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HASTANEMİZDEKİ SARS CORONAVİRUS - 2 AŞI ÇALIŞMALARININ DEĞERLENDİRİLMESİ

EVALUATION OF SARS CORONAVIRUS-2 VACCINE PRACTICES IN OUR HOSPITAL

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ÖZET

AMAÇ: "Coronavirus Disease 19" salgını pandemi olarak etkisini tüm dünyada sürdürmekte iken; ülkemizde pandemik aşı uygulamaları 14 Ocak 2021 tarihinde başladı. Bu çalışmada; Afyonkarahisar Sağlık Bilimleri Üniversitesi COVID-19 aşı polikliniğinde SARS-CoV-2 aşı uygulaması yapılan kişilerin demografik özellikleri, aşılama öncesi riskli temas öyküleri ve pandemi aşılamaları konusundaki görüşlerinin değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Pandemik aşı uygulamalarının ilk başladığı dönemde; birinci doz pandemik aşı uygulaması yapılan kişilere 17 sorudan oluşan anket yüz yüze görüşme yoluyla uygulandı. Sağlık çalışanları A grubu, diğer katılımcılar B grubu olarak sınıflandırılıp, bu iki grubun aşı olmayı isteme nedenleri, pandemiden etkilenme durumları ve diğer cevapları karşılaştırıldı.

BULGULAR: Çalışma periyodu içinde 3159 kişi aşılandı; 1682'si (%53) sağlık çalışanı olup A grubu, geri kalan1477 (% 47) kişi B grubu olarak değerlendirildi. A grubunun anlamlı olarak daha fazla bilimsel yayınlardan, B grubunun ise medyadan bilgi edindiği görüldü. Aşılanma nedenleri sorgulandığında; yakınlarına hastalık bulaştırmaktan korkma, aşı etkinliğine ve koruyuculuğuna inanma, kısıtlamalardan kurtulup normal yaşama dönme gerekçesi ile aşı olanların oranı, A grubunda B grubundan anlamlı olarak yüksek bulundu.

SONUÇ: Bu çalışmanın en önemli sonucu, hastalığı ağır geçirme riski olan kişilerin aşı ile ilgili bilgilere sağlık çalışanlarına göre daha yüksek oranda medyadan ulaşması olup toplumun daha doğru kaynaklardan bilgilendirilmesi için tedbir alınması konusunda uyarıcı olmasıdır.

ANAHTAR KELİMELER: Pandemi, COVID-19 aşıları, Sağlık çalışanları

ABSTRACT

OBJECTIVE: While the epidemic of "Coronavirus Disease 19" continues as a pandemic all over the world, Pandemic vaccine practices in our country started on January 14, 2021. This study was aimed to evaluate the demographic characteristics, risky contact histories before vaccination, and the opinions of the people who received the SARS-CoV-2 vaccine in the COVID-19 vaccine polyclinic of Afyonkarahisar University of Health Sciences about the pandemic vaccinations.

MATERIAL AND METHODS: In the period, when pandemic vaccine practices first started, a questionnaire consisting of 17 questions was administered to people who received the first dose of the pandemic vaccine through face-to-face interviews. Health workers were classified as group A and the other participants as group B, and the reasons for wanting to be vaccinated, their exposure to the pandemic, and other responses of these two groups were compared.

RESULTS: During the study period, 3159 persons were vaccinated. 1682 (53%) of them were health workers, and the remaining 1477 (47%) were considered to be group B. It was observed that group A obtained significantly more information from scientific publications, and group B from the media. When the reasons for vaccination are questioned, the rate of those vaccinated because of fear of infecting their relatives, believing in the effectiveness and protection of the vaccine, getting rid of the restrictions, and returning to daily life was found to be significantly higher in group A than in group B.

CONCLUSIONS: The most important result of this study is that people who are at risk of having severe disease access vaccination information from the media at a higher rate than healthcare professionals, and it warns the public to take precautions to inform them from more accurate sources.

KEYWORDS: Pandemic, COVID-19 vaccines, Healthcare workers

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GİRİŞ

"Severe Acute Respiratory Syndrome Coronavirus 2 (Şiddetli Akut Solunum Yolu Sendromu Koronavirüsü 2)" SARS-CoV-2 etkenli "Coronavirus Disease 19 (COVID-19)" pandemisi; dünya çapında endişe verici bir halk sağlığı sorunu olarak etkisini hala sürdürmektedir (1, 2). Etken, kişilere solunum sekresyonlarından damlacık yoluyla, yoğun sekresyon saçılımının olduğu alanlarda hava yolu ile ve kontamine çevresel yüzeylerle temas sonucu bulaşmaktadır. Nazofarengeal sürüntü örneklerinde, "polymerase chain reaction" (polimeraz zincir reaksiyonu, PCR) yöntemi ile SARS-CoV-2 varlığının araştırılması ile tanı konulur. Kardiyovasküler hastalık, kronik böbrek yetmezliği, kronik akciğer hastalıkları, diyabetes mellitus, hipertansiyon, immun supresyon, obezite gibi önceden var olan hastalıkları olan kişilerde hastalığın daha ağır seyrettiği bilinmektedir. Ayrıca hastalara hizmet veren sağlık çalışanları bulaş açısından oldukça yoğun risk altındadır. Risk grubundaki bu kişilerin hastalıktan korunması amacıyla öncelikli olarak aşılanması önem taşımaktadır (3).

Etkenin 2020 yılının başında tanımlanması ve sekans analizinin yapılmasının ardından tüm dünyada etkili ve güvenli bir aşı geliştirmeye yönelik çalışmalar baş döndürücü bir hızla gerçekleşti. Zira pandemiyi kontrol altına almak ve dünya genelinde pandemi yükünü azaltmak için standart önlemlerin (maske-mesafe-temizlik-havalandırma) yaygın şekilde uygulanması ve kısıtlama tedbirlerinin hayata geçirilmesi ne yazık ki yeterli olamadı ve acilen etkili ve güvenli COVID-19 aşılarına ihtiyaç duyulmaktaydı. Ülkemizde inaktive edilmiş SARS-CoV-2 aşısının 13 Ocak 2021'de Türkiye İlaç ve Tıbbi Cihaz Kurumu (TİTCK) tarafından acil kullanım onayı alması sonrasında 14 Ocak 2021 itibariyle pandemik aşılama uygulamaları öncelikle sağlık çalışanları, 90 yaş üzeri, komorbid hastalığı olanlar gibi risk gruplarının aşılanmasıyla başladı (4). Aşı uygulaması, 28 gün arayla sol koldan intramüsküler olarak verilen iki doz inaktif COVID-19 aşısı CoronaVac 600 U/0.5 mL (Sinovac Life Science, Pekin, Çin) olarak yapıldı (5).

Bu çalışmada; ülkemizde COVID-19 aşılamasının ilk başlatıldığı 20 Şubat 2021 ile 1 Haziran 2021 tarihleri arasında, Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıp Fakültesi COVID-19 aşı polikliniğinde SARS-CoV-2 aşı uygulaması yapılan kişilerin demografik özellikleri, aşılama öncesi riskli temas öyküleri ve yeni başlayan pandemi aşılamaları konusundaki görüşlerinin değerlendirilmesi amaçlandı.

GEREÇ VE YÖNTEM

Aşı uygulama biriminde 20 Şubat 2021 tarihinden 1 Haziran 2021 tarihine kadarki zaman aralığında birinci doz pandemik aşı uygulaması yapılan kişilere 17 sorudan oluşan anket yüz yüze görüşme yoluyla uygulanarak kişilerin demografik bilgileri, aşılar hakkındaki görüşleri, pandemi döneminde yakınlarında CO-VID-19 enfeksiyonu geçirme ve temaslı olma durumları sorgulandı. Sağlık çalışanları (hekim, öğrenci, hemşire, tıbbi sekreter, temizlik personeli, diğer yardımcı sağlık personeli vb.) A grubu, bakanlık tarafından ileri yaş ve/veya eşlik eden hastalıkları nedeniyle aşı uygulaması programına dahil edilen diğer katılımcılar B grubu olarak sınıflandırılıp, bu iki grubun aşı olmak isteme nedenleri, pandemiden etkilenme durumları ve diğer cevapları karşılaştırıldı.

Etik Kurul

Afyonkarahisar Sağlık Bilimleri Üniversitesi Klinik Araştırmalar Etik Kurulu onayı (Tarih: 05.02.2021 ve Karar No: 2021/99) ve T.C. Sağlık Bakanlığı onayı (Tarih: 15.01.2021 ve Başvuru No: 2021-01-12T16-31-01) ile gerçekleştirildi.

İstatistiksel Analiz

İstatistiksel analiz için IBM SPSS Statistic 22 versiyon paket programı kullanıldı. Kategorik veriler için frekans ve yüzdelikler, nicel veriler için ortalama ve standart sapma verildi. Kategorik değişkenlerin arasındaki farklılıkların incelenmesinde ki-kare testinden yararlanıldı. $p < 0.05$ olması anlamlı olarak kabul edildi.

BULGULAR

Çalışma periyodu içinde 3159 kişi aşılandı; 1569'u (%49.7) kadın, 1590'ı (%50.3) erkekti; yaşları 18 ile 91 aralığında olup ortalama yaş 42.28 ± 16.05 idi. Katılımcıların %30.4'ü 31 yaş altı kişilerden oluşuyordu, 72 yaş üzeri olan kişilerin sayısı 174 (%5.5) idi. Aşı olanların %71.4'ünün herhangi bir kronik hastalığı yoktu, eşlik eden en sık komorbiditeler; hipertansiyon (%10.3), diyabet (%7.8), kronik akciğer hastalıklarıydı (%4.6). Katılımcı grubu olduk-

ça düşük oranda malignite hastası içeriyordu (%0.6)(Tablo 1). Hastaların komorbidite ve demografik özellikleri **Tablo 1**'de gösterilmiştir.

Tablo 1: Aşı olan katılımcıların komorbidite ve demografik özellikleri

	n	%
Yaş		
<31	960	30.4
<41	735	23.3
<51	453	14.3
<61	550	17.4
<71	287	9.1
72<	174	5.5
Cinsiyet		
Kadın	1569	49.7
Erkek	1590	50.3
Mesleği		
Sağlık personeli	1682	53.2
Ev hanımı	471	14.9
Öğretmen	74	2.3
Serbest meslek	160	5.1
Çiftçi	39	1.2
Emekli	259	8.2
Memur	137	4.3
Öğrenci	34	1.1
Diğer	303	9.6
Komorbidite		
Kronik hastalığı yok	2257	71.4
Diyabet	246	7.8
Hipertansiyon	324	10.3
Kronik akciğer hastalığı	144	4.6
Kalp yetmezliği	132	4.2
Malignite	20	0.6
Böbrek yetmezliği	56	1.8
Diğer	201	6.4

Aşılananların 1682'si (%53) sağlık çalışanı olup A grubu, geri kalan1477 (%47) kişi B grubu olarak değerlendirildi. A grubunda 755 (%44.9) kişinin B grubunda da 542 (%36.7) kişinin, çalışma periyodu öncesinde birinci dereceden akrabalarında COVID-19 öyküsü tespit edildi (p<0.001). Pandeminin başından çalışma periyodunun başlangıcına kadar olan sürede A grubunda 1027 kişiden (%61.1), B grubunda ise 438 kişiden (%29.7) nazofarengeal sürüntü örneği alınarak PCR testi çalışılmıştı (p<0.001). A grubunda daha fazla sayıda katılımcı (823 kişi, %48.9) COVID-19 nedeniyle tanıdığı bir kişiyi kaybetmişti. Yakınını kaybeden katılımcı sayısı B grubunda 631 (%42.7) idi(p<0.001).

A grubunun verileri değerlendirildiğinde; 862 (%51.2) kadın, 820 (%48.8) erkek olduğu, yaş ortalamasının 32.7±9.05 olduğu tespit edildi. A grubunda yaş aralığı 18 - 66 yaş arasında değişiyordu. Hekimler, 434 kişiyle A grubunun %25.8'ini oluşturuyordu. Aşıya ulaşıncaya kadarki dönemde; 948 (%56.4) sağlık çalışanının çalıştığı birimde COVID riskli teması olmuş, bunlardan 277'si izole edilerek nazofarengeal sürüntü örneği ile PCR testi yapılmış, diğerleri semptom takibi yaparak maske ile çalışmıştı. A grubu katılımcıların genel özellikleri **Tablo 2**'de verilmiştir.

Çalışma grubuna uygulanan anket sorularının cevapları değerlendirildiğinde; aşı hakkındaki bilgilerin katılımcıların %50.3'ünde televizyon ve sosyal medyadan edinildiği tespit edildi. Medyadan bilgi edinenlerin oranı B grubunda (%61.5) A grubuna (%40.4) göre anlam-

lı düzeyde yüksek bulundu (p<0.001). Yine A grubu ile kıyaslandığında B grubunda daha fazla kişi arkadaş çevresinden ve doktorundan bilgi edindiğini söylerken (sırasıyla p<0.001 ve p=0.01), A grubunun anlamlı olarak daha fazla bilimsel yayınlardan bilgi edindiği görüldü (p<0.001). Anket sorularına verilen cevapların sonuçları **Tablo 3**'te gösterilmiştir.

