoeksema & Girgus, 1994). Furthermore, the higher incidence of NSSI in females may be attributed to their greater tendency to seek help in response to emotional distress, potentially leading to higher rates of psychiatric clinic visits. In our study, individuals who engaged in NSSI exhibited a higher frequency of psychiatric comorbidities. Depression was the most commonly observed comorbid psychiatric disorder. Similar to our findings, numerous studies have identified depression as the most frequently associated psychiatric condition in individuals with NSSI (Auerbach et al., 2014; Dougherty et al., 2009; Glenn & Klonsky, 2010; Groschwitz et al., 2015; Nock et al., 2006; Perry et al., 2009). For instance, a study conducted among adolescents in the UK demonstrated that treating depression in individuals with psychiatric comorbidities reduced the risk of NSSI in these individuals (Wilkinson et al., 2011). Furthermore, a correlation exists between treatment-resistant depression and NSSI (Asarnow et al., 2011). Depression is also recognized as a significant predictor for NSSI (Baiden et al., 2017). Therefore, it can be inferred that depressive symptoms may trigger NSSI, suggesting a potential bidirectional relationship between NSSI and depression. Following depression, the most frequently observed psychiatric comorbidities in our study were Intellectual Disability (ID), Attention-Deficit/Hyperactivity Disorder (ADHD), Conduct Disorder, and Anxiety Disorder. The literature supports these findings, as studies have reported that, in addition to depression, other common comorbidities accompanying NSSI include Anxiety Disorder, PTSD, and ADHD (Auerbach et al., 2014; Baiden et al., 2017; Glenn

& Klonsky, 2010; Groschwitz et al., 2015; Klonsky, 2007b; Perry et al., 2009). In our sample, 70.2% of individuals who engaged in NSSI had multiple comorbid psychiatric disorders. This finding further strengthens the notion that psychiatric disorders contribute to the initiation of NSSI (Nock, 2009; Nock et al., 2006). Another significant comorbidity in our study was ADHD, particularly the core symptom of impulsivity. Impulsivity significantly increases the risk of NSSI, as it hampers individuals' ability to plan their behaviors, thereby promoting riskier actions (Baiden et al., 2017; Glenn & Klonsky, 2010). A clinical study reported that individuals who had previously engaged in NSSI exhibited higher levels of impulsivity compared to the general population, with those who had made multiple NSSI attempts demonstrating even greater impulsivity (Evans et al., 1996). These findings suggest that careful assessment and treatment of ADHD in adolescents may reduce impulsive behaviors and, consequently, lower the risk of NSSI. Regarding the forms of NSSI, we found that self-cutting was the most common form of NSSI among hospitalized patients. Similar results have been reported in other studies (Auerbach et al., 2014; Dougherty et al., 2009; Gromatsky et al., 2020; Groschwitz et al., 2015; Klonsky, 2011; Muehlenkamp & Gutierrez, 2004). The relative accessibility of sharp objects may explain the higher prevalence of self-cutting. Our study also identified distress as the most common reason for NSSI attempts. It is well-established that NSSI is frequently used as a means of alleviating negative emotions (Klonsky, 2007b, 2011; Nock, 2009; Taliaferro et al., 2019). This suggests that NSSI may serve as an outlet to escape feelings of distress and emotional turmoil. Additionally, another common reason for NSSI in our study was the desire to attract the attention of others. Adolescents may engage in NSSI as a way to garner attention (Klonsky, 2011; Wilkinson et al., 2011), which can be interpreted as an effort to communicate or a cry for help. A noteworthy finding in our study was the significant correlation between sexual abuse and NSSI attempts. Childhood sexual abuse is a significant adverse event that increases the likelihood of self-harm and suicidal behaviors later in life (Chaplo et al., 2015; Maniglio, 2011). Sexual abuse is consistently highlighted as a risk factor that significantly elevates the risk of NSSI (Auerbach et al., 2014; Baiden et al., 2017; Chaplo et al., 2015). The higher prevalence of sexual abuse among girls compared to boys may help explain the greater incidence of NSSI among females in our study (Ford et al., 2008). Moreover, our study found that individuals who engaged in NSSI had a significantly higher history of suicide attempts compared to the control group. A study conducted in the United States found that 70% of adolescents who had recently engaged in NSSI had attempted suicide at least once in their lifetime (Nock et al., 2006). This study suggested that repeated NSSI attempts, along with an increased tolerance to pain, may lead individuals to experience less pain and engage in more impulsive behaviors, ultimately resulting in a higher risk of suicide attempts (Nock et al., 2006). Furthermore, adolescents who engage in NSSI and do not receive appropriate professional support may struggle to cope with emotional distress, which can exacerbate suicidal thoughts (Taliaferro et al., 2019). These findings underscore the importance of clinicians regularly screening for NSSI in adolescents and providing timely, empathetic interventions (Muehlenkamp & Lau, 2016). Finally, our study explored the relationship between ferritin levels and NSSI. Iron status plays a crucial role in brain function, cognition, and behavior, with ferritin serving as a key clinical marker of iron levels (Huan et al., 2021). Iron deficiency, often reflected in lower ferritin levels, is associated with mood disorders (Yue et al., 2021). In line with this, our findings revealed that individuals with NSSI had significantly lower ferritin levels compared to those without NSSI. This suggests a potential association between iron metabolism and NSSI, supporting previous research that highlights the role of iron homeostasis in emotional regulation and impulsivity. In this study, the prevalence of NSSI among hospitalized patients was found to be 44.9%. This high prevalence may be attributed to the increased rate of psychiatric comorbidities in inpatient settings. However, the unequal distribution of gender among participants poses a limitation in interpreting gender-based differences. One of the main limitations of this study is that the control group does not consist of healthy individuals, which may limit the generalizability of the findings. Additionally, to our knowledge, no

prior study in Türkiye has specifically examined NSSI among child and adolescent inpatients in psychiatric clinics. Therefore, this study contributes to the literature by addressing this gap.

CONCLUSIONS

This study highlights the high prevalence of NSSI among hospitalized children and adolescents and underscores the association between NSSI and psychiatric comorbidities, suicidal behavior, and exposure to sexual abuse. The findings suggest that identifying and addressing risk factors for NSSI in clinical settings is crucial for early intervention and prevention. Additionally, the observed relationship between lower ferritin levels and NSSI warrants further investigation to explore potential biological underpinnings. Future research with larger and more diverse samples is needed to validate these findings and develop targeted interventions for at-risk youth.

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Araştırma Makalesi / Research Article
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EVALUATION OF BODY MASS INDEX CHANGES, NUTRITIONAL HABITS AND FOOD LITERACY LEVELS OF INDIVIDUALS RECEIVING NUTRITION AND DIETARY COUNSELING DURING THE COVID-19 LOCKDOWN PERIOD; ANKARA, PURSAKLAR

Beslenme ve Diyet Danışmanlığı Alan Bireylerin COVID-19 Kısıtlama Sürecindeki Beden Kitle İndeksi Değişimleri, Beslenme Alışkanlıkları ve Gıda Okuryazarlığı Düzeylerinin İncelenmesi; Ankara, Pursaklar

Eylem Gözde ALTUNDAL[1], Egemen ÜNAL[2], Mehmet Enes GÖKLER[2]

Afiliasyon / Affiliation:
[1]Kastamonu İl Sağlık Müdürlüğü Kastamonu, Türkiye
[2]Ankara Yıldırım Beyazıt Üniversitesi, Tıp Fakültesi Halk Sağlığı AD Ankara, Türkiye

Sorumlu Yazar / Correspondence:
Specialist Doctor Eylem Gözde ALTUNDAL
Kastamonu İl Sağlık Müdürlüğü Kastamonu, Türkiye
E-mail:eylemaltundal@gmail.com

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ABSTRACT

Objectives: In this study, it was aimed to evaluate the BMI values, changes in nutritional habits and food literacy levels of individuals who had previously received nutrition and diet counseling during the COVID-19 restriction process. **Method:** The study was cross-sectional and was conducted with 44 individuals over the age of 18 who received nutrition and diet counseling at Pursaklar District Health Directorate. After the individuals were called by phone and their verbal consent was obtained, they were directed to a questionnaire consisting of questions about sociodemographic characteristics, anthropometric data, nutrition and lifestyle habits, and the short food literacy questionnaire. **Results:** The mean age of the participants was 40.20±9.08 years and 93.2% were women. The mean BMI of the participants was 33.87±6.36 before the restriction period and 32.84±5.87 after the restriction period. During the restriction period, 47.7% of the participants reported that their eating habits worsened and 36.4% reported that their appetite increased. 22.7% of the group stated that they skipped main meals during the period, while 20.5% added to main and snacks. The mean food literacy scale score of the participants was 33.54±5.8. As the education level of the participants increased, the food literacy score increased. **Discussion:** Individuals' exercise, screen time and eating habits were negatively affected during the COVID-19 restriction process.

Keywords: COVID-19, Eating Habits, Food Literacy

ÖZET

Amaç: Bu çalışmada, daha önce beslenme ve diyet danışmanlığı alan bireylerin, COVID-19 kısıtlama sürecinde BKİ değerleri, beslenme alışkanlıkları değişiklikleri ve gıda okuryazarlığı düzeylerinin incelenmesi amaçlanmıştır. **Yöntem:** Araştırma kesitsel tipte olup çalışma, Pursaklar İlçe Sağlık Müdürlüğü'nde beslenme ve diyet danışmanlığı alan 18 yaş üzeri 44 kişi ile yürütüldü. Bireyler telefonla aranarak sözlü onamlarının alınması sonrasında sosyodemografik özellikler, antropometrik veriler, beslenme ve yaşam tarzı alışkanlıkları ile ilgili sorulardan ve gıda okuryazarlığı ölçeğinden oluşan anket soruları yönlendirildi. **Bulgular:** Katılımcıların yaş ortalaması 40,20±9,08 yıl olup %93,2'sini kadınlar oluşturdu. Katılımcıların kısıtlama sürecinden önce BKİ değerleri ortalaması 33,87±6,36 iken süreç sonunda 32,84±5,87 olduğu izlendi. Kısıtlama döneminde katılımcıların %47,7'si yeme alışkanlığının kötüleştiğini ve %36,4'ü iştahının arttığını bildirdi. Grubun %22,7'si süreçte ana öğünleri atladığını, %20,5'i ise ana ve ara öğünlere ekleme yaptığını ifade etti. Katılımcıların gıda okuryazarlığı ölçek puan ortalamaları 33,54±5,8 bulunmuştur. Katılımcıların eğitim düzeyi artıkça gıda okuryazarlığı puanı yükselmiştir. **Sonuç:** Bireylerin, COVID-19 kısıtlama sürecinde egzersiz yapmaları, ekran kullanım süreleri ve yeme alışkanlıkları olumsuz etkilenmiştir.

Anahtar Kelimeler: Beslenme Alışkanlıkları, COVID-19, Gıda Okuryazarlığı

INTRODUCTION

The first Coronavirus disease 2019 (COVID-19) case was detected in Turkey on March 11, 2020. In the period since the first case was detected, it has been aimed to gradually reduce the effects of the outbreak and limit the outbreak with public health measures (T.C. Sağlık Bakanlığı, 2020). For this purpose, the activities of public places of rest and entertainment were suspended, flexible working arrangements in public institutions, entry-exit bans in cities where cases are frequently seen, and curfew interventions on weekends have limited the spread of COVID-19 (T.C. İçişleri Bakanlığı, 2020a, 2020b). The COVID-19 pandemic has affected daily life worldwide with its physical and mental health effects (Holmes et al., 2020). Stress is an important factor in the development and re-emergence of addiction and is known to affect eating patterns in general (Yau & Potenza, 2013). The interruption of work routine caused by quarantine may lead to boredom, and it has been shown that there are significant positive associations between boredom and calorie, fat, carbohydrate and protein consumption and the desire to eat less healthy foods (Moynihan et al., 2015). During this period, people's consumption of unhealthy foods and snacking between meals increased (Carroll et al., 2020). Isolation appears to change physical activity and eating behaviors in a way that is risky for health (Ammar et al., 2020). In the face of the current COVID-19 pandemic, there have been restrictions to reduce the infection rate with public health recommendations. These restrictions cause negative effects by limiting access to normal daily and physical activity (Hossain et al., 2020). The quarantine itself and its negative psychological effects can lead to unhealthy behaviors such as physical inactivity, increase in sedentary lifestyle, consumption of unhealthy food and beverages, and changes in proper dietary patterns (López-Bueno et al., 2020). In this study, it was aimed to examine the body mass index (BMI) values, eating habits, lifestyle changes and food literacy levels of individuals who received nutrition and diet counseling during the COVID-19 restriction process.