Tablo 2: Aşı olan sağlık çalışanlarının genel özellikleri

	n	%
Cinsiyet		
Kadın	862	51,2
Erkek	820	48,8
Mesleği		
Öğrenci	80	4,8
Hekim	434	25,8
Hemşire	359	21,3
Temizlik personeli	168	10
Tıbbi sekreter	134	8
Diğer yardımcı sağlık personeli	507	30,1
COVID biriminde çalıştı mı?		
Evet	948	56,4
Hayır	734	43,6
COVID riskli temas öyküsü		
Riskli teması olan	948	56,4
Riskli temas sonrası semptom takibi yapıldı	671	39,9
Riskli temas sonrası PCR verdi	277	16,5

Tablo 3: SARS-CoV-2 aşısı hakkındaki bilgilerinizi nereden edindiniz

	A grubu n (%)	B grubu n (%)	p
Televizyon ve sosyal medyadan	680 (40.4)	909 (61.5)	<0.001
Doktorumdan	379 (22.5)	390 (26.4)	0.01
Arkadaş çevremden	217 (12.9)	127 (8.6)	<0.001
Bilimsel yayınlardan	734 (43.6)	106 (7.2)	<0.001

Çalışma gruplarında aşılanma nedenleri sorgulandığında; yakınlarına hastalık bulaştırmaktan korkma, aşı etkinliğine ve koruyuculuğuna inanma, kısıtlamalardan kurtulup normal yaşama dönme gerekçesi ile aşı olanların oranı, A grubunda B grubundan anlamlı olarak yüksek bulundu (p<0.001). Bu bulgular **Tablo 4**'te gösterilmiştir.

Tablo 4: Neden aşı olmayı tercih ettiniz

	A grubu n (%)	B grubu n (%)	p
Herkesin aşı olmasıyla pandeminin biteceğine inandığım için	599 (35.6)	515(34.9)	0.662
Sevdiklerimi korumak, hasta olup onlara bulaştırmamak için	682 (40.5)	475(32.2)	<0.001
Hastalığı ağır geçirmekten ve ölmekten korktuğum için	233 (13.9)	237 (16.0)	0.084
Aşının etkili olduğuna ve beni koruyacağına inandığım için	297 (17.7)	166(11.2)	<0.001
Aşının güvenli olduğuna ve bana zarar vermeyeceğine inandığım için	114(6.8)	87 (5.9)	0.308
COVID-19 enfeksiyonu geçirmeyi aşıdan daha tehlikeli bulduğum için	101 (6.0)	78 (5.3)	0.380
Kısıtlama önlemlerinden sıkıldığım ve normal sosyal hayata dönmek istediğim için	171 (10.2)	87 (5.9)	<0.001

TARTIŞMA

Pandemi ile mücadele amacıyla uygulanan kısıtlama önlemleri nedeniyle toplumun büyük bir kesimi ekonomik, sosyal ve psikolojik olarak olumsuz etkilenmiştir. Enfekte olma ve hayatını kaybetme korkusu, kısıtlamalar nedeniyle sınırlanan sosyal yaşam, sevdiklerinden ayrı kalma gibi durumlar nedeniyle insanların artmış anksiyete belirtileri gösterdiği saptanmıştır (6). Çalışmamızda, ülkemizde pandemi aşılamalarının başlangıç döneminde, polikliniğimizde

aşılanların %53.2'si sağlık çalışanı geri kalanı diğer riskli grup olarak belirlendi. Her iki grubun benzer orana sahip olması, çalışma grubumuz tüm toplumu yansıtmadığı için kesin yargıya varmak mümkün olmasa da, hastalığı ağır geçirme olasılığı nedeni ile riski olanlar (B grubu) ile virusla karşılaşma olasılığı yüksek olduğu için risk grubunda olanların (A grubu) aşıya ilgisinin benzer olduğunu düşündürmektedir. Benzer şekilde, yapılan bazı çalışmalarda bu iki grubun aşı olma istekleri arasında herhangi bir fark saptanmamış, bu da pandeminin etkisini toplumun tüm kesimlerinde güçlü bir şekilde hissettirmiş olmasıyla açıklanmıştır (7). Buna karşılık Harapan ve ark., sağlık çalışanı olarak çalışanların, tıp dışı sektörlerde çalışanlara kıyasla aşıyı kabul etme oranlarının daha yüksek olduğunu, kendini, ailesini, arkadaşlarını ve hastaları koruma arzusunun sağlık çalışanlarının aşı olma kararının itici güçleri olduğunu ifade etmişlerdir (8).

Pandemi ile mücadelede aşılamanın önemi göz önüne alındığında, yaşlılar ve kronik hastalığı olan hastalar gibi özel alt grupların aşılanması büyük önem taşımaktadır. Altta yatan komorbiditeleri olan bireylerde şiddetli COVID-19 insidansının çok daha fazla olduğu kanıtlanmıştır. Bu nedenle; otoimmün hastalıkları olan, immünosupresif veya anti-kanser ajanları alan hastalar gibi spesifik immünolojik eksiklikleri olan hastaların aşılanmasına özellikle önem verilmelidir (9). Komorbiditeler açısından bakıldığında çalışmamızda katılımcıların %71.4'ünün herhangibir kronik hastalığı yoktu, geri kalan 902 kişinin (%28.6) ise hastalığın daha ağır geçirilmesine neden olduğu bilinen diyabet, hipertansiyon, kronik akciğer hastalığı, böbrek yetmezliği, malignite gibi ek hastalıkları mevcuttu. Kronik hastalığı olmamasına rağmen aşı olmayı tercih eden kişi sayısının bu yüksek oranlara sahip olması oldukça sevindiricidir. Malignite hastalarının sayısının katılımcılar arasında düşük oranlarda kalması ise dikkat çekicidir. Bu hastalar; malignitesi olmayan hastalara kıyasla, COVID-19'dan kaynaklanan ciddi komplikasyonlar ve mortalite açısından daha büyük risk altındadır. Bu nedenle aşılanmalarına önem verilmeli, bu kişileri bulaş riskinden korumak için maske, mesafe hijyen gibi kişisel korunma önlemlerine de dikkat edilmelidir (10).

Çalışmamızda A grubuna göre B grubunda, SARS-CoV-2 aşısı ile bilgilerin medyadan edinildiğini saptadık. Pandemi sürecinde kısıtlamalar nedeniyle uzun süre evde vakit geçiren insanların televizyon ve sosyal medyaya daha fazla vakit ayırması nedeni ile bu sonuç doğal olarak değerlendirilebilir. Ancak bu kaynaklardan her zaman doğru bilgi edinilemeyebileceği, bu durumunda aşılama aleyhine tutum alınmasına da neden olabileceği akılda tutulmalıdır. Aşı tereddütü ya da aşı karşıtlığının en önemli nedenleri advers reaksiyon endişeleri, aşının içeriğine güvenmeme, dini sebepler, aşı karşıtlarının açıklamalarından etkilenme ve basında çıkan olumsuz haberler olarak bildirilmektedir (11). Bu nedenle, sağlık otoritelerinin, toplumun daha doğru bilgi kaynaklarına ulaşması, medyanın etkin bilgi kaynağı olması için tedbirler alması zorunludur. Sosyal medya ve basının doğru bilgilendirmeler yapması konusunda denetlemeler uygulanması alınabilecek tedbirler arasında yer almalıdır.

Çalışmamızda yakınlarına hastalık bulaştırma korkusu ve normal yaşama dönme isteği nedeni ile aşılanma A grubunda B grubuna göre anlamlı düzeyde yüksek bulunmuştur. Pandemi ile doğrudan ve dolaylı olarak mücadele eden sağlık çalışanları, her gün enfekte olma riskiyle karşı karşıyadır. Ayrıca pandeminin getirdiği ek iş yükü, kişisel koruyucu ekipman kullanımına dikkat etme gerekliliği, ekipman yetersizliği, yoğun bir çalışma temposunun da beraberinde getirdiği aşırı fiziksel ve ruhsal yorgunluk, tükenmişlik hissi sağlık çalışanlarının pandeminin artık sonlanması ve normal sosyal hayata dönme gibi isteklerinin toplumun diğer kesimlerinden daha fazla olmasını açıklayabilir. Zhu ve ark.'larının çalışmasında 5062 sağlık çalışanından %29.8'inde stres, %24.1'inde kaygı, %13.5'inde depresyon bildirilmiş, İtalya'da yapılan bir çalışmada ise sağlık çalışanlarının genel nüfusa kıyasla daha yüksek düzeyde kaygı duyduğu saptanmıştır (12). Çalışmamızda salgının başından çalışma periyodumuzun başına kadar, A grubunda SARS-CoV-2 bulaş şüphesi ile PCR testi yaptırma oranını B grubundan fazla bulduk. Bu da sağlık çalışanlarının daha fazla bulaş riski ile karşı karşıya kalma olasılığını desteklemektedir.

Sonuç olarak; bu çalışmada, değerlendirilen grupta, COVID-19 bulaş riski nedeni ile risk taşıyan grup ile hastalığı ağır geçirme riski olanlar benzer oranlarda tespit edildi. Aşılananların aşılanma nedenleri değerlendirildiğinde sağlık çalışanlarının daha çok yakınları için kaygı duyduğu ve geçirdikleri yoğun süreç nedeni ile bık-

kın olmaları diğer gruptan daha fazla öne çıktı. Aşı ile ilgili bilgi kaynaklarına sağlık çalışanlarının daha doğru yollardan ulaştığı tespit edildi.

Bu çalışmanın en önemli sonucu, hastalığı ağır geçirme riski olan kişilerin aşı bilgilendirmelerine sağlık çalışanlarına göre daha yüksek oranda medyadan ulaşması olup toplumun daha doğru kaynaklardan bilgilendirilmesi için tedbir alınması konusunda uyarıcı olmasıdır.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

SON BEŞ YILDA (2012 - 2017) AFYON KOCATEPE ÜNİVERSİTESİ TIP FAKÜLTESİ HASTANESİ'NDE İZLENEN HASTANE KAYNAKLI PNÖMONİ OLGULARININ DEĞERLENDİRİLMESİ

THE EVALUATION OF HOSPITAL ASSOCIATED PNEUMONIA (HAP) CASES IN THE LAST FIVE YEARS (2012 - 2017) AT AFYON KOCATEPE UNIVERSITY MEDICAL FACULTY HOSPITAL

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Ana Bilim Dalı

ÖZET

AMAÇ: Bu çalışmanın amacı hastanenin farklı bölümlerinde HKP (Hastane kaynaklı pnömoni) ve VİP (Ventilatör ilişkili pnömoni) sıklığını, florayı oluşturan mikroorganizmaları ve antibiyotik direnç paternlerini belirleyerek uygun ampirik tedaviye yol göstermek.

GEREÇ VE YÖNTEM: Ocak 2012 ve Aralık 2017 tarihleri arasında Afyon Kocatepe Üniversitesi (AKÜ) Hastanesi'nde yatan ve takipleri sırasında HKP ve VİP gelişen, 18 yaş ve üzeri hastalar çalışmaya dahil edildi. Yaş, cinsiyet, yattığı klinik birim, kronik hastalık varlığı, pnömoninin ventilatör ile ilişkisi, mortalite gelişen hasta sayısı, mortalite gelişen hastaların özellikleri, olası risk faktörleri değerlendirildi.

BULGULAR: Hastaların 405'i (%65.5) VİP, 213'ü (%34.5) HKP idi. Yaş ortalaması 67.20±15.42 yıl bulundu. 240'ı (%38.8) kadın, 378'i (%61.2) erkek hastaydı. Erkek cinsiyetin VİP ve HKP gelişmesi üzerine etkisi görüldü (p=0.006). 329 hastada (%53.2) kronik hastalık yokken, 289'unda (%46.8) vardı. En sık eşlik eden kronik hastalıklar sırasıyla; Diabetes mellitus (DM) (%15.3), Hipertansiyon (HT) (%12.6), Kronik Obstruktif Akciğer Hastalığı (KOAH) (%7.6) idi. Komorbidite varlığının VİP gelişmesini etkilediği bulundu (p=0.003). Yoğun bakım ünitelerinde (YBÜ) yatan hastaların 122 (%57.3)'sinde HKP, 384 (%94.9)'ünde VİP gelişti. Dahili birimlerde yatan hastaların 63 (%29.6)'ünde HKP, 14 (%3.4)'ünde VİP gelişti. Cerrahi birimlerde yatan hastaların ise 28 (%13.1)'inde HKP, 7 (%1.7)'sinde VİP gelişti. YBÜ'lerde yatan hastalarda HKP ve VİP görülme oranı anlamlı düzeyde yüksek bulundu (p<0.001). HKP grubunda 213 hastanın 161'inde (%75.5), VİP grubunda ise 405 hastanın 211'inde (%52.1) etken mikroorganizma belirlenemedi. HKP ve VİP olgularında en sık izole edilen etkenler; *A.baumannii, K.pneumoniae, P.aeruginosa, E.coli* ve metisilin dirençli *S.aureus* (MRSA) idi. A.baumannii suşlarında meropenem direnci 103 (%97.2), imipenem direnci 105 (%99.1) bulundu. Hastaların 373'ünde (%60.4) mortalite gelişti. VİP grubunun 297'sinde (%48.1), HKP grubunun 76'sında (%12.3) mortalite görüldü. VİP olgularında mortalite oranı anlamlı düzeyde yüksek bulundu (p<0.001). Erkek cinsiyet, yaş ortalamasının ≥60 olması, komorbidite varlığı ve YBÜ'de yatış mortaliteyi artıran risk faktörleri idi. Hiçbir etken mikroorganizma ile mortalite gelişmesi arasında ise bir korelasyon saptanmadı.

SONUÇ: Bu retrospektif çalışmada HKP'lerin çoğunun VİP olarak gözlenmesi, kurumumuzda VİP gelişmesini engellemek için alınması gereken önlemlerin artırılması gerektiğini düşündürmektedir.

ANAHTAR KELİMELER: Yoğun bakım ünitesi, Nozokomiyal pnömoni, Ventilatör.

ABSTRACT

OBJECTIVE: This study was aimed to guide the appropriate empirical treatment, by determining the frequency of hospital acquired pneumonia (HAP) and Ventilator-associated pneumonia (VAP) in different parts of the hospital, the causative microorganisms and their antibiotic resistance patterns.

MATERIAL AND METHODS: Patients aged ≥18 years who were hospitalized in Afyon Kocatepe University Hospital between January 2012 and December 2017 and who developed HAP and VAP during their follow-up were included in the study. Age, gender, hospitalization unit, presence of chronic disease, the relationship between pneumonia and ventilator, number of patients who developed mortality, characteristics of patients who developed mortality, and possible risk factors were recorded and evaluated.

RESULTS: : 405 (%65.5) of the patients were VAP, and 213 (%34.5) of patients were HAP. The mean age was 67.20±15.42 years. 240 (%38.8) of the patients were female, and 378 (%61.2) were male. The male gender had a statistically significant effect on the development of VAP and HAP (p=0.006). There was no chronic disease in 329 (%53.2) of the patients, and 289 (%46.8) had a chronic disease. The most common chronic diseases were respectively; Diabetes mellitus (DM) (%15.3), Hypertension (HT) (%12.6), and Chronic Obstructive Pulmonary Disease (COPD) (%7.6). The relationship between comorbidity and the development of VAP was found to be significant (p=0.003). HAP developed in 122 (%57.3) and VAP developed in 384 (%94.9) of the patients hospitalized in the intensive care units (ICU). HAP developed in 63 (%29.6) and VAP developed in 14 (%3.4) of the patients hospitalized in internal units. 28 (%13.1) of the patients who were hospitalized in surgical units developed HAP, and 7 (%1.7) of the patients developed VAP who hospitalized in surgical units. The incidence of HAP and VAP was found to be significantly higher in patients hospitalized in ICUs (p<0.001). The incidence of HAP and VAP was found to be significantly higher in patients who were hospitalized in ICUs (p<0.001). The causative agent could not be determined 161 (%75.5) of 213 patients in the HAP group, and 211 (%52.1) of 405 patients in the VAP group. The most frequently isolated microorganisms in HAP and VAP cases were; *A.baumannii, K.pneumoniae, P.aeruginosa, E.coli,* and methicillin-resistant *Staphylococcus aureus* (MRSA). Meropenem resistance was found in 103 (%97.2) and imipenem resistance in 105 (%99.1) A.baumannii strains. Mortality developed in 373 (%60.4) of the patients. Mortality was seen in 297 (%48.1) of the VAP group and 76 (%12.3) of the HAP group. The mortality rate was higher in the VAP group (p<0.001). Male gender, mean age ≥60 years, comorbidity and ICU hospitalization were risk factors that increased mortality. No correlation was found between any of the causative microorganisms and the development of mortality.

CONCLUSIONS: Measures should be increased to prevent the development of VAP in our institution because most of HAPs were in the VAP group in this retrospective study.

KEYWORDS: Intensive care unit, Nosocomial pneumonia, Ventilator.

GİRİŞ

Hastane kaynaklı pnömoni (HKP) ülkemizde tüm hastane infeksiyonları arasında 2. veya 3. sırada görülmektedir (1 - 3). YBÜ'de yatan hastalarda ise; en sık görülen hastane kaynaklı infeksiyon (HKİ) pnömonidir. HKP'nin gerçek insidansını tahmin etmek zordur. Ülkemizde farklı çalışmalardan elde edilen verilerde bu oranın %0.2-52 arasında ciddi farklılıklar gösterdiği belirlenmiştir (1, 4, 5) ve %80'den fazlası ventilatör kullanımı ile ilişkilidir. HKP ve ventilatör ilişkili pnömoni (VİP) hastalarında tanıdaki zorluklar nedeniyle gereksiz antibiyotik kullanımına bağlı çok ilaca dirençli (MDR) mikroorganizmalar ile infeksiyon riski yüksektir. Bu çalışmada Afyon Kocatepe Üniversitesi Tıp Fakültesi Hastanesi'nde gelişen HKP'lerin sıklığı, ünitelere göre dağılımı, etken mikroorganizmalar, olası risk faktörleri ve mortalite gelişen hastaların özelliklerinin araştırılması amaçlandı.

GEREÇ VE YÖNTEM

Çalışmaya Ocak 2012 ve Aralık 2017 tarihleri arasında Afyon Kocatepe Üniversitesi (AKÜ) Hastanesi'nde yatan ve takipleri sırasında HKP ve VİP gelişen, 18 yaş ve üzeri hastalar dahil edildi. Retrospektif kohort çalışması olarak yürütüldü. HKP ve VİP tanısı CDC 2015 kılavuzunun HKİ tanı kriterlerine göre belirlendi. Hastaların ilk HKP ve VİP atakları değerlendirildi. Yaş, cinsiyet, yattığı klinik birim, eşlik eden kronik hastalık varlığı ve pnömoninin ventilatör ile ilişkili olup olmadığı bilgileri kaydedildi. Veriler hastane infeksiyon kontrol komite hemşirelerinin kayıtları ve bilgisayar otomasyon sistemindeki bilgilerden elde edildi. Mikrobiyal değerlendirme ve antibiyotik duyarlılık testi için VİTEK®2 cihazı kullanıldı. Antibiyotik duyarlılık değerlendirmesi 2012 - 2015 yılları arasında Clinical and Laboratory Standards Institute (CLSI), 2015 - 2017 yılları arasında European Committee on Antimicrobial Susceptibility Testing (EUCAST) kullanılarak yapıldı.

Etik Kurul

Çalışmamızın araştırma protokolüne Afyon Kocatepe Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulunun 04.05.2018/123 sayılı kararı ile amaç, yöntem ve yaklaşım bakımından etik ilkelere uygun olduğu kararı verildi.

İstatistiksel Analiz

Bağımsız gruplarda sürekli verilerin ortanca değerlerinin karşılaştırılmasında Mann Withney U Testi, kategorik verilerin yüzde dağılımlarının karşılaştırılmasında Ki-Kare testi kullanıldı. İki veya daha fazla sayıda grubun ortalamaları arasındaki faklılığın anlamlılığı ise Kruskal Wallis testi ile karşılaştırıldı. P<0.05 olduğunda istatistiksel olarak anlamlı kabul edildi.

BULGULAR

Ocak 2012 ve Aralık 2017 tarihleri arasında AKÜ Hastanesi yoğun bakım ünitesi (YBÜ), dahili birimler ve cerrahi birimlerde yatan, ≥18 yaş olan, yatışında HKP ve VİP gelişen 618 hasta değerlendirmeye alındı. Hastaların 405'i (%65.5) VİP, 213'ü (%34.5) HKP olarak değerlendirildi. Yaş ortalaması 67.20±15.42 yıl idi. Hastaların 240'ı (%38.8) kadın, 378'i (%61.2) erkek idi. VİP gelişen 405 hastanın 173'ü (%42.7) kadın, 232'si (%57.3) erkek iken; HKP görülen 213 hastanın 67'si (%31.5) kadın, 146'sı (%68.5) erkek idi. Erkek hastalarda VİP ve HKP anlamlı düzeyde yüksek bulundu (p=0.006). HKP ve VİP hastaları eşlik eden hastalıklar açısından incelendi **(Tablo 1)**.

Tablo 1: Eşlik eden hastalıklar

Komorbidler	VİP (n:405)		HKP (n:213)		Toplam (n:618)	
	Sayı	%	Sayı	%	Sayı	%
Diabetes Mellitus	59	14.6	36	16.9	95	15.4
Hipertansiyon	50	12.4	28	13.2	78	12.7
KOAH	26	6.5	21	9.8	47	7.7
Kalp yetmezliği	23	5.7	20	9.4	43	6.9
KBY	14	3.5	13	6.2	27	4.4
Akciğer kanseri	6	1.5	13	6.2	19	3
Kolon kanseri	9	2.3	7	3.2	16	2.6
Koroner arter hastalığı	7	1.8	4	1.8	11	1.8
Pankreas kanseri	8	1.9	1	0.4	9	1.5
Epilepsi	6	1.5	1	0.4	7	1.1
Astım	5	1.2	3	1.4	7	1.1
Mide kanseri	3	0.7	4	1.8	7	1.1
Larenks kanseri	1	0.2	4	1.8	5	0.8
GBM	5	1.2	-		5	0.8
Siroz	2	0.4	1	0.4	3	0.5
Safra kesesi kanseri	-		-		2	0.3
Tiroid kanseri	-		2	0.9	2	0.3
Periferik arter hastalığı	1	0.2	1	0.4	2	0.3
Parkinson	2	0.4	-		2	0.3
Over kanseri	1	0.2	-		1	0.1
Mesane kanseri	-		1	0.4	1	0.1
İntersitisyel akciğer hastalığı	-		1	0.4	1	0.1
Alzheimer	1	0.2	-		1	0.1

Hastaların 329'unda (%53.2) eşlik eden bir kronik hastalık yokken, 289'unda (%46.8) eşlik eden kronik hastalık olduğu görüldü. Komorbidite ile VİP gelişmesi arasında anlamlı bir ilişki bulundu (p=0.003). YBÜ'lerde yatan hastalarda HKP ve VİP görülme oranı yüksek bulundu (p<0.001). Hastaların yattığı birimlere göre HKP ve VİP görülme oranları **Tablo 2**'de gösterilmiştir. HKP grubundaki 213 hastanın 161'inde (%75.5) pnömoni etkeni olarak hiçbir mikroorganizma belirlenemezken; 52'sinde (%24.5) pnömoni etke-

ni olan mikroorganizma belirlendi. VİP gelişen grupta ise 405 hastanın 211'inde (%52.1) pnömoni etkeni mikroorganizma belirlenemezken, 194'ünde (%47.9) etken belirlendi. HKP olgularında en sık izole edilen etkenler sırasıyla; *A.baumannii, K.pneumoniae, P.aeruginosa, E.coli* ve MRSA idi. VİP grubunda ise en sık izole edilen mikroorganizmalar sırasıyla; *A.baumannii, P.aeruginosa, K.pneumoniae, E.coli* ve MRSA idi. İzole edilen etkenler **Tablo 3**'te, antibiyotik direnç paternleri **Tablo 4 ve Tablo 5**'te gösterilmiştir.

Tablo 2: Hastanedeki bölümlere göre HKP ve VİP gelişme oranı

Klinikler	VİP (n:405)		HKP (n:213)	
	Sayı	%	Sayı	%
Yoğun bakımlar	384	94.9	122	57.3
Dahili birimler	14	3.4	63	29.6
Cerrahi birimler	7	1.7	28	13.1

Tablo 3: HKP ve VİP gelişen hastalarda izole edilen etkenler

Etken	VİP (n:194)		HKP (n:52)	
	Sayı	%	Sayı	%
A.baumanii	90	46.4	16	30.8
P.aeruginosa	41	21.2	10	19.3
GSBL(-) K.pneumoniae	14	7.3	6	11.6
GSBL(+) E.coli	12	6.1	3	5.8
GSBL(+) K.pneumoniae	11	5.7	6	11.6
MRSA	8	4.1	4	7.6
GSBL(-) E.coli	7	3.7	4	7.6
MSSA	3	1.5	-	-
E.faecalis	2	1	1	1.9
S.agalactia	1	0.5	-	-
Proteus mirabilis	1	0.5	-	-
Citrobacter koseri	1	0.5	-	-
Serratia plymultica	1	0.5	-	-
Citrobacter freundii	1	0.5	-	-
Morganella morganii	1	0.5	-	-
Klebsiella oxytoca	-	-	2	3.9

Tablo 4: İzole edilen non-fermentatiflerin antibiyotik dirençleri

Antibiyotik	A.baumannii (n:106)		P.aeruginosa (n:51)	
	Sayı	%	Sayı	%
Amikasin	52	49.1	7	13.7
Sefepim	106	100	21	41.2
Seftazidim	106	100	39	83
Sefoperazon-sulbaktam	94	92.2	38	85
Siprofloksasin	105	99.1	20	39.2
Gentamisin	80	75.5	14	27.5
Imipenem	105	99.1	13	25.5
Levofloksasin	104	99	24	47.1
Meropenem	103	97.2	15	29.4
Piperasilin-tazobaktam	89	84	45	88.2
Tigesiklin	2	1.9	-	-

Tablo 5: İzole edilen E.coli ve Klebsiella spp. izolatlarının antibiyotik dirençleri

Antibiyotik	GSBL(-) E.coli (n:11)		GSBL(+) E.coli (n:15)		GSBL(-) K.pneumoniae (n:20)		GSBL(+) K.pneumoniae (n:17)	
	Sayı	%	Sayı	%	Sayı	%	Sayı	%
Amikasin	2	18.2	-	-	2	10	4	23.5
Sefepim	-	-	11	73.3	4	20	17	100
Sefoperazon-sulbaktam	8	72.7	11	73.3	6	30	11	64.7
Siprofloksasin	4	36.4	12	80	5	25	5	29.4
Gentamisin	6	54.5	3	20	4	20	15	88.2
İmipenem	-	-	-	-	2	10	6	35.3
Levofloksasin	4	36.4	14	93.3	5	25	16	94.1
Meropenem	-	-	-	-	2	10	2	10
Piperasilin-tazobaktam	4	36.4	8	53.3	4	20	13	76.5

Hastaların 373'ünde (%60.4) mortalite gelişti. VİP gelişen 405 hastanın 297'sinde (%48.1), HKP belirlenen 213 hastanın 76'sında (%12.3) mortalite görüldü. VİP olgularında mortalite oranı anlamlı düzeyde yüksekti (p<0.001).