METHODS

The study was cross-sectional. The population of the study consisted of people who applied for nutrition and diet counseling in Ankara Pursaklar District Health Directorate between 2019 and 2020. In this study, it was aimed to reach the entire population, but the study was conducted on 44 adults over the age of 18 who agreed to participate in the study. After obtaining the necessary ethical and institutional permissions, the study was conducted by the researcher between March 29, 2021, and July 5, 2021, by calling the phone numbers provided by individuals during registration. Participants were informed about the study and verbal consent was obtained by asking them to accept the data sharing and confidentiality policy before participating in the study. Survey questions were directed to the individuals who agreed to participate in the study and data were obtained. The questionnaire consisted of 4 sections including sociodemographic characteristics (gender, age, marital status, education, employment status, income level), anthropometric data (height, weight), questions about nutrition and lifestyle habits (hunger/satiety perception, weight change, number of daily meals, screen time, sleep duration, water consumption, exercise) and food literacy scale. The food literacy section of the questionnaire was taken from the literature. The Short Food Literacy Questionnaire - SFLQ is a scale developed by Krause et al. (Gréa Krause et al., 2018). This scale, which covers important elements of nutritional literacy and definitions of food literacy, has a four- or five-point Likert-type 12-item questionnaire. A score ranging from 7 to 52 can be obtained from the scale. A higher score indicates better food literacy. The Turkish validity and reliability of the SFLQ scale was conducted by Durmuş et al. in 2019 (Durmus et al., 2019). Ethics committee approval and necessary institutional permissions were obtained from Ankara Yıldırım Beyazıt University Health Sciences Ethics Committee (date: 16/02/2021, no: 64). No financial support was received for the conduct of the study and there was no conflict of interest. IBM SPSS 24.0 package program was used for data analysis. Number (n), percentage (%), mean ± standard deviation

(SD), median, minimum (min), maximum (max) were used for descriptive statistics. Chi-square test was used to compare categorical data. Chi-square (Mc-Nemar) test was used for categorical data in dependent groups, paired t test was used for normally distributed continuous data, and Wilcoxon test was used for non-normally distributed data to evaluate the changes before and after COVID-19 quarantine. In the comparison of continuous data, one-way Anova test and independent t test were used since they were compatible with normal distribution. $p \leq 0.05$ was accepted for statistical significance.

RESULTS

The study included 44 participants. 93.2% of the participants were women. The mean age of the participants was 40.20±9.08 years (min 21-max 62). 88.6% of the participants were married. 47.7% of the participants were primary school graduates, 25% were high school graduates and 27.3% were university graduates. 31.8% of the participants were employed and 29.5% had an income level of minimum wage or less (Table 1).

Table 1: Sociodemographic Characteristics of Participants

		n=44	%
Gender	Female	41	93.2
	Male	3	6.8
Marital Status	Married	39	88.6
	Single	5	11.4
Education	Primary school	21	47.7
	High school	11	25.0
	University	12	27.3
Age Groups	18-30	8	18.2
	31-40	14	31.8
	41-50	16	36.4
	51 years and older	6	13.6
Employment Status	Unemployed	30	68.2
	Employed	14	31.8
Income Level (Turkish Lira)	3500 and lower	13	29.5
	3501-7000	18	40.9
	7001 and higher	6	13.7
	Not specified	7	15.9

When the change in eating habits of the participants were analyzed, 47.7% stated that it worsened during this period, while 40.9% stated that there was no change. 36.4% of the participants reported that their appetite increased during this period. In this period, 20.5% of the group added to main and intermediate meals, while 52.3% stated that they did not change the number of meals (Table 2). 11.4% of the participants reported that their consumption of products and 27.3% of bread and pastries increased during this period. There was no significant difference in smoking before and after the restriction ($p>0.05$). Change in eating habits, number of daily feedings, change in feeling of hunger and fullness, and weight gain did not differ according to gender, lifestyle, education, marital status and profession ($p>0.05$).

Table 2: Nutrition and Behavioral Changes in Covid-19 Quarantine

		n=44	%
Eating Habit Change	It didn't change	18	40.9
	It got worse	21	47.7
	It got better	5	11.4
Hunger/Satiety Perception	It didn't change	24	54.5
	It decreased	4	9.1
	It increased	16	36.4
Weight Change	I think my weight is stable	12	27.3
	I think I lost weight	7	15.9
	I think I gained a little weight	10	22.7
	I think I gained too much weight	15	34.1
Water Consumption	It didn't change	28	63.6
	It increased	15	34.1
	It decreased	1	2.3
Screen Time Change	It didn't change	12	27.3
	It increased	29	65.9
	It decreased	3	6.8
Number of Daily Meals	It didn't change	23	52.3
	I skipped the main meals	10	22.7
	I added extra main and snack meals	9	20.5
	Not specified	2	4.5

Before and during the restriction period, 38.6% and 65.9% of the individuals reported that they did not do any sports. It was observed that participants reduced their exercise during the restriction period (p = 0.012) (Table 3). Of the supplement, 65.9% reported an increase in screen use time. 27.3% of the participants reported that their weight remained stable, 15.9% reported weight loss, 22.7% stated that they thought they gained a little weight, and 34.1% thought they gained too much weight.

Table 3: Comparison of Participants' Physical Activity Before and During COVID-19

		before-COVID-19		during COVID-19		
		n=44	%	n=44	%	p
Physical Activity	No	17	38,6	29	65,9	**0.012***
	Yes	27	61.4	15	34,1	

*Mcnemar, p <0.05

The mean BMI values of the participants were 33.87±6.36 before the restriction process and 32.84±5.87 during the process (p=0.013) (Table 4). However, 56.8% of the participants reported that they gained weight during this period.

Table 4: Comparison of Mean BMI Values of Participants Before and During COVID-19

	before-COVID-19 (mean±sd)	during COVID-19 (mean±sd)	p
BMI	33.87±6.36	32.84±5.87	**0.013***

*Paired t test, p <0.05

In the same period, 34.1% of the participants reported that increased water consumption during this period. Participants reported an increase in sleep duration during the restriction period, but analyses showed that sleep duration did not change before and after the restriction (p = 0.078). The participants' food literacy questionnaire mean score was found to be 33.54±5.8 (Min 20-Max 45). There was no statistically significant difference in knowledge level in terms of gender and marital status (p>0.05). The mean food literacy score of women was 33.63±5.95 and was higher than the mean of men, 32.33±3.71. The average food literacy score of working participants was 35.64±4.48, while that of non-working participants was 32.56±6.15. Food literacy level did not differ significantly according to employment status and income level (p>0.05) (Table 5). Considering the food literacy average score in terms of educational status, the score of primary school graduates was calculated as 30.73±5.99, high school graduates as 35.00±4.18, and university graduate participants as 37.13±4.4. As the education level of the participants increased, the food literacy score increased (p = 0.04). The average food literacy score of the participants according to their body mass index is 35.06±3.16 for normal weight participants, 37.32±6.14 for overweight participants, 32.00±5.31 for obese participants, and there was a significant difference between the groups (p=0.027) (Table 5). In our study, achieved power (1-B) was determined as 80.1% in the post-hoc power analysis performed with 0.05 alpha error, 44 minimum sample size, and 3.07 odd ratio value.

Table 5: Comparison of The Short Food Literacy Questionnaire- SFLQ

		Mean±SD	p
Gender	Female	33.63±5.95	0.71[1]
	Male	32.33±3.71	
Working Status	Employed	35.64±4.48	0.10[1]
	Unemployed	32.56±6.15	
Marital Status	Single	33.68±3.79	0.96[1]
	Married	33.52±6.05	
Age Groups	18-30	37.35±4.51	0.23[2]
	31-40	33.04±6.15	
	41-50	32.28±6.09	
	51 years and older	33.00±4.72	
Education	Primary school	30.73±5.99*	**0.04[2]**
	High school	35.00±4,18	
	University	37.13±4.40*	
BMI	Normal weight	35.06±3.16	**0.03[2]**
	Overweight	37.32±6.14*	
	Obesity	32.00±5.31*	

[1]Independent t test, [2]One-way ANOVA, *post hoc tukey, p <0.05

DISCUSSION

COVID-19 has caused a global pandemic. Governments have imposed restrictions and mass quarantines to control the spread of the COVID-19 virus. Lockdowns and restrictions have led to lifestyle changes, such as reduced physical activity and unhealthy diets (Mattioli et al., 2020). Quarantine potentially causes weight changes due to dietary changes, lack of physical activity, and stress. In a study conducted in Poland, 29.9% of the participants reported weight gain and 18.6% reported a decrease in weight (Sidor & Rzymski, 2020). Similarly, in our study, 27.3% of our participants stated that their weight remained constant, 15.9% lost weight, 22.7% gained a little weight, and 34.1% stated that they

gained a lot of weight. In another study conducted on the Spanish population, 52.7% of the participants reported weight gain during quarantine and 47.3% reported that their weight did not change (Sánchez-Sánchez et al., 2020). An international study shows that COVID-19 isolation and house arrest have a negative impact on physical activity and nutrition (Ammar et al., 2020). In a study conducted in the United States, 37% of the participants stated that there was no change in their general diet, and 31% stated that their diet had worsened (Khubchandani et al., 2020). In a study conducted in Australia, 34.6% of participants reported an increase in overeating behaviors compared to before COVID-19 (Phillipou et al., 2020). In our study, 47.7% of our participants stated that their eating habits worsened during this period, 22.7% skipped main meals during the process, and 20.5% stated that they added extra meals. A study conducted in Italy stated that boredom was the cause of changes in eating behaviors (Pellegrini et al., 2020). Our study concluded that our participants reduced their exercise during the restriction period. In a study conducted in the United Kingdom, 40% of individuals reported exercising less during quarantine (Robinson et al., 2021). Despite recommendations that house arrest should not prevent people from being physically active, current results have shown a decrease in all levels of physical activity during the COVID-19 house arrest period (Ammar et al., 2020). It is known that overweight and obese groups exhibit more problematic eating behaviors, including food consumption without hunger and frequent overeating (Opichka et al., 2019). One study found that binge eating during the pandemic was 2.88 times higher in people experiencing weight stigma (Puhl et al., 2020). Increased rates of stress and negative effects due to the pandemic and social isolation may contribute to the increased risk of eating disorders (Rodgers et al., 2020). In a study conducted in Italy, 34.4% of participants stated that their appetite increased during the COVID-19 quarantine (Di Renzo et al., 2020). In another study conducted in Italy, 46.1% of participants reported eating more during quarantine and 19.5% reported gaining weight. An increase in the consumption of "comfort food", especially chocolate, sweets and salty snacks, has been reported (Scarmozzino & Visioli, 2020). In another study conducted in Poland, 51.8% of participants reported increased snacking during quarantine (Sidor & Rzymski, 2020). Our findings were consistent with these results. 36.4% of our participants stated that their appetite increased during this period. Additionally, 11.4% reported that their consumption of snack products and 27.3% of bread and pastries increased during this period. People with high nutritional literacy tend to exhibit healthy eating behaviors (C. K. Lee et al., 2019). In our study, women paid more attention to nutritional characteristics than men and scored higher on the SFLQ. Our results were consistent with the study conducted in Italy (Trieste et al., 2021). In a study conducted in South Korea, female participants scored higher than men in terms of endurance levels in food literacy (Y. Lee et al., 2022). In another study on adults, higher levels of food literacy were associated with greater self-control, less impulsivity, and healthier food consumption (Poelman et al., 2018). Consistent with the data obtained from Italy (Palumbo et al., 2019), the food literacy score increased as the education level of the participants in our study increased. In a study conducted during the COVID-19 quarantine, unhealthy eating patterns were reported more frequently by overweight and obese people than those of normal weight during the COVID-19 pandemic (Poelman et al., 2021). Supporting this, in our study, the food literacy scores of obese participants were lower than those of overweight and normal weight participants. People with obesity should be given more attention in nutrition and dietary counseling. This study has some limitations. Data were collected by telephone interview. Since people's BMI measurements are not measured directly after the restriction, they are based on people's statements. Limited generalizations can be made due to the low number of participants and male participation.

CONCLUSION

This study shows that during the COVID-19 restriction period, individuals may experience changes in their eating habits, manifested by exercise, screen use, eating more and weight change, and are negatively affected by important health behaviors. Research is needed to understand the negative effects of COVID-19-related quarantine on eating

habits and health and to prevent its negative effects on public health.

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Olgu Sunumu / Case Report
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SEVERE HYPERTRANSAMINASEMIA DURING ASYMPTOMATIC COVID-19 INFECTION

Asemptomatik COVID-19 Enfeksiyonu Sırasında Şiddetli Hipertransaminazemi

Raziye Merve YARADILMIŞ[1], İlknur BODUR[1], Ahmet Serkan ÖZCAN[1], Betül ÖZTÜRK[1], Orkun AYDIN[1], Ali GÜNGÖR[1], Nilden TUYGUN[1]

Afiliasyon / Affiliation:
[1]Department of Pediatric Emergency Care, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, Turkey

Sorumlu Yazar / Correspondence:
Assoc. Prof. Dr. Raziye Merve YARADILMIŞ
Department of Pediatric Emergency Care, Dr. Sami Ulus Maternity and Child Health and Diseases Training and Research Hospital, Ankara, Turkey
E-mail: karaomermerve@hotmail.com

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ABSTRACT

Although the mechanism of Coronavirus disease 2019 (COVID-19) related liver damage in critically ill children is not well defined yet, it is thought to be related to the hyperinflammation phase (cytokine release). Here, we present a 40-day-old asymptomatic patient with isolated severe liver enzyme elevation associated with COVID-19. A 40-day-old female was admitted to our emergency department for screening after her mother was diagnosed with COVID-19. The patient's vital signs and physical examination were normal on admission. Laboratory findings showed alterations in hepatic function measures. Transaminase levels increased up to 11-fold and 5-fold the upper reference limit for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) on day 6 of admission. No direct bilirubin elevation or coagulopathy was detected, and also the creatine kinase (CK) level was within the normal range. Microbial investigations excluded a superimposed congenital or acquired infection. Ultrasound examination (day 6) found only altered echogenicity in the liver. During the following weeks, AST and ALT levels decreased and resolved to normal range after 14 days from the first biochemical evaluation on admission. Pediatric patients with asymptomatic or mildly symptomatic COVID-19 infection may have severe hepatic enzyme elevation, with or without hepatic failure. A variety of mechanisms, such as direct virus infection may cause liver injury in patients with COVID-19. Clinicians should pay more attention to the occurrence of liver damage in COVID-19 infection and analyze comprehensively the pathogenesis of liver injury in management strategy.