Mortalite gelişen 373 hastanın 164'ü (%43.9) kadın; 209'u (%56.1) erkek idi. Cinsiyetin mortalite üzerine anlamlı bir etkisi bulunmadı (p=0.001).Mortalite gelişen hastaların yaş ortalaması 69.04±15 yıl, ilk pnömoni atağı başarı ile tedavi edilen hastaların yaş ortalaması ise 64.41±15.65 yıl idi. Yaş ile mortalite arasındaki ilişki istatistiksel açıdan anlamlı bulunmadı (p=0.061). Komorbiditesi olan 289 hastanın 168'inde (%58.1) mortalite gelişirken, komorbiditesi olmayan 329 hastanın 205'inde (%62.3) mortalite gelişti Komorbidite varlığının mortaliteyi etkilemediği görüldü (p=0.290). YBÜ'lerde yatan 506 hastanın 350'sinde (%69.1), dahili birimlerde yatan 77 hastanın 18'inde (%23.3), cerrahi birimlerde yatan 35 hastanın 5'inde (%14.2) mortalite gelişti. Mortalite oranı YBÜ'lerde daha yüksek bulundu (p <0.001). İzole edilen etkenler içinde mortalite oranı en yüksek olan *A.baumannii* (%10.5/%22.5) idi. Hiçbir etken mikroorganizma ile mortalite oranı arasında anlamlı bir ilişki saptanmadı (p=0.176).

TARTIŞMA

HKP hastanede yatan hastalarda hastanede kalış süresi ve mortaliteyi etkileyen en önemli HKİ'dir. Kontrol programları, antimikrobiyal tedavi ve destek tedaviye rağmen önemli bir morbidite ve mortalite nedenidir (1). Hastanede yatış süresini uzattığından ekonomik yükü artırmaktadır (2). Etken mikroorganizma hastaneye, kliniğe, komorbiditeye, risk faktörlerine ve antimikrobiyal kullanım öyküsüne göre değişiklik gösterebilir. HKP'nin tanımlanmasında klinik bulgular, akciğer grafisi ve varsa etken patojen beraber değerlendirilmelidir. Etken izolasyonu için solunum yolu örneklemesi yapılmalıdır. Tedavide esas ilke uygun kültürler alındıktan sonra ampirik antibiyotik tedavisinin hemen başlanması, kültür sonuçlarına göre gerekirse revize edilmesidir.

Çalışmamızda HKP ve VİP gelişen hastaların yaş ortalaması birbirine yakın olup; ileri yaşın VİP gelişmesini etkilemediği görüldü. HKP/VİP tanılı hastalarda ileri yaş bazı çalışmalarda önemli bir risk faktörü iken bazı çalışmalarda ise anlamlı bulunmamıştır. İbrahim ve ark.'larının yapmış olduğu bir çalışmada 3717 YBÜ hastasında yaşın VİP gelişmesi üzerine etkisi olmadığı belirlenmiştir (3).

Yine Hindistan'da Agarwal ve ark.'larının yapmış olduğu bir çalışmada ileri yaşın HKP gelişmesi açısından risk oluşturmadığı görülmüştür (4). HKP gelişimi açısından daha önce yapılmış olan birçok çalışmada cinsiyete dayalı bir farklılık bulunmadığı görülmüştür (4, 5). Ancak bazı çalışmalarda da HKP ve VİP'in erkek hastalarda daha sık olduğu belirlenmiştir (6, 7). Bilici ve ark.'larının yapmış olduğu bir çalışmada VİP gelişme oranının erkek hastalarda daha yüksek olduğu görülmüştür (7). Yine Fransa'da Giard ve ark.'larının 7236 YBÜ hastası ile yaptığı bir çalışmada, erkek cinsiyetin erken başlangıçlı VİP gelişmesi açısından bir risk faktörü olduğu görülmüştür (8). Benzer şekilde bizim çalışmamızda da VİP oranının erkek hastalarda daha yüksek olduğu görüldü.

Kronik hastalık varlığı HKP ve VİP gelişmesine yol açan risk faktörleri arasında sayılmaktadır. Türk Toraks Derneği Erişkinlerde Hastanede Gelişen Pnömoni Tanı ve Tedavi Uzlaşı Rehberinde kronik akciğer hastalığı, Kronik böbrek yetmezliği (KBY), Diabetes mellitus (DM) ve malignite gibi kronik hastalıkların HKP/VİP gelişmesine yol açan risk faktörlerinden olduğu belirtilmiştir (9). Alp ve ark.'larının Erciyes Üniversitesi Hastanesi YBÜ'de 2402 hastada yaptığı bir çalışmada, KOAH varlığının HKP gelişme riskini 3 kat arttırdığı gözlenmiştir (10). Uslu ve ark.'larının yapmış olduğu bir çalışmada da DM ve KOAH varlığının VİP gelişmesi için bağımsız birer risk faktörü olduğu saptanmıştır (11). Çalışmamızda kronik hastalık varlığının VİP gelişmesi üzerine istatistiksel olarak anlamlı etkisi olduğu görüldü (p=0.003). William Buczko'nun 2004 yılında 3371 hasta ile yapmış olduğu bir çalışmada HT ile VİP gelişmesi arasında istatistiksel açıdan anlamlı bir ilişki olduğu görülmüştür (12). Bizim çalışmamızda da HT'nin de HKP/VİP hastalarına sık eşlik ettiği görüldü. Bu sebeple hastanede uzun süre yatan ve komorbiditesi olan hastalarda VİP'ten korunma önlemlerine daha çok dikkat edilmesi önemlidir.

YBÜ'lerde yatan hastalar infeksiyon gelişmesine yatkındırlar (13, 14). Bu hastalarda en sık görülen HKİ pnömonidir (9). Sevinç ve ark.'larının HKP gelişen 173 olguyu değerlendirdiği bir çalışmada HKP/VİP'in en sık YBÜ'lerde geliştiği belirlenmiştir (6). Bu çalışmada HKP/VİP olgularının çoğunluğu YBÜ'lerde yatan hastalardı. Bu durum; YBÜ'lerde yatan hastalarda ileri yaş, alt-

ta yatan hastalığın ciddiyeti, eşlik eden kronik hastalıklar, endotrakeal entübasyon, mekanik ventilatör gibi risk faktörlerinin mevcudiyetinin HKP/VİP gelişmesine katkıda bulunduğunu düşündürmektedir. HKP/VİP etkeni olan patojenler hastaneye, hastanenin değişik birimlerine, altta yatan hastalığa göre değişiklik gösterebilirler (15). Biz HKP hastalarında en sık; *A.baumannii, K.pneumoniae, P.aeruginosa, E.coli* ve MRSA'nın etken olduğunu gördük. Sevinç ve ark.'larının yaptığı bir çalışmada da HKP'nin en sık etkenleri *A.baumannii, P. aeruginosa,* MRSA, *K.pneumoniae ve E.coli* olarak bulunmuştur (6). VİP'te ise etken mikroorganizmaların özellikle *P. aeruginosa, S. aureus ve Enterobacteriaceae spp.* olduğu vurgulanmaktadır (16). Ülkemizde yapılmış olan çok merkezli bir çalışmada VİP etkenlerinin en sık olarak sırasıyla; *Acinetobacter spp., P. aeruginosa ve S. aureus* olduğu belirlenmiştir (7). Çalışmamız da literatür ile benzer olup VİP etkenlerinin en sık; *A.baumannii, P.aeruginosa, K.pneumoniae, E.coli* ve MRSA olduğu görüldü. HKP/VİP etkeni mikroorganizmaların antibiyotiklere direnç oranları ülkemizde genel olarak yüksektir (7, 17, 18). Antibiyotiklere en fazla direnç gösteren etken Acinetobacter spp. olup, sefalosporinlere, değişen düzeyde karbapenemlere, aminoglikozidlere ve kinolonlara direnç göstermektedir (19). Çalışmamızda *A. baumannii* suşlarının en duyarlı olduğu antibiyotikler sırasıyla; kolistin, tigesiklin, netilmisin, amikasin ve gentamisin idi. Hastanemiz *A.baumannii* izolatlarında imipenem direnci %99.1 olup; yüksek tespit edildi. Yılmaz ve ark.'larının yapmış olduğu çalışmada da bizim hastalarımıza benzer şekilde *A.baumannii* suşlarında imipenem direnci %91.6 olarak belirlenmiştir (20). Bu çalışmada *A.baumannii* izolatlarında karbapenem direncinin yüksek olmasının nedeni çok ilaca dirençli bir mikroorganizma olması nedeniyle karbapenemlerin yoğun kullanımına bağlı olabilir. *P.aeruginosa*'nın antibiyotik duyarlılığı incelendiğinde en duyarlı olan antibiyotikler sırasıyla; kolistin, amikasin, gentamisin, meropenem ve imipenemdi. Yılmaz ve ark.'ları ile Bilici ve ark.'larının yaptığı çalışmalarda da *P.aeruginosa* olgularının en duyarlı olduğu antibiyotikler içerisinde amikasin, meropenem ve imipenem olduğu belirlenmiştir (7,20). Sekiz ülkenin YBÜ'lerinde izole edilen etkenlerin değerlendirildiği bir çalışmada *P.aeruginosa*

izolatlarında florokinolon direncinin %0-67 arasında olduğu saptanmıştır (21). Benzer şekilde çalışmamızda *P.aeruginosa* suşlarında siprofloksasin direnci %54, seftazidim direnci %39, imipenem direnci ise %25.5 olarak belirlendi. Çeşitli çalışmalarda *K. pneumoniae ve E. coli* suşlarında GSBL kodlayan genin kolayca aktarıldığı görülmüştür (22). Altoparlak ve ark.'larının yaptığı çalışmada Klebsiella spp. suşlarında GSBL pozitifliği %14 ve %33.3 olarak bildirilmiştir (23). Çalışmamızda Klebsiella spp. suşlarında GSBL pozitifliği %43.5 olarak belirlendi ve GSBL pozitif K.pneumoniae izolatlarına en etkili antibiyotikler; kolistin, amikasin, imipenem, meropenem ve piperasilin-tazobaktam idi. GSBL pozitif K.pneumoniae suşlarında siprofloksasin direnci %94.1, gentamisin direnci %88.2, piperasilin-tazobaktam direnci %76.5, meropenem direnci %41.2, imipenem direnci %35.3 ve amikasin direnci %23.5 olarak belirlendi. K.pneumonia izolatlarında GSBL üretim oranının yüksek olması hastaların çoğunluğunun YBÜ'de yatması, mekanik ventilasyon, endotrakeal entübasyon gibi invaziv girişimler uygulanması ve altta yatan kronik hastalıkların varlığı ile açıklanabilir. Bu sebeple hastalara doğru endikasyonda ve uygun antibiyotik kullanılmasına dikkat edilmeli, gereksiz antibiyotik kullanımından kaçınılmalıdır.

S.aureus HKP etyolojisinde yer alan önemli mikroorganizmalardan birisidir (23). Çalışmamızda HKP ve VİP olgularında MRSA beşinci sıklıkta izole edilmiştir. Ülkemizde *S.aureus* izolatlarında %89 metisilin direnci olduğu bildirilmektedir (17,24). Bilici ve ark.'larının VİP gelişen hastalar ile ilgili yaptığı bir çalışmada *S.aureus* izolatlarının %84.6'sının MRSA olduğu görülmüştür (7). Bu çalışmada da *S.aureus* izolatlarında %80 oranında metisilin direnci olduğu belirlendi. HKİ içerisinde en sık mortalite nedeni pnömonilerdir (6, 25). HKP olgularında mortalite hızının %5-87 arasında değişmekte olduğu bildirilmiştir (6,26). Çalışmamızda ise HKP'ye ait kaba mortalite oranı %60.4 idi. VİP ile ilişkili mortalite oranı son kılavuzlarda %20-50 olarak belirtilmiş olup (6, 25, 27 - 29); VİP olgularımızda mortalite oranı %48.1 tespit edildi. VİP hastalarımızda mortalite oranı daha yüksekti. Benzer şekilde İbrahim ve arkadaşlarının YBÜ'de yatan hastalarda yaptığı bir çalışmada VİP gelişen hastalardaki mortalite oranı VİP gelişmeyen hastalara göre daha