Keywords: COVID-19, Emergency department, Hypertransaminasemia, Pediatric

ÖZET

Kritik hasta çocuklarda COVID-19'a bağlı karaciğer hasarının mekanizması henüz tam olarak tanımlanmamış olsa da hiperinflamasyon aşamasıyla (sitokin salınımı) ilişkili olduğu düşünülmektedir. Burada, COVID-19'a bağlı izole ciddi karaciğer enzim yüksekliği olan 40 günlük asemptomatik bir hastayı sunuyoruz.40 günlük kız hasta, annesine COVID-19 tanısı konulduktan sonra çocuk acil servise tarama amacıyla başvurdu. Başvuru sırasında hastanın vital bulguları ve fizik muayenesi normaldi. Laboratuvar bulguları hepatik fonksiyon ölçümlerinde değişiklikler gösterdi. Başvurunun 6. gününde transaminaz düzeyleri aspartat aminotransferaz (AST) ve alanin aminotransferaz (ALT) için üst referans sınırının 11 ve 5 katına kadar yükseldi. Direkt bilirubin yüksekliği veya koagülopati saptanmadı, ayrıca kreatin kinaz (CK) düzeyi normal sınırlardaydı. Diğer konjenital veya edinilmiş enfeksiyonlar dışlandı. Abdomen ultrasonunda (6. gün) karaciğer ekojenitenitesinde artış saptandı. Takip eden haftalarda AST, ALT düzeyleri düştü ve başvuru sırasındaki ilk biyokimyasal değerlendirmeden 14 gün sonra normal aralığa geriledi. Asemptomatik veya hafif semptomatik COVID-19 enfeksiyonu olan pediatrik hastalarda, karaciğer yetmezliği olsun ya da olmasın, ciddi hepatik enzim yüksekliği görülebilir. COVID-19 hastalarında karaciğer hasarına, doğrudan virüs enfeksiyonu gibi çeşitli mekanizmalar neden olabilir. Klinisyenlerin, COVID-19 enfeksiyonunda karaciğer hasarı oluşumuna daha fazla dikkat etmesi ve tedavi stratejisinde karaciğer hasarının patogenezini kapsamlı bir şekilde analiz etmesi gerekmektedir.

Anahtar Kelimeler: Acil servis, COVID-19, Hipertransaminazemi, Pediatri

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a complex multi-system disease that affects several human systems, mainly respiratory tract infection, also affecting the liver. In critically ill children, COVID-19-related elevated transaminases with or without liver failure have been reported in 60% of the case series (Tian et al, 2020). Although the mechanism of COVID-19-related liver damage in critically ill children is not well defined yet, it is thought to be related to the hyperinflammation phase (cytokine release) (Zippi et al, 2020). Here, we present a 40-day-old asymptomatic patient with isolated severe liver enzyme elevation associated with COVID-19.

CASE

A 40-day-old girl was admitted to our emergency department for screening after her mother was diagnosed with COVID-19. There were no features in the antenatal, perinatal, and neonatal periods, her development was completely normal. Her mother was taking only therapeutic doses of paracetamol for fever. The patient's vital signs and physical examination were normal on admission. COVID-19 infection was confirmed by a positive polymerase chain reaction on nasopharyngeal swabs. Chest X-ray examination was negative. Laboratory findings showed alterations in hepatic function measures. Transaminase levels increased up to 11-fold and 5-fold the upper reference limit for aspartate aminotransferase (AST) and alanine aminotransferase (ALT) on day 6 of admission to the pediatric emergency department, respectively. Gamma-glutamyl transferase (GGT) was 71 U/mL (normal range <204), alkaline phosphatase was 471 IU/L (normal range 60-321). No direct bilirubin elevation or coagulopathy was detected, and also the creatine kinase (CK) level was within the normal range. White blood cell count, and electrolytes were also normal. Microbial investigations excluded a superimposed congenital or acquired infection (HBV, HCV, EBV, CMV, Toxoplasma, and other viral pathogens). Ultrasound examination (day 6) found only altered echogenicity in the liver. During the following weeks, AST and, ALT levels decreased and resolved to normal range after 14 days from the first biochemical evaluation on admission.

DISCUSSION

COVID-19 has a variety of clinical manifestations, with acute respiratory symptoms being the predominant symptoms (Feng et al, 2020). It has been shown to affect affect the extrapulmonary organs, including liver damage (Tian et al, 2020). The incidence of liver injury in patients with severe or critical COVID-19 disease is highly prevalent. Liver damage as the first finding in COVID-19 patients was uncommon, so herein, we report a pediatric case of acute liver injury in the course of COVID-19 asymptomatic infection, notable for the severe increase in serum aminotransferases without liver failure. The exact pathophysiological mechanisms of liver injury during COVID-19 infection remain uncertain (Sgouropoulou et al, 2021). Additional it remains unclear whether COVID-19 has a direct toxic effect on liver function. Several different mechanisms are implicated. It has been reported in previous studies that angiotensin-converting enzyme 2 (ACE 2), which is the receptor of COVID-19 and is mainly found in the lungs, is also widely expressed in liver cells (Tian et al, 2020). So, these might suggest that COVID-19 might directly bind to hepatocytes expressing ACE2 resulting in hepatocyte injury. According to the report by Chai X and Gaun GW et al, bile duct epithelial cells found the ACE2 receptor at a concentration 20 times higher than hepatocytes and suggested that COVID-19 infection may also cause bile duct epithelial cell damage (Chai et al, 2020; Guan et al, 2020). The other mechanisms of liver damage due to COVID-19 are an antibody-dependent enhancement, systemic immune response syndrome and cytokine storms, ischemia and hypoxia reperfusion injury, drug hepatotoxicity, recurrence or aggravation of existing liver disease. Antiviral treatments were recommended during the COVID-19 infection, but many patients were treated with antipyretics, primarily paracetamol (Feng G et al, 2020). As is known, paracetamol can cause significant liver damage or liver failure when it exceeds the toxic dose. Our patient's mother had taken paracetamol as needed during COVID-19 infection and had not reached the toxic dose. The possibility that the liver enzyme elevation was