yüksek bulunmuştur (30). Erkek cinsiyetin VİP gelişimini artırdığına dair birçok çalışma gösterilmiştir (6). Bu çalışmada erkek hastalarda mortalite oranının daha yüksek tespit edildi ve bu durumun erkek hastalarımızda VİP/HKP gelişme oranının daha yüksek bulunmasıyla ilişkili olabileceği düşünüldü. Eşlik eden kronik hastalıkların mortalite üzerine anlamlı bir etkisi saptanmadı. Ülkemizde Sevinç ve ark.'larının yapmış olduğu bir çalışmada da altta yatan hastalık ile mortalite oranı arasında bir ilişki olmadığı görülmüştür (6). Yaş ile mortalite arasında istatistiksel açıdan anlamlı bir ilişki saptanmadı. HKİ gelişen hastalarda yaş ile mortalite arasındaki ilişkiyi araştıran çalışmalarda farklı sonuçlar olduğu bildirilmiştir (31 - 33). Aube ile ark.'ları ve Miller ile ark.'larının HKİ gelişen hastalarda yaptığı çalışmalarda yaş ile mortalite arasında doğru bir ilişki olduğu görülmüştür (32, 33). Sevinç ve ark.'larının HKP olgularında prognostik faktörleri değerlendirdiği bir çalışmada ise yaşın sağkalım üzerine bir etkisi bulunmadığı belirlenmiştir (6). Çalışmamızda YBÜ'lerde yatan hastaların mortalite oranı %50'nin üzerinde olup, anlamlı düzeyde yüksek tespit edildi. YBÜ'lerde yatan hastalarda infeksiyonlara yatkınlık ve mortalite riski artmaktadır (12). Arısoy ve ark.'ları ile Sevinç ve ark.'larının yapmış olduğu çalışmalarda da YBÜ'de yatan pnömoni olgularında mortalite oranı %58 ve %51 olarak belirlenmiştir (6, 34). HKP/VİP hastalarında özellikle MDR mikroorganizma ile infeksiyon söz konusu olduğunda mortalite oranı artmaktadır. Fagon ve ark.'larının VİP gelişen hastalarda yaptığı bir çalışmada *A.baumannii* ve *P.aeruginosa* olgularında mortalite oranının arttığı görülmüştür (16). Ülkemizde Alp ve ark.'larının yapmış olduğu HKP hastalarında mortalitenin değerlendirildiği bir çalışmada en yüksek mortalite oranı Acinetobacter spp.'de saptanmıştır (10). Çalışmamızda da HKP/VİP gelişen hastalarda mortalitesi en yüksek olan etken *A.baumannii* idi. Bu durum bu mikroorganizmanın birçok antibiyotiğe karşı direnç geliştirmesi, tedavide kullanılan antibiyotik seçeneklerinin kısıtlı olması ve dolayısıyla infeksiyonun kontrol edilememesi gibi sebeplerle açıklanabilir.

Kurumumuzda HKP'lerin çoğunun VİP olarak gözlenmesi, VİP gelişimini engellemek için alınması gereken önlemlerin artırılması gerektiğini düşündürmektedir. Etken mikroorganizmaların

çoğunun Gram negatif enterik ve nonfermentatif mikroorganizmalar olduğu tespit edilmiş olup; antibiyotik duyarlılıkları incelendiğinde; Gram negatif enterik bakteriler için karbapenemler iyi bir seçenek iken, nonfermentatif bakteriler için yeterli düzeyde etkin olmadığı görülmüştür. Her kurumun kendi sürveyans verilerini oluşturması uygun antibiyotik seçimi için oldukça önemlidir.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

COVID-19 PANDEMİ SÜRECİNİN GIDA TÜKETİM DAVRANIŞI VE HİJYEN ALIŞKANLIĞI ÜZERİNDEKİ ETKİSİ

THE EFFECT OF THE COVID-19 PANDEMIC PROCESS ON FOOD CONSUMPTION BEHAVIOR AND HYGIENE HABITS

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ÖZET

AMAÇ: Bu araştırma ile koronavirüs (COVID-19) küresel salgınının yaşandığı bu dönemde, bireylerin pandemi ile ilgili bilgi düzeylerinin, gıda hijyeni ve gıda alışverişlerindeki tutumlarının değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışma Türkiye'nin farklı illerinde ikamet eden ve yaşları 18 ile 65 arasında değişen gönüllü bireyleri içermektedir. Araştırmaya katılan bireylerin demografik özelliklerini, mutfak kullanımı ve gıda alışverişi esnasında hijyen ile ilgili konularda bilgi ve tutumlarını belirlemeyi amaçlayan 17 sorudan ve 505 katılımcıdan oluşan çevrimiçi bir anket çalışmasıdır.

BULGULAR: Çalışmaya katılan bireylerin %53,9'unun yaşları 18 ile 65 arasında olan erkeklerden oluşmaktadır. COVID-19'un bir viral enfeksiyon olduğunu bilen bireylerin oranı %68 iken bu etkene karşı önlem almayanların oranı ise %3.8 olarak belirlenmiştir. Ankete katılanların %54.4'ü COVID-19 PCR testini yaptırdığını bildirirken bunların %19,4'ü pozitif olduğunu belirtmiştir. Etkenin gıdalar aracılığıyla bulaşmadığını fakat gıda ambalajları ile bulaşabileceğini düşünenlerin oranı ise %39.8 olarak belirlenmiştir. Ayrıca, bireylerin yaşları büyüdükçe, öğrenim ve ekonomik gelir durumu arttıkça, COVID-19'un gıdalar ile bulaşmayacağını düşünenlerin sayısı anlamlı derecede artmıştır. Bununla birlikte kendisini büyük risk altında olduğunu düşünenlerin oranı %40 olarak tespit edilirken COVID-19'dan korunmak için alınan tedbirler arasında en fazla (%46,7) maske, eldiven, dezenfektan ve sosyal mesafenin birlikte kullanılması görülmüştür. Yapılan market alışverişleri sonrasında ürünleri hiç bekletmeden kullanan bireyler, kendilerini risk altında görmemektedirler. Çalışmaya katılanların %51.7'si el yıkama alışkanlıklarındaki değişiklikleri ve su tüketim miktarlarındaki artışları bildirmişlerdir. Ayrıca çalışmaya katılan bireylerin bağışıklıklarını güçlendirmek için en yüksek oranla (%38.7) organik beslenmeyi tercih ettikleri görülmüştür.

SONUÇ: Pandemi sürecinde, gıda hijyenine verilen önemin anlamlı derecede arttığı görülürken, eş zamanlı olarak su tüketimi ve el yıkama alışkanlıklarının da değiştiği görülmüştür. Bunun yanı sıra bireylerin COVID-19'un bulaşma yolları ile ilgili bireylerin bilgi seviyelerinin, bireylerin eğitim düzeyleri, gelir seviyeleri ve yaşa göre farklılık gösterdiği belirlenmiştir. Ayrıca bireylerin, organik beslenmeye yönelmesi ve vitamin takviyeleri alması, beslenme alışkanlıklarının da etkilendiğini göstermiştir.

ANAHTAR KELİMELER: COVID-19, Gıda, Hijyen.

ABSTRACT

OBJECTIVE: In this study, it was aimed to evaluate the knowledge level of individuals about the pandemic, and their attitudes towards food hygiene and food shopping during this period when the coronavirus (COVID-19) global epidemic was experienced.

MATERIAL AND METHODS: It consists of volunteer individuals residing in different provinces of Turkey and aged between 18 and 65. It is an online questionnaire study consisting of 17 questions and 505 participants, aiming to determine the demographic characteristics of the individuals participating in the study, their knowledge and attitudes about hygiene during kitchen use and food shopping.

RESULTS: 53.9% of the individuals participating in the study consisted of men between the ages of 18 and 65. While the rate of individuals who know that COVID-19 is a viral infection is 68%, the rate of those who do not take precautions against this factor is 3.8%. While 54.4% of the respondents reported that they had the COVID-19 PCR test, 19.4% of them stated that they were positive. The rate of those who think that the agent is not transmitted through food, but can be transmitted through food packaging, was determined as 39.8%. In addition, the number of people who think that COVID-19 will not be transmitted by food has increased significantly as the age of the individuals, education, and economic income increase. However, the rate of those who think that they are at great risk was determined as 40%, and among the measures taken to protect themselves from COVID-19, the most (46.7%) were the use of masks, gloves, disinfectants, and social distance together. Individuals who use products without waiting after grocery shopping do not see themselves at risk. 51.7% of the participants in the study reported changes in hand-washing habits and increases in water consumption. Moreover, it was observed that the individuals participating in the study preferred organic nutrition with the highest rate (38.7%) to strengthen their immunity.

CONCLUSIONS: While the importance given to food hygiene has increased significantly during the pandemic process, it has been observed that water consumption and hand-washing habits have changed simultaneously. In addition, it has been determined that the level of knowledge of individuals about the transmission routes of COVID-19 differs according to the education level, income level, and age of the individuals. Also, the fact that individuals turn to organic nutrition and take vitamin supplements has shown that their nutritional habits are also affected.

KEYWORDS: COVID-19, Food, Hygiene.

GİRİŞ

Koronavirüs 2019 hastalığı (COVID-19), önemli bir halk ve çevre sağlığı sorunudur. Dünya Sağlık Örgütü (WHO) salgını küresel bir pandemi ilan ederken; Çin, yeni koronavirüs enfeksiyonunu birinci sınıf bulaşıcı hastalık (en tehlikeli enfeksiyon sınıfı olarak kabul edilir) olarak ilan etmiştir (1, 2). Koronavirüsler insanlarda soğuk algınlığına benzer hafif hastalıklara neden olurken, diğer türleri (MERS - Orta Doğu Solunum Sendromu ve SARS) daha ciddi hastalıklara neden olmaktadır (3). COVID-19 nedeniyle gerçekleşen ölüm, kritik hastalar için %61.5 kadar yüksek bir orana sahiptir ve COVID-19'un önlenmesi için en önemli strateji, bulaşma yollarının bloke edilmesidir (4, 5). Nesneler ve yüzeyler üzerindeki kontaminasyon süresiyle ilgili olarak yapılan bir çalışmada; SARS-CoV-2'nin plastik üzerinde 2-3 güne kadar, paslanmaz çelikte 2-3 güne kadar, kartonda 1 güne kadar, bakır üzerinde 4 saate kadar bulunabileceği gösterilmiştir (6). Ayrıca, yoğun bakım ünitelerinde genel koğuşlara göre kontaminasyonun daha yüksek olduğu ve SARS-Cov-2'nin zeminlerde, bilgisayar farelerinde, çöp kutularında ve hasta yatağı tırabzanlarında ve hastalardan 4 metreye kadar havada bulunabileceği bildirilmiştir (7). Temas ile bulaşma; semptomatik veya asemptomatik kişilerin ortama yaydıkları solunum salgılarına, diğer bireylerin elleri ile temas etmesi ve salgılarla kirlenen ellerin ağız, burun veya göz mukozasıyla temas etmesiyle meydana gelmektedir (6). Beslenme, büyüme ve gelişmenin yanında, özellikle hastalıklardan korunmada, ruhsal, fiziksel ve zihinsel fonksiyonların korunmasında ve immün sistemin düzenlenmesinde önemli rol oynamaktadır (8). Enfeksiyon hastalıklarında olduğu gibi bireylerin beslenme durumu iyi olduğunda COVID-19 enfeksiyonundan ve/veya hastalığın komplikasyonlarından korunma olasılığı da artmaktadır (9). Gıda güvenliği ile bağlantılı olan sağlık-beslenme ilişkisi COVID-19 salgını sürecinde de önemini devam ettirmektedir (9). Bu araştırma ile, koronavirüs (COVID-19) küresel salgınının yaşandığı bu dönemde, koronavirüs salgınının bireylerin gıda tüketim davranışları ve hijyen alışkanlıkları üzerindeki etkisinin değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM

Bu çalışma, Türkiye'nin farklı illerinde ikamet eden, 18-65 yaş arasında ve çalışmaya katılmayı kabul eden 505 katılımcı ile çevrimiçi gerçekleştirilmiştir. Çalışma, COVID-19 salgınının, bireylerin gıda güvenliği ve gıda hijyeni ile ilgili bilgi ve tutumlarındaki farklılıkların belirlenmesi; cinsiyet, eğitim düzeyi, yaş gibi demografik özelliklerin karşılaştırılması prensibine göre planlanmış olup, Nisan – Haziran 2021 tarihleri arasında yürütülmüştür. Araştırmada veri toplama aracı olarak 17 sorudan oluşan, online anket yönteminden yararlanılmıştır.

Etik Kurul

Bu çalışma; Afyonkarahisar Sağlık Bilimleri Üniversitesi, Klinik Araştırmalar Etik Kurulu'nun 30.04.2021 tarihli, 2011-KAEK-2 kodlu kararıyla etik kurul onayı alınarak yapılmıştır (2021/6).

İstatistiksel Analiz

Ankete katılan gönüllülerin doldurduğu anket değerlendirmeleri excel formatında kaydedilmiştir. Excel formatında kaydedilen bilgiler daha sonra SPSS 22.0 programına aktarılarak analiz edilmiştir. Elde edilen veriler değerlendirilirken tanımlayıcı istatistiksel metotların (frekans, ortalama, standart sapma) yanı sıra Pearson ki-kare (x^2) testleriyle değerlendirilerek $P<0.05$ düzeyi istatistiki açıdan anlamlı kabul edilmiştir.

BULGULAR

Çalışmaya katılan bireylerin %53,9'u (272/505) erkeklerden, %46,1'i (233/505) kadınlardan oluşurken, yaşları 18 ile 65 arasındadır **(Tablo 1)**.