caused by paracetamol taken through breast milk was also considered to be very low. Few pediatric cases have been reported showing the development of liver damage during COVID-19 infection. In the pediatric case series of Zhou et al., it was reported that mild hypertransaminasemia may be common during acute infection in children aged 0-3 years (Zhou et al, 2020). Palpacelli et al. reported that a case of of liver involvement with transient severe hypertransaminasemia in 30-day-old baby girl with mild COVID-19 infection (Palpacelli et al, 2021). Similarly, transient liver injury without hepatic dysfunction has been reported during a mild SARS-CoV-2 infection in a 5-year-old child (Sgouropoulou et al, 2021). In our case, other liver function tests were preserved despite the findings of severe AST elevation and moderate ALT elevation: albumin, cholestasis parameters (such as bilirubin, GGT, and alkaline phosphatase levels), and coagulation test were always within normal limits for age. We detected incidentally severe liver enzyme elevation in our patient who was positive for a COVID-19 swap scan. Inflammation parameters were normal (absolute neutrophil count, C-reactive protein, immature granulocyte, etc.). There was no indication for hospitalization. There was no need for oxygen support or other medical treatment. These findings indicate that hepatocyte damage was likely independent of immune system involvement, cytokine storm, or hypoxia. Direct viral damage is likely a key contributor to the occurrence of temporary severe liver damage. It is evident that further research is essential to deepen our understanding of this pathophysiological process.

CONCLUSION

Pediatric patients with asymptomatic or mildly symptomatic COVID-19 infection may have severe hepatic enzyme elevation, with or without hepatic failure. In COVID-19 patients, liver damage may result from various mechanisms, including direct viral infection. Clinicians should be aware that liver damage may occur in COVID-19 infection and should incorporate a comprehensive analysis of the liver damage pathogenesis into their treatment strategy.

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Author Contributions: MD Yaradılmış, and MD Bodur conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Drs Akkaya, Aydin and Öztürk designed the data collection instruments, collected data, reviewed, and revised the manuscript. Drs Yaradılmış, Güngör, and Prof Tuygun carried out the initial analyses, reviewed and revised the manuscript. All authors approve the final version of manuscript and accept all the responsibilities.

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A RARE CASE OF NEURONAL CEROID LIPOFUSCINOSIS 5 IN A CHILD: FROM INITIAL ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS TO SEVERE NEURODEGENERATION

Nadir Görülen Nöronal Seroid Lipofuskinozis 5 Olgusu: Dikkat Eksikliği Hiperaktivite Bozukluğu Belirtilerinden Ağır Nörodejenerasyona

Merve OKUYUCU[1], Esra KAYGISIZ[2]

Afiliasyon / Affiliation:
[1]Department of Child and Adolescent Psychiatry, Ministry of Health Dogubayazit Dr. Yasar Eryilmaz State Hospital, Ağrı, Türkiye

[2]Department of Child and Adolescent Psychiatry, Private Consultant, Ankara, Türkiye

Sorumlu Yazar / Correspondence:
Esra KAYGISIZ, MD.
Department of Child and Adolescent Psychiatry, Private Consultant, Kızılay, Ankara, Türkiye.
E-mail: esra.yphn@gmail.com

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ABSTRACT

Neuronal ceroid lipofuscinosis (NCL) is a group of rare, inherited neurodegenerative disorders characterized by the accumulation of lipopigments in neuronal cells. Among these, CLN5 lipofuscinosis is generally considered a juvenile-onset variant, presenting with a complex clinical Picture that includes psychiatric, cognitive, and motor impairments. The aim of this report is to describe a rare case of pediatric CLN5 lipofuscinosis initially presenting with psychiatric symptoms, contributing to early diagnostic challenges. We report the case of a boy aged 7;11 (years; months) who initially presented with symptoms of inattention, hyperactivity, and verbosity at the age of 5, which led to an early diagnosis of attention-deficit/hyperactivity disorder (ADHD). Psychiatric assessments and evaluations were conducted in accordance with DSM-5 guidelines to support the diagnosis and monitor the progression of symptoms. As the disease advanced, additional clinical evaluations, including genetic testing, were performed to confirm the diagnosis of CLN5 lipofuscinosis and assess the progression of motor, cognitive, and psychiatric symptoms. The patient, initially diagnosed with ADHD, experienced a rapid progression over approximately one year to severe neurodegenerative symptoms, including loss of ambulation, vision impairment due to retinal atrophy, and cognitive decline. Genetic testing confirmed CLN5 lipofuscinosis, with accompanying psychiatric symptoms such as anxiety. Early psychiatric symptoms in CLN5 lipofuscinosis may be underrecognized, delaying appropriate diagnosis and intervention. This case highlights the importance of a multidisciplinary approach in the evaluation of psychiatric and neurological symptoms in pediatric patients, especially in the context of rare neurodegenerative diseases.

Keywords: Attention-deficit/hyperactivity disorder, Cognitive decline, Neuronal ceroid lipofuscinosis, Pediatric neurodegenerative disorders, Psychiatric symptoms,Visual impairment

ÖZET

Nöronal seroid lipofüsinozis (NCL), nöronal hücrelerde lipopigment birikimi ile karakterize nadir, kalıtsal nörodejeneratif bozukluklar grubudur. Bunlar arasında, CLN5 lipofüsinozis genellikle psikiyatrik, bilişsel ve motor bozuklukları içeren karmaşık bir klinik tablo ile ortaya çıkan, juvenil başlangıçlı bir varyant olarak kabul edilir. Bu olgu sunumu başlangıçta psikiyatrik semptomlarla ortaya çıkan nadir bir pediatrik CLN5 lipofusinoz vakasını tanımlamayı ve erken tanı sürecindeki zorluklara dikkat çekmeyi amaçlamaktadır. Bu olgu sunumunda, 5 yaşında iken dikkat eksikliği, hiperaktivite ve aşırı konuşkanlık semptomları gösteren ve bu belirtiler doğrultusunda erken dönemde dikkat eksikliği/hiperaktivite bozukluğu (DEHB) tanısı alan 7 yaş 11 aylık bir erkek olgu sunulmaktadır. Tanı ve takip süreci için DSM-5 kılavuzuna uygun olarak psikiyatrik değerlendirmeler yapılmıştır. Hastalık ilerledikçe, CLN5 lipofusinozis tanısını doğrulamak ve motor, bilişsel ve psikiyatrik semptomların ilerleyişini değerlendirmek için genetik testler de dâhil olmak üzere ek klinik değerlendirmeler yapılmıştır. Başlangıçta DEHB tanısı konulan hasta, yaklaşık bir yıl içinde ambulasyon kaybı, retinal atrofiye bağlı görme bozukluğu ve bilişsel gerileme gibi şiddetli nörodejeneratif semptomlara doğru hızlı bir ilerleme yaşamıştır. Genetik testler, anksiyete gibi psikiyatrik semptomların eşlik ettiği CLN5 lipofusinozisi doğrulamıştır. CLN5 lipofusinozisindeki erken psikiyatrik semptomlar yeterince tanınmayabilir ve bu durum uygun tanı ve tedaviyi geciktirebilir. Bu olgu, özellikle nadir görülen nörodejeneratif hastalıklar kapsamında, pediatrik hastalarda psikiyatrik ve nörolojik semptomların değerlendirilmesinde multidisipliner bir yaklaşımın önemini vurgulamaktadır.

Anahtar Kelimeler: Bilişsel gerilik, Dikkat eksikliği ve hiperaktivite bozukluğu, Görme bozukluğu, Nöronal seroid lipofusinozis, Pediatrik nörodejeneratif hastalıklar, Psikiyatrik semptomlar

INTRODUCTION

Lipofuscinoses are a group of hereditary neurodegenerative lysosomal storage disorders (LSDs) characterized by the accumulation of lipopigments within cells (Staretz-Chacham et al., 2010). Epidemiological data indicate an incidence of 1-3 per 100,000 and a prevalence of approximately 2-4 per 1,000,000 (Simonati et al., 2017). These disorders primarily affect the brain and retina, with clinical presentations varying in disease onset, associated features, and progression. Common manifestations include progressive visual impairment, seizures, cognitive decline, pyramidal and extrapyramidal motor deficits, and premature death (Mole & Cotman, 2015; Staretz-Chacham et al., 2010). Based on the age of onset, NCL is classified into congenital, infantile, late-infantile, juvenile, and adult types, with over 10 genes identified as associated with the neuronal ceroid lipofuscinosis (NCL) phenotype (Mole & Cotman, 2015). Mutations in the CLN5 gene, which were first identified in Finland, result in CLN5 lipofuscinosis (Mole & Cotman, 2015; Simonati et al., 2017). CLN5 lipofuscinosis typically presents with initial signs between the ages of 4 and 7 years (Basak et al., 2021), including mild intellectual decline, clumsiness, unsteady gait, and speech delay (Rakheja & Bennett, 2018). As the disease progresses, symptoms may evolve to include motor delays, intellectual disability, ataxia, vision loss, and seizures. Psychiatric or behavioral symptoms, however, can also manifest as early signs of the disorder (Staretz-Chacham et al., 2010). Cognitive dysfunction is often recognized when the child begins school, with progressive deterioration ultimately leading to severe dementia (Rakheja & Bennett, 2018). Considering the clinical course of neurological and psychiatric symptoms, cognitive decline in CLN5 lipofuscinosis manifests as a two-phase process (Simonati & Williams, 2022). In the early stages, children's developmental trajectoriess low; they acquire new skills at a slower pace compared to their peers but often remain within a normal range for some time before concerns arise. Eventually, they reach a plateau and then begin to lose the cognitive abilities they had acquired in the first months or years of life, which typically triggers diagnostic investigations. Cases involving the psychiatric aspects of CLN5 have been documented in the literature (Bäckman et al., 2005; Simonati et al., 2017). While several NCL cases have been reported in Türkiye (Kose et al., 2021; Sürücü Kara et al., 2024), to our knowledge, only one case involving CLN5 has been previously published (Duz, 2021). However, none of these reports have specifically focused on the psychiatric aspects of the disease. In this report, we present the case of a 7-year, 11-month-old boy with a CLN5 mutation, who was initially diagnosed with attention-deficit/hyperactivity disorder (ADHD), highlighting the psychiatric manifestations of juvenile NCL.

CASE REPORT

This report describes a 7-year, 11-month-old boy who presented with psychiatric symptoms that began at an early age, leading to an early diagnosis of ADHD. The diagnosis, treatment, and follow-up are briefly discussed. This case was assessed and treated in the Child and Adolescent Psychiatry Department outpatient clinic of the Ministry of Health Doğubayazıt Dr. Yaşar Eryılmaz State Hospital in Türkiye. ADHD and other specified anxiety disorder were classified using Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (APA, 2013). Verbal and written informed consent was obtained from the parent to publish this case. The presentation of the case report adheres to the CARE (Consensus-based Clinical Case Reporting Guideline) guidelines, which provide recommendations for authors of case reports to improve their completeness and transparency (Riley et al., 2017). At the beginning of the second semester of first grade, our patient presented to our clinic at the first time with complaints of inattention, clumsiness, and hyperactivity. At this visit, his chronological age was 6 years and 5 months. He frequently interrupted others, had difficulty waiting his turn, was excessively talkative, easily bored, restless, and impulsive. By the end of the first semester of first grade, he had not yet acquired reading or writing skills. At the time of this visit, there

was no known chronic illness. The first onset of psychiatric symptoms was noted about two years ago, at the age of 5, when the patient started kindergarten. He was described as hyperactive, inattentive, and restless. Approximately 2-3 months after starting kindergarten, he sustained a left femoral head fracture after jumping from a wall about 1 meter high. After a recovery period of approximately three months, he resumed walking. During this period, the patient exhibited behaviors consistent with hyperactivity, such as being highly energetic, unable to stay seated, and very talkative. By the time he entered first grade, although his hyperactivity had decreased somewhat in comparison to the previous year, he continued to be more energetic than his peers. During the first semester of first grade, he encountered significant difficulties with concentration and academic performance, particularly in reading and writing. Consequently, he was referred to a child and adolescent psychiatry department, where he was diagnosed with ADHD early in the school year and was prescribed immediate-release methylphenidate (IR-MPH) 10 mg/day. However, due to the onset of symptoms such as dullness and withdrawal, the family discontinued the medication after approximately 3-4 days. At the first visit of our patient was alert and fully oriented. He maintained appropriate eye contact and responded accurately to questions, indicating intact sensory perception and comprehension. His speech was coherent and notably verbose, with marked impulsivity and restlessness observed. His judgment was appropriate for his developmental age. Based on the DSM-5 criteria, a diagnosis of ADHD was established (APA, 2013). Subsequently, extended-release methylphenidate (ER-MPH) at a dose of 18 mg/day was prescribed, with a follow-up appointment recommended in one month; however, the patient did not return for this appointment. Approximately four months later, shortly after the end of the school year, the patient returned to our clinic for a second visit at the age of 6 years and 9 months. The family reported that they had initially administered ER-MPH 18 mg/day for approximately 10 days after the previous visit, but discontinued it because the patient exhibited dullness. His ability to concentrate in class deteriorated, and he had not learned to read or write by the end of first grade. As a result, his academic performance declined and he was required to repeat the first grade. Over the past 2-3 months, the patient had experienced fear of the dark, fear of being alone, separation anxiety from parents, sleep difficulties, restlessness, and significant anticipatory anxiety before bedtime. In addition, over the same period, the patient experienced more frequent falls, which became progressively worse. On mental status examination, the patient was alert and fully oriented. He maintained adequate eye contact and responded correctly to questions. His speech was coherent with normal rate and volume. His motor function was intact, as he was able to walk independently. A diagnosis of an Other Specified Anxiety Disorder was made based on the DSM-5 criteria (APA, 2013). Fluoxetine 2.5 mg/day was started to treat his anxiety symptoms. However, ADHD treatment was not resumed due to school vacation. He was referred to physical therapy and rehabilitation and to a pediatric neurologist for the falls. One year later, the patient returned for follow-up at the chronological age of 7 years and 11 months. Over the past year, he had experienced progressive vision loss due to retinal atrophy and a marked decline in motor function, resulting in the loss of independent ambulation. Approximately four months prior, he had developed urinary incontinence, necessitating the use of diapers. In the past month, he also lost bowel control and was unable to dress himself. He had been diagnosed with epilepsy, for which valproate 600 mg/day was prescribed. Genetic testing revealed a homozygous c.594_597 del (p.W198*) variant in the CLN5 (NM-006493) gene. During the physical examination, the patient made meaningless sounds, displayed an inappropriate affect, was unable to comprehend or respond to questions, and exhibited repetitive forward and backward rocking movements while seated. Additionally, he was unable to walk without assistance.