Tablo 1: COVID-19 ve gıda hijyeni ile ilgili soruya verilen cevapların demografik özelliklere göre dağılımı

Yaş grupları ile COVID-19 ve gıda hijyeni ile ilgili sorulara verilen cevapların dağılımı				
Yaş	COVID – 19 gıdalarla bulaşan bir hastalık mıdır?			
	Evet	Hayır	Fikrim Yok	Toplam
18-24	%5,0 (25)	%12,5 (62)	%4,6 (23)	%21,8 (110)
25-34	%6,3 (32)	%8,9 (45)	%3,4 (17)	%18,6 (94)
35-44	%4,0 (20)	%16,0 (81)	%2,6 (13)	%22,6 (114)
45-54	%4,4 (22)	%23,0 (116)	%4,0 (20)	%31,3 (158)
55-65	%1,0 (5)	%3,4 (17)	%1,4 (7)	%5,7 (29)
Toplam	%20,6 (104)	%63,6 (321)	%15,8 (80)	%100(n=505)
χ2=26,424, P<0,05 (0,001)				
Cinsiyet ile COVID-19 ve gıda hijyeni ile ilgili sorulara verilen cevapların dağılımı				
Cinsiyet	COVID – 19 gıdalarla bulaşan bir hastalık mıdır?			
	Evet	Hayır	Fikrim Yok	Toplam
Kadın	%10,1 (51)	%28,1 (142)	%7,9 (40)	%46,1 (233)
Erkek	%10,5 (53)	%35,4 (179)	%7,9 (40)	%53,9 (272)
Toplam	%20,6 (104)	%63,6 (321)	%15,8 (80)	%100(n=505)
χ2=1,299, P>0,05 (0,522)				
Öğrenim durumu ile COVID-19 ve gıda hijyeni ile ilgili sorulara verilen cevapların dağılımı				
Öğrenim durumu	COVID – 19 gıdalarla bulaşan bir hastalık mıdır?			
	Evet	Hayır	Fikrim Yok	Toplam
İlk ve ortaöğretim	%1,8 (9)	%5,0 (25)	%3,2 (16)	%9,9 (50)
Önlisans	%8,3 (42)	%12,9 (65)	%4,4 (22)	%25,5 (129)
Lisans	%2,8 (14)	%15 (76)	%1,4 (7)	%19,2 (97)
Lisansüstü	%7,7 (39)	%30,7(155)	%6,9 (35)	%45,3 (229)
Toplam	%20,6 (104)	%63,6 (321)	%15,8 (80)	%100 (n=505)
χ2=34,209, P<0,05 (0,000)				
Ekonomik Gelir ile COVID-19 ve gıda hijyeni ile ilgili sorulara verilen cevapların dağılımı				
Gelir durumu	COVID – 19 gıdalarla bulaşan bir hastalık mıdır?			
	Evet	Hayır	Fikrim Yok	Toplam
Gelirim yok	%1,2 (6)	%2,0 (10)	%0,2 (1)	%3,4 (17)
0 – 750 TL	%0,6 (3)	%1,0 (5)	%0,0 (0)	%1,6 (8)
751 – 1500 TL	%0,4 (2)	%1,6 (8)	%1,2 (6)	%3,2 (16)
1501 – 2500 TL	%5,5 (28)	%15,0 (76)	%5,1 (26)	%25,7 (130)
2501 – 5000 TL	%9,7 (49)	%37,0 (187)	%5,9 (30)	%52,7 (266)
5000 TL ve üstü	%3,2 (16)	%6,9 (35)	%3,4 (17)	%13,5 (68)
Toplam	%20,6 (104)	%63,6 (321)	%15,8 (80)	%100(n=505)
χ2=24,460, P<0,05 (0,006)				

Bu bireylerin %68'i COVID-19'un viral bir enfeksiyon olduğunu bilirken %32'sinin bilmediği görülmektedir. Pandemi süresince COVID-19

virüsüne yakalanmamak için %3.8'i hiç önlem almazken yaklaşık %50'si sürekli önlem almaktadır. COVID-19'un varlığını belirlemeye yönelik PCR testini yaptıranların oranı %54.4 olup %19,4'nün COVID-19 pozitif olduğu tespit edilmiştir. Çalışmaya katılan bireylerin aile yakınlarında COVID-19'un görülme oranı %30.3 olarak saptanmıştır **(Tablo 2)**.

Tablo 2: Genel COVID-19 bilgisi sorularına verilen cevapların dağılımı (n=505)

	n	%
COVID – 19'un neden olduğu enfeksiyon türü hangisidir?		
Bakteriyel Enfeksiyon	68	13,4
Viral Enfeksiyon	343	68,0
Parazitel Enfeksiyon	13	2,6
Fikrim Yok	81	16,0
COVID -19 testi sonucunuz nasıl çıktı?		
Negatif	177	35,0
Pozitif	98	19,4
Test yaptırmadım	230	45,6
Birinci derece yakınlarınızda COVID-19 hastası var mı?		
Evet	153	30,3
Hayır	352	69,7
COVID-19 virüsüne yakalanmamak için önlem alıyor musunuz?		
Her zaman	252	49,9
Ara sıra	66	13,0
Sıklıkla	168	33,3
Hiç almıyorum	19	3,8

Çalışmaya katılan bireylerin yaşları büyüdükçe ve öğrenim durumu arttıkça COVID-19'un gıda ile bulaşmayacağını düşünenlerin sayısı (%63.6) anlamlı derecede artmaktadır. Ayrıca anket çalışmasına katılan bireylerin ekonomik geliri arttıkça COVID-19'un gıdalar ile bulaşmadığını düşünenlerin sayısı da anlamlı derecede artmaktadır. Bunun yanı sıra COVID-19'un gıdalar ile bulaştığını düşünen kadın ve erkek bireyler arasında anlamlı bir fark yoktur (Tablo 1). COVID-19'un gıdalar aracılığıyla bulaşmadığı fakat gıda ambalajları ile bulaşabileceğini düşünenlerin oranı %39.8 olarak belirlenmiştir. Gıdalar ve gıda ambalajları aracılığıyla COVID-19'un bulaşmayacağını düşünenler ise %21.4 oranındadır **(Tablo 3)**.

Tablo 3: COVID-19'un gıda veya gıda ambalajı ile bulaşmasına dair sorulara verilen cevapların dağılımı

COVID–19 gıda ile temas ambalajlarına bulaşır mı?	COVID – 19 gıdalarla bulaşan bir hastalık mıdır?			
	Evet	Hayır	Fikrim Yok	Toplam
Evet	%19,6 (99)	%39,8 (201)	%9,5 (48)	%68,9 (348)
Hayır	%0,8 (4)	%21,4 (108)	%1,0 (5)	%23,2 (117)
Fikrim yok	%0,2 (1)	%2,4 (12)	%5,3 (27)	%7,9 (40)
Toplam	%20,6 (104)	%63,6 (321)	%15,8 (80)	%100 (n=505)
X2=135,871, P<0,05 (0,000)				

COVID-19 pandemisinde kendisini büyük risk altında olduğunu düşünenlerin oranı %40 iken risk altında olmadığını düşünenler ise %14,3 oranında tespit edilmiştir. Risk altında olduğunu düşünen fakat herhangi bir önlem almayanların oranı %2,5 (13/505) iken en az bir önlem alanların sayısı %95,2 (481/505) olarak belirlenmiştir.

COVID-19'a yakalanmamak için kullanılan tedbirler arasında en fazla (%46,7) maske, eldiven, dezenfektan ve sosyal mesafenin birlikte kullanılması görülmüştür **(Tablo 4)**.

Tablo 4: COVID-19 bakımından risk altında olma durumu ile gıda alış-verişi sırasında önlem alma durumuna dair sorulara verilen cevapların dağılımı

COVID-19'a yakalanmamak için gıda alış-verişiniz sırasında hangi önlemleri alıyorsunuz?	COVID-19 bakımından risk altında olduğunu düşünüyor musunuz?			
	Risk altında değilim	Düşük risk altındayım	Büyük risk altındayım	Toplam
Yalnızca maske	%1,2 (6)	%5,7 (29)	%6,5 (33)	%13,5 (68)
Maske ve eldiven	%1,2 (6)	%1,8 (9)	%3,0 (15)	%5,9 (30)
Dezenfektan ve sosyal mesafe	%0,8 (4)	%0,4 (2)	%0,4 (2)	%1,6 (8)
Maske, dezenfektan ve sosyal mesafe	%4,4 (22)	%11,1 (56)	%12,1 (61)	%27,5 (139)
Maske, eldiven, dezenfektan ve sosyal mesafe	%4,6 (23)	%20,6 (104)	%21,6 (109)	%46,7 (236)
Hiçbir önlem almıyorum	%2,2 (11)	%2,0 (10)	%0,6 (3)	%4,8 (24)
Toplam	%14,3 (72)	%41,6 (210)	%44,2 (223)	%100 (505)
X2=38,446, P<0,05 (0,000)				

Kendini büyük risk altında gören bireylerin çoğunluğu (%26,9) ve düşük risk altında olduğunu düşünen bireylerin hemen hemen tamamı (%11,8) mutfak araç-gereçlerini deterjan ve alkol bazlı sıvılar ile dezenfekte etmektedir **(Tablo 5)**.

Tablo 5: COVID-19 bakımından risk altında olma durumu ile mutfakta hijyen önlemi sorularına verilen cevapların dağılımı

COVID-19 bakımından risk altında olduğunu düşünenler ile mutfakta hijyen önlemi alanların verdiği cevapların dağılımı				
COVID – 19'dan korunmak amacıyla hijyen önlemi için neler yapıyorsunuz? Meyve ve sebzeleri;	COVID-19 bakımından risk altında olduğunu düşünüyor musunuz?			
	Risk altında değilim	Düşük risk altındayım	Büyük risk altındayım	Toplam
Bol su ile yıkamak	%10,8 (55)	%29,9 (151)	%26,9 (136)	%67,7 (342)
Sirkeli suda bekletmek	%2,7 (14)	%13,6 (69)	%11,8 (60)	%28,3 (143)
Deterjan ile yıkamak	%0,6 (3)	%1,3 (7)	%1,9 (10)	%3,9 (20)
Toplam	%14,2 (72)	%44,9 (227)	%40,8 (206)	%100 (n=505)
X2=9,996, P<0,05 (0,040)				
Market alış-verişleriniz sonrasında ürünleri kullanmadan önce belirli bir süre bekletiyor musunuz?	COVID-19 bakımından risk altında olduğunu düşünüyor musunuz?			
	Risk altında değilim	Düşük risk altındayım	Büyük risk altındayım	Toplam
1 saat	%2,4 (12)	%8,9 (45)	%6,1 (31)	%17,4 (88)
3 saat	%4,0 (20)	%7,9 (40)	%7,3 (37)	%19,2 (97)
5 saat	%1,0 (5)	%2,8 (14)	%5,0 (25)	%8,7 (44)
En az bir gün	%6,3 (32)	%15,8 (80)	%18,6 (94)	%40,8 (206)
Hiç bekletmiyorum	%0,6 (3)	%6,1 (31)	%7,1 (36)	%13,9 (70)
Toplam	%14,3 (72)	%41,6 (210)	%44,2 (223)	%100 (n=505)
X2=16,513 P<0,05 (0,036)				

Pandemiden korunmak için market alışverişlerinden sonra ürünleri kullanmadan önce belli bir süre bekletenler anlamlı derecede fazladır. Düşük ve büyük risk altında olduğunu düşünen bireyler en yüksek oranda (%15,8 ve %18.6) en az bir gün beklettiklerini bildirmişlerdir. Market alışverişleri sonrasında ürünleri hiç bekletmeden kullanan bireyler risk altında olmadıklarını düşünmektedirler (Tablo 5). Su tüketim alışkanlığını değiştiren bireylerin oranı anlamlı derecede yüksek belirlenmiştir. Su tüketim alışkanlığını değiştiren bireylerin arasında el yıkama alışkanlığını değiştirenler %51,7 (261/312) oranında belirlenirken el yıkama alışkanlığını değiştirmeyenler ise %10,1 (51/312) oranında tespit edilmiştir **(Tablo 6)**. Çalışmaya katılan bireylerin bağışıklıklarını güçlendirmek için en yüksek oranla organik beslenmeyi tercih ederken en düşük oranla probiyotik-prebiyotik gıdalar tüketmeyi tercih ettikleri görülmüştür **(Tablo 7)**.