Table 1: Chronological Order of Symptoms and Clinical Course

Age	Mental Status Examination	Psychiatric Symptoms	Progressive Symptoms
5 years	-	Excessive hyperactivity, inattentiveness, restlessness	
5 years 3 months	-	Hyperactivity-related behaviors, excessive talkativeness	-
6 years	-	Difficulty concentrating, poor school performance	-
6 years 5 months	Alert and fully oriented, intact eye contact, sensory perception, and comprehension, coherent speech	Interrupting others, difficulty waiting for turn, talkative, easily bored, impulsiveness, clumsiness, hyperactivity	-
6 years 9 months	Alert and fully oriented, intact eye contact, sensory perception, and comprehension, coherent speech	Declining school performance, fears	Frequent falls, worsening with time
7 years 11 months	Unable to comprehend or respond to questions, uttered meaningless sounds, displayed inappropriate affect, exhibited repetitive forward and backward rocking movements while seated	Progressive deterioration in thinking, memory, and understanding, urinary incontinence, loss of bowel control (requiring diaper use)	Vision loss due to retinal atrophy, seizures, urinary incontinence, loss of bowel control, decline in motor function resulting in the loss of independent ambulation

The patient was 7-year, 11 month-old boy, the second of four children. His prenatal, perinatal, and early developmental history was unremarkable. He began speaking his first words around the age of 12 months and started walking at approximately the same age. He completed toilet training around 2.5 years of age. His mother, a 31-year-old homemaker with a high school education, and his father, a 35-year-old construction worker with limited literacy who did not complete primary school, are second cousins. A family history of mild mental retardation documented on the father's extended family (i.e. father's cousin).

DISCUSSION

This case presents a rare and challenging progression from ADHD to a severe neurodegenerative condition, ultimately diagnosed as CLN5 lipofuscinosis. The early presentation of psychiatric symptoms such as hyperactivity, inattention, and delayed literacy initially led to a diagnosis of ADHD. However, as the disease progressed, the patient developed neurological symptoms, including motor decline, visual impairment, and seizures, which are characteristic of CLN5 lipofuscinosis. This case highlights the importance of considering neurodegenerative disorders in the differential diagnosis when psychiatric symptoms present alongside progressive neurological decline. Psychiatric manifestations in LSDs can range from mild depression to severe conditions such as psychosis or early dementia, often accompanied by behavioral problems such as hyperactivity, aggression, and anxiety (Staretz-Chacham et al., 2010). In this context, the early psychiatric symptoms observed in our patient, including hyperactivity and inattention, align with previous findings in the literature (Bäckman et al., 2005; de Paiva et al., 2023), where these symptoms are often underrecognized as potential early indicators of neurodegenerative conditions like CLN5 lipofuscinosis. In a study conducted by Bäckman et al. (2005) involving 27 patients diagnosed with juvenile NCL, 74% of the participants were found to have some degree of psychiatric disturbance, including hyperactivity, aggression, and anxiety (Bäckman et al., 2005). Similarly, in a case series by Paiva et al. (2023) involving 17 patients with CLN5 mutations, early psychiatric symptoms, such as anxiety, inattention, and stereotypic behaviors, were commonly observed (de Paiva et al., 2023).

These findings are consistent with our case, where psychiatric symptoms were among the initial clinical manifestations, reinforcing the need for early recognition and intervention in patients presenting with similar symptoms. Furthermore, Simonati et al. (2017) analyzed 15 children with CLN5 mutations and found that cognitive and motor impairments were among the first symptoms to appear, with a mean age of onset of 5 years 9 months and 6 years 7 months, respectively (Simonati et al., 2017). In six patients, regression in language skills was observed as an initial symptom. At the same time, behavioral disorders such as hyperactivity, aggression, and motor stereotypes were reported in 11 patients, often emerging early in the disease course. These findings paralel the clinical course of our patient, who presented with hyperactivity and inattention before progressing to more severe neurological symptoms, emphasizing the importance of a comprehensive and multidisciplinary approach in the management of CLN5 lipofuscinosis. The development of anxiety and behavioral disturbances underscores the importance of monitoring and treating psychiatric symptoms as part of the overall management of CLN5 lipofuscinosis.

CONCLUSION

In conclusion, this case highlights the importance of considering neurodegenerative disorders such as CLN5 lipofuscinosis in the differential diagnosis of psychiatric symptoms, especially in the setting of progressive neurological decline. Early recognition and a multidisciplinary approach, including genetic testing, are crucial for appropriate diagnosis and management.

Limitations

Limitations of this case report include the reliance on family-provided information for the child's early psychiatric symptoms. One of the limitations is that self-report scales were not used in the case study. In addition, the lack of regular psychiatric follow-up of the child after initial diagnosis and treatment initiation limited the ability to objectively monitor the clinical course and treatment response, potentially preventing a comprehensive assessment of symptom progression and treatment outcomes.

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Author Contributions: MO conducted the psychiatric evaluations and clinical interviews, drafted the initial manuscript. EK Contributed to the interpretation of psychiatric findings, participated in the literature review and the writing of the manuscript, and created the tables for the manuscript. MO and EK reviewed the manuscript and on the final drafts.

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