Tablo 6: COVID-19 pandemi sürecinde el yıkama alışkanlığındaki ve su tüketim davranışındaki değişikliğe dair sorulara verilen cevapların dağılımı

COVID-19 pandemi sürecinde el yıkama alışkanlığında ve su tüketim davranışındaki değişikliğe dair sorulara verilen cevapların dağılımı			
El yıkama alışkanlığınızda değişiklik oldu mu?	Pandemi sürecinde su tüketim miktarınızda artış oldu mu?		
	Evet	Hayır	Toplam
Evet	%51,7 (261)	%20,2 (102)	%71,9 (363)
Hayır	%10,1 (51)	%18,0 (91)	%28,1 (142)
Toplam	%61,8 (312)	%38,2 (193)	%100(n=505)
	X2=55,979, P<0,05 (0,000)		

Tablo 7: COVID – 19'a karşı bağışıklığınızı güçlendirmek için neler yapıyorsunuz ? sorusuna verilen cevapların dağılımı

	n	%
Doğal-organik beslenmek	195	38,7
Vitamin takviyesi almak	161	31,8
Probiyotik-prebiyotik gıdalar tüketmek	37	7,3
Hiçbir şey yapmıyorum	112	22,2

TARTIŞMA

Bu çalışmada, pandemi sürecinde gıda tüketim davranışı ve hijyen alışkanlığındaki değişiklikler analiz edilmiştir. COVID-19 hastalığı, SARS-CoV-2 (Şiddetli Akut Solunum Sendromu–Coronavirüs-2) adı verilen yeni bir koronavirüsün neden olduğu bir hastalıktır (10). Anket sonuçları katılımcıların %68'inin COVID-19'un neden olduğu enfeksiyon türünün viral bir enfeksiyon olduğunu bildiklerini göstermektedir. Virüsün olası bulaşma nedeni olarak; konuşma, hapşırma ve öksürme veya enfekte kişilerle doğrudan temas yoluyla dağılan solunum damlacıkları olduğu düşünülmektedir (11, 12). Bu nedenle sosyal mesafe, el yıkama, dezenfektan, maske kullanımı ve gıda hijyenini sağlamak gibi önlemler neredeyse zorunlu hale gelmiştir (12-14). Bu çalışmanın anket sonuçlarına göre bireylerin ancak sadece yarısının COVID-19'a yakalanmamak için her zaman önlem aldığı, yaklaşık %3,8'lik bir kısmının ise hiç önlem almadığı belirlenmiştir. Dünya Sağlık Örgütü ve Sağlık Bakanlığı gibi kuruluşlar tarafından, pandemi sürecinde virüsün yayılmasını önlemenin en kolay, en ekonomik ve en etkili yolu olduğu için sık sık el yıkama şiddetle tavsiye edilmektedir (13, 15). Çalışmamızda; bireylerin %71,9'unda el yıkama alışkanlığında değişiklik olduğu, %61,8'inde ise su tüketim davranışında değişiklik olduğu görülmüştür. Pandemi sürecinde bireylerin yeterli el hijyenine sahip olduğu ve bununla birlikte su kullanımının da arttığı görülmektedir. Bu konuda halkın yeterli bilgiye sahip olduğu düşünülmektedir. Ancak, Uğurlu ve ark.'larının (2020) yaptığı çalışmada ise katılımcıların tavsiye edilen günlük 11 kez ellerini yıkayıp yıka-

madığı sorgulanmış ve bulunan değer (%57,7) salgın süreci için yetersiz görülmüş ve bireylerin halk sağlığı eğitim programına ihtiyacı olduğu düşünülmüştür (15). Choi ve ark.'larının (2021) Kore'de yaptığı çalışmada günde ortalama el yıkama sıklığı, COVID-19 salgınından sonra 6,96 kattan 9,98 kata yükseldiği ve el yıkama sıklığında ise tüm yaş gruplarında ve bazı meslek gruplarında anlamlı bir artış olduğu bildirilmiştir (13). Gıda veya gıda ambalajı kontaminasyonu; üretim sürecinde su kirliliği veya el hijyeni uygulamalarına uymayan enfekte bireylerden öksürme veya hapşırma yoluyla yayılan damlacıklar aracılığıyla ortaya çıkabilmektedir (12, 16). Bununla birlikte, COVID-19'un gıda ürünleri yoluyla yayıldığına dair bugüne kadar yayınlanmış bilimsel bir veri yoktur (11, 16, 17).

Tüketicilerin ele alması gereken en önemli konu gıda ambalajlarına COVID-19'a neden olan virüslerin bulaşma olasılığıdır (16, 17). Bazı virüsler ile yapılan çalışmalar, gıda ürünlerinin yüzeylerinde virüslerin hayatta kaldıklarını ortaya koymuştur. Bu olasılık COVID-19'a neden olan virüs için de düşünülmelidir. Bu dönemde özellikle konserve veya paketlenmiş gıdalar tercih edilirken, meyveler ise yıkanmalı ve sirkeli suda saklanmalıdır (16). Dimassi ve ark.'larının (2021) Lübnan'da 1337 katılımcı ile yaptıkları çalışmada "Coronavirüs'ün kontamine gıdaların tüketilmesi yoluyla insanlara bulaşır" ifadesine katılımcıların %35.2'si "yanlıştır" demiştir (18). Görür ve ark.'larının (2021) 719 katılımcı ile yaptıkları anket çalışmasında ise akademisyen katılımcıların %34,6'sı, öğrenci katılımcıların ise %16,5'i virüsün gıdalarla bulaşamayacağını belirtmiştir. Akademisyen katılımcıların %78,3'lük kısmı, öğrenci katılımcıların ise %81,8'lik kısmı virüsün gıda paketleri ile bulaşabileceğini belirtmiştir (19). Anketimizde katılımcıların %68,9'luk kısmı COVID-19'un gıda ambalajlarına temas ile bulaşabileceğini düşünmektedir. Katılımcıların %63,6'lık bir kısmı ise COVID-19'un gıdalar ile bulaşmayabileceğini düşünmektedir. Çalışmamızda COVID-19'un gıdalarla bulaşabileceğini düşünmeyenlerin oranı eğitim ve ekonomik gelir durumuna paralel olarak artış göstermiştir. COVID-19'un gıdalarla bulaşmadığını belirten katılımcıların %39,8'lik kısmı ise virüsün gıda ambalajlarına temas ile bulaşabildiğini belirtmiştir. Daha önce yapılmış çalışmalar CO-

VID-19'un birçok yüzeyde uzun süre canlı kalabildiğini göstermiştir (12, 20). Virüsün satın alınan gıdalardan bulaşma riskini azaltmak için en etkili yollardan biri gıdaların üç gün boyunca bekletilmesi olabilir. Ayrıca sebze ve meyvelerin suda iyice yıkanması, gerekirse çok az miktarda sabun kullandıktan sonra iyice durulanarak tüketilmesi önerilmektedir. Pişirilmeden tüketilen taze sebze ve meyve gibi ürünler su altında iyice yıkanmalıdır (21). Katılımcıların market alış–verişi sonrasında ürünleri kullanmadan önce belirli bir süre bekletip bekletmediği sorusuna verilen yanıtlara bakıldığı zaman, yaklaşık %86'sının 1 saat ile en az bir gün arasında ürünlerini bekletip öyle kullandıkları görülmüştür. Katılımcılara, COVID–19'dan korunmak amacıyla meyve ve sebzeleri nasıl temizlediği sorulduğunda ise; %67,7'sinin bol su ile yıkadığı, %28,3'ünün ise sirkeli suda beklettiği, geri kalanın ise deterjan bazlı temizleyiciler ile yıkadığı görülmüştür. Bu konu ile ilgili olarak Finger ve ark.'larının (2021) 3000 katılımcı ile Brezilya'da yaptığı bir ankette katılımcıların %50'sinin meyve ve sebzeleri klorlu suda beklettikten sonra akan suda duruladığı, %27,4'ünün deterjan kullandığı, %7'sinin ise mutfak sirkesi kullandığı tespit edilmiştir. Yine aynı çalışmada katılımcıların neredeyse tamamına yakınının maske, sosyal mesafe ve alkol bazlı dezenfektan kullanımına dikkat ettiği belirlenmiştir (10). Katılımcıların bu konudaki bilincini ölçmek amacıyla COVID–19'a yakalanmamak için gıda alışverişleriniz sırasında hangi önlemleri alıyorsunuz? sorusu yöneltilmiş ve katılımcıların %95,2'si gibi büyük bir çoğunluğunun önlem aldığı görülmüştür. Alınan önlemlerin büyük çoğunluğunu (%46,7) ise maske, eldiven, dezenfektan ve sosyal mesafe oluşturmaktadır (%46,7). COVID-19 salgını sırasında tüketicilerin hijyen alışkanlıklarının değişmesinin yanı sıra daha sağlıklı gıda ürünlerine olan ilgilerinin de arttığı görülmektedir. COVID-19 pandemisi sırasında sağlıklı beslenme viral enfeksiyonlara karşı bağışıklık sistemini korumak için oldukça önemlidir (22).

Anketimize katılan bireylerin %77,8'inin pandemi sürecinde beslenme davranışlarının değiştiği belirlenmiştir. Karaman ilinde pandemi sürecinin bireylerin beslenme alışkanlıkları üzerine etkisinin incelendiği çalışmada, katılımcıların %45,3'ünde beslenme alışkanlığının değiştiği görülmüştür (23). Kutlu ve ark.'larının (2021) yaptığı çalışmada ise katılımcıların büyük çoğunluğunun (%65,5) COVID-19 pandemi sürecinde bağışıklığın güçlendirmesi bakımından etkili olduğu düşünülen vitamin takviyelerini kullandıkları gözlenmiştir (24).

Sonuç olarak bireylerin pandemi sürecinde gıda hijyenine vermiş oldukları önemin arttığı, bununla paralel olarak su tüketimi ve el yıkama alışkanlıklarının değiştiği, ancak COVID-19'un bulaşma yolu ile ilgili olarak bireylerin bilgi derecesinin eğitim düzeyleri, gelir seviyeleri ve yaşa göre farklılık gösterdiği belirlenmiştir. Ayrıca bireylerin bu dönemde organik beslenmeye yönelmesi ve vitamin takviyesi şeklinde beslenme alışkanlıklarının da etkilendiği görülmüştür.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

FAZLA KİLOLU VE OBEZ ÖĞRENCİLERİN BESLENME ÖZ-YETERLİK, BESLENME TUTUM VE DAVRANIŞLARI ARASINDAKİ İLİŞKİNİN İNCELENMESİ

INVESTIGATION OF THE RELATIONSHIP BETWEEN NUTRITIONAL SELF-EFFICACY, ATTITUDE AND BEHAVIOURS OF STUDENTS WITH OVERWEIGHT AND OBESITY

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ÖZET

AMAÇ: Bu çalışmada fazla kilolu ve obez öğrencilerin beslenme özyeterlik, beslenme tutum ve beslenme davranışı arasındaki ilişkinin incelenmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Bu çalışma beden kitle indeksi persentil değeri 85'in üzerinde olan, 5. 6. ve 7. sınıfta eğitim gören 192 öğrenci ile gerçekleştirilmiştir. Veriler kişisel bilgi formu, çocuk beslenme öz-yeterliği, beslenme tutum ve beslenme davranış ölçeği ile elde edilmiştir.

BULGULAR: Öğrencilerin beslenme öz-yeterliği puan ortalaması 5.58±5.07, beslenme tutum puan ortalaması 12.72±2.52, beslenme davranış puan ortalaması ise 2.92±6.03 bulunmuştur. Cinsiyet ve beden kitle indeksi sınıflamasına göre ölçek puanları arasında anlamlı farklılık olmadığı, ailesinde fazla kilolu birey olmayan öğrencilerin daha olumlu beslenme tutumuna sahip olduğu tespit edilmiştir. Beslenme öz-yeterliği ile beslenme tutum ve beslenme davranışı arasında pozitif ilişki bulunmuştur.

SONUÇ: Fazla kilolu ve obez çocukların beslenme öz-yeterlikleri, beslenme tutumları ve beslenme davranış düzeyleri orta düzeyin üzerindedir. Fazla kilo ve obeziteye yatkınlığı arttıran fastfood yeme alışkanlığı, TV, bilgisayar gibi teknolojik aletlerle geçirilen süre gibi faktörler beslenme öz-yeterliği, beslenme tutumu ve beslenme davranış düzeylerinde etkilidir.

ANAHTAR KELİMELER: Çocukluk çağı obezitesi, Beslenme öz yeterliği, Beslenme tutumu, Beslenme davranışı, Öğrenci.

ABSTRACT

OBJECTIVE: The aim of this study was to investigate the relationship between nutritional self-efficacy, nutritional attitude and behaviour of students with overweight and obesity.

MATERIAL AND METHODS: This study was carried out with 192 students in 5th, 6th and 7th grades whose body mass index percentile value was over 85. The data were obtained with personal information form, dietary self-efficacy scale, nutrition attitude scale and dietary behaviour scale in this study.

RESULTS: The nutritional self-efficacy mean score of the students was 5.58 ± 5.07, the nutritional attitude was 12.72 ± 2.52, and the nutritional behaviour mean score was 2.92 ± 6.03. There was no significant difference found between scale scores according to gender and body mass index classification, and students without an overweight family member had a more positive nutritional attitude. A positive relationship was found between nutritional self-efficacy and nutritional attitude and nutritional behaviour.

CONCLUSIONS: Nutritional self-efficacy, nutritional attitudes and nutritional behaviour levels of children with overweight and obesity were found to be above the moderate level. Factors such as fast food eating habits and time spent with technological devices such as computers and TV, which increase the susceptibility to overweight and obesity, are effective in the levels of nutritional self-efficacy, nutritional attitude and nutritional behaviour.

KEYWORDS: Childhood obesity, Nutritional self-efficacy, Nutritional attitude, Nutritional behaviours, Student.

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INTRODUCTION

Overweight and obesity is a condition characterized by an excess of adipose tissue or body fat. It usually occurs when the energy intake is greater than the energy consumption. In recent years, overweight and obesity in childhood have been increasing all over the world. Being overweight and obese among children and adolescents is considered an important public health problem due to its contribution to the development of chronic diseases in adulthood (1, 2). According to data from the World Health Organization, while more than 340 million children and adolescents were overweight or obese in 2016, there were 38 million children under the age of 5 and overweight or obese in 2019 (3). In our country, 9.9% of children were obese and 14.6% overweight according to the findings of the Childhood Obesity Survey conducted by the Ministry of Health (4). The condition of overweight and obesity in childhood is carried over to adulthood and it increases the likelihood of the occurrence of cardiovascular disease, type 2 diabetes and diabetes-related retinal and kidney complications, nonalcoholic fatty liver, hypercholesterolemia, systemic hypertension, obstructive sleep apnea, cancer and other obesity-related pathological conditions (5, 6). Fighting overweight and obesity in the childhood period, therefore, becomes important. The nutritional self-efficacy, attitude and behaviour of the child are effective factors in this fight. There is a need for self-efficacy beliefs in order for individuals to overcome the obstacles to adopting and maintaining healthy lifestyle habits such as healthy nutrition (7). Self-regulatory skills such as behavioural change related to self-efficacy for initiating and maintaining healthy nutrition, goal setting and self-monitoring are important elements of behaviour change (8). Social cognitive self-regulation theories suggest that people with high self-efficacy and positive outcome expectations tend to self-regulate their behaviour successfully in a particular area. Therefore, nutritional self-efficacy is effective in nutritional attitudes and behaviours (9).

Positive nutritional behaviours were found to be high in a study conducted to determine the nutritional behaviour levels of secondary school students (10). In another study (11), primary and secondary school students were found to

have high self-efficacy in nutrition and more than half of the students demonstrated healthy nutritional behaviours. In a study conducted by Keskin et al., the nutritional behaviours of children between the ages of 12-14 were found to be at moderate levels (12). In another study (13), the nutritional self-efficacy levels of children with overweight and obesity and children with normal weight were found to be similar. In a study evaluating the relationship between nutritional self-efficacy, nutritional attitude and behaviour (14), healthy nutritional habits were found to increase with the increase in nutritional self-efficacy and nutritional attitude. Nutritional self-efficacy, attitude and behaviour levels of children have been shown in studies. But these studies have mostly determined levels of self-efficacy, attitude and behaviour without distinguishing body mass index (BMI), and the relationship between these three variables has not been evaluated together. The number of studies where the nutritional self-efficacy, attitude and behaviour levels of children with overweight and obesity have been evaluated together and the relationship between them has been revealed is limited. Knowing the levels of these variables and their relationship with each other will reveal on the one hand the level of nutrition self-efficacy, attitude and behaviour of the students, on the other hand, the effects of these three variables on each other. This information can contribute as a guide to programs to fight overweight and obesity, especially within the scope of school health. Therefore, this study aimed to investigate the relationship between nutrition self-efficacy, nutrition attitude and nutritional behaviour of students with overweight and obesity, and the levels of these elements according to some variables.

MATERIAL AND METHODS

Procedure

The study was carried out in the fall term of the 2019 - 2020 academic year in three secondary schools in a city in Türkiye with 192 students who accepted to participate in the study from the 5th, 6th and 7th grades. Students' BMI percentile value was over 85 out of 1841 students and their height and weight were recorded. Weight measurements of the students were performed with school uniforms and clothes, while cardigans and vests that would increase the weight were removed before the measure-

ment. A digital weighing (Mesilife BY-810^R)) scale was used for the weight measurement. For height measurements of the students, the shoes were removed, the feet were flat together and the heels and the back were leaning against the wall. In this position, the measurement was taken using the height gauge mounted to the wall. In line with the measurements of height and weight of the children, their BMIs were calculated by using the Child Body Mass Index calculator of the Ministry of Health, General Directorate of Public Health. Students were taken to the meeting rooms and empty classrooms to complete the scales. It took an average of 15 minutes for the students to complete them.

Measures

The data were obtained with personal information form, dietary self-efficacy scale, nutrition attitude scale and dietary behaviour scale in this study, in which the descriptive findings of a doctoral dissertation were given. The scales were applied between 15-30 September 2019.

Personal Information Form

Questions related to age, gender, grade, presence of an overweight member in the family, frequency of meals, fast food eating habits, snacking habits and frequency of physical activity and included in this form were prepared by the researchers.

Child Dietary Self-efficacy Scale

The scale was developed within the scope of Child and Adolescent Trial for Cardiovascular Health (CATCH), a research project aimed at improving the cardiovascular health of children and adolescents and reducing the risk of cardiovascular diseases in the United States (15, 16). CATCH was a school-based, interventional project involving over 6000 children and teenagers from a total of 96 schools in four states (California, Louisiana, Minnesota and Texas). The Child Dietary Self-Efficacy Scale measures self-efficacy ensuring children eat low-fat and low-salt food items. Scale items were formed from various food items containing fat and salt. The food items in the scale were selected among the frequently consumed food items by this age group of children. The scale measures the self-efficacy of children, which

enables them to choose food items with less fat and salt despite the choices with more fat and salt. The scale, a 3-point Likert type, has a single factor structure consisting of 15 items. The scale items are scored in the -1, +1 point range (-1: not sure, 0: somewhat sure, +1: very sure) and the total score ranges from -15 to +15. A high total score on the scale indicates a high level of self-efficacy. Cronbach alpha value of the scale was 0.84 and test-retest reliability (r): 0.63. The Turkish validity and reliability study of the scale has been performed and shown that it can be used on Turkish children by Öztürk Haney and Erdoğan (17). The Cronbach alpha value of the scale in this study was 0.75.

Nutrition Attitude Scale

It is the sub-scale of "The Children's Cardiovascular Health Promotion Attitude Scale." The Children's Cardiovascular Health Promotion Attitude Scale, which was developed by Arvidson (18) to evaluate children's attitudes towards improving cardiovascular health, and consists of 16 items, was adapted to Turkish society by Öztürk Haney and Bahar (19). The scale consists of four subscales: (1) Physical Activity- 4 items; (2) Nutrition- 4 items; (3) Smoking- 4 items (4) Stress Management- 4 items. The internal consistency reliability coefficient of the scale was calculated as 0.75 and the internal consistency reliability coefficient of the nutrition sub-scale was 0.67. The nutrition subscale measures a child's attitude towards activities that reduce fat intake, increase healthy food consumption, and the way of nutrition that improves cardiovascular health. The scale items are scored in the 1 to 4 point range (1- strongly disagree, 2- disagree, 3- agree, 4- strongly agree) and the total score ranges from 4 to 16. A high total score on the scale indicates a high level of positive attitude. The Cronbach alpha value of the scale in this study was found to be 0.71.

Dietary Behaviour Scale

The scale was developed within the scope of Child and Adolescent Trial for Cardiovascular Health (CATCH), a research project aimed at improving the cardiovascular health of children and adolescents and reducing the risk of cardiovascular diseases in the United States (15,

16). The scale consists of 14 illustrated items with low-fat/salty and high-fat/salty food choices to determine the nutrient consumption of children. Children were shown comparable foods and asked which of the two food items they eat more. The scale items have a score of -1 for unhealthy food and +1 for healthy food, and the total score ranges from -14 to +14. A high total score on the scale indicates a healthy nutritional habit. Cronbach alpha value of the scale was 0.76 and test-retest reliability (r): 0.58. The Turkish validity and reliability study of the scale has been performed and shown that it can be used on Turkish children by Öztürk Haney and Erdoğan (17). The Cronbach alpha value of the scale in this study was found to be 0.71.

Ethical Committee

Ethics committee permission was obtained from the Osmangazi University Clinical Research Ethics committee (Date / Number: June 27, 2019/12) and informed consent was obtained from the parents and students before starting the study.

Statistical Analysis

The data obtained were analyzed in the SPSS 20.0 package program. The data were evaluated using descriptive statistics such as mean, percentage and frequency. The suitability of the data to normal distribution was checked with the Kolmogorov-Smirnov Test. Since the data did not show a normal distribution, Spearman's correlation test to evaluate the relationship between the three variables, Mann Whitney U test, and Kruskal Wallis were used. The statistical significance value was accepted as $p < 0.05$.

RESULTS

Of the students participating in the study, 46.3% were girls and 53.7% were boys. The mean age of the participants was 10.8 years. The minimum age was 9 and the maximum age was 12. While 42.7% of the students were in grade 5, 25.5% were in grade 6, and 31.8% were in grade 7. The nutritional self-efficacy mean score of the students was 5.58±5.07, the nutritional attitude mean score was 12.72±2.52, and the nutritional behaviour mean score was 2.92±6.03. There was no significant difference between scale scores according to gender and BMI classification.

Grade 5 students had higher nutritional self-efficacy (KW=6.874, p=0.032), nutritional attitude (KW=14.669, p=0.001) and nutritional behaviour (KW=18.175, p<0.001) scores than Grade 7 students. Nutritional attitude scores of students who did not have overweight family members were found to be higher and statistically significant than those who had an overweight family member **(Table 1**; Z=-2.326, p=0.020**)**.

Table 1: Distribution of some sociodemographic characteristics of students according to Nutrition Self-efficacy, Attitude and Behavior Scales

Socio-demographic characteristics	N	Nutrition self-efficacy	Nutrition attitude	Nutrition behavior
		Median (min-max)	Median (min-max)	Median (min-max)
Gender				
Female	89	6.0 (-10.0-15.0)	13.0 (4.0-16.0)	4.0 (-10.0-14.0)
Male	103	6.0 (-13.0-14.0)	13.0 (4.0-16.0)	2.0 (-12.0-14.0)
Test value		z= -1.135*	z= -1.485*	z= -1.286*
z/KW;p		p= 0.256	p= 0.138	p= 0.198
Class				
5	82	7.0 (-13.0-15.0)a	14.0 (6.0-16.0)a	6.0 (-10.0-14.0)a
6	49	6.0 (-10.0-14.0)b	13.0 (4.0-16.0)b	2.0 (-8.0-12.0)b
7	61	5.0 (-9.0-11.0)c	12.0 (4.0-16.0)c	0.0 (-12.0-12.0)c
Test value		KW= 6.874**	KW= 14.669**	KW= 18.175**
z/KW;p		p= 0.032	p= 0.001	p= 0.000
Post hoc		a>c	a>c	a>c
BMI classification				
Owerweight	96	6.5 (-13.0-14.0)	13.0 (4.0-16.0)	4.0 (-10.0-14.0)
With obesity	96	6.0 (-10.0-15.0)	13.0 (4.0-16.0)	2.0 (-12.0-14.0)
Test value		z= -0.638*	z= -1.207*	z= -1.238*
z/KW;p		p= 0.523	p= 0.228	p= 0.216
Presence of overweight members in the family				
Yes	76	6.0 (-9.0-13.0)	12.0 (4-16)	2.0 (-10.0-14.0)
No	107	6.0 (-13.0-15.0)	13.0 (4-16)	4.0 (-12.0-14.0)
Test value		Z= -0.608	Z= -2.326	Z= -1.937
z/KW;p		p= 0.543	p= 0.020	p= 0.053

* Mann Whitney U; **Kruskall-Wallis

The nutritional behaviour score of students with a daily meal frequency of 1-2 was higher than those with a daily meal frequency of 3-5 **(Table 2**; z=-4.204, p<0.001**)**.

Table 2: Distribution of students' nutritional characteristics according to Nutrition Self-Efficacy, Attitude and Behavior Scales

Nutrition characteristics	N	Nutrition self-efficacy	Nutrition attitude	Nutrition behavior
		Median (min-max)	Median (min-max)	Median (min-max)
Meal frequency per day				
1-2	96	6.0 (-13.0-15.0)	13.0 (4.0-16.0)	6.0 (-10.0-14.0)
3-5	96	6.0 (-7.0-14.0)	13.0 (4.0-16.0)	0.0 (-12.0-14.0)
Test value		z= -0.512*	z= -0.677*	z= -4.204*
z/KW;p		p= 0.609	p= 0.499	p= 0.000
Fast food eating habit				
3-4 per week	17	4.0 (-7.0-14.0)a	12.0 (4.0-16.0)a	-2.0 (-12.0-12.0)
1-2 per week	54	5.0 (-6.0-14.0)b	13.0 (9.0-16.0)b	2.0 (-12.0-14.0)
1-2 per month	109	7.0 (-13.0-15.0)c	13.0 (5.0-16.0)c	4.0 (-10.0-14.0)
Test value		KW= 12.100**	KW= 6.401**	KW= 4.633**
z/KW;p		p= 0.002	p= 0.041	P=0.099
Post hoc		c>b;c>a	c>a	
Habit of snacking after dinner				
Yes	32	5.0 (-7.0-14.0)	13.0 (4-16)a	0.0 (-12.0-12.0)a
No	27	6.0 (-9.0-14.0)	14.0 (4-16)b	6.0 (-4.0-14.0)b
Sometimes	131	7.0 (-13-14)	13.0 (4.0-16.0)c	2.0 (-12.0-14.0)c
Test value		KW= 0.735**	KW= 6.178**	KW= 8.815**
z/KW;p		p= 0.692	p= 0.046	p= 0.012
Post hoc			b>a	b>a;b>c
Habit of waking up and eating				
Yes	11	5.0 (-9.0-13.0)	14.0 (10.0-16.0)	0.0 (-12.0-12.0)a
No	164	7.0 (-13.0-15.0)	13.0 (4.0-16.0)	4.0 (-10.0-14.0)b
Sometimes	17	4.0 (-6.0-14.0)	13.0 (7.0-15.0)	0.0 (-12.0-6.0)c
Test value		KW= 5.169**	KW= 0.345**	KW= 9.698**
z/KW;p		p= 0.075	p= 0.842	p= 0.008
Post hoc				b>c

* Mann Whitney U; **Kruskall-Wallis

The nutritional self-efficacy scores of the students who consume fast food products 1-2 times a month were found to be higher than those who consume 1-2 or 3-4 times a week (KW=12.100, p=0.002), while the nutritional attitude scores of the students who consume fast food products 1-2 times a month were higher

than the students consuming 3-4 times a week (KW=6.401, p=0.041). The nutritional attitude scores of the students who do not snack after dinner were found to be higher than those snacking after dinner (Table 2; KW=6.178, p=0.046), while nutritional behaviour scores of them (KW=8.815, p=0.012) were higher than students who snack regularly after dinner and those who snack from time to time. The nutritional behaviour scores of the students without the habit of waking up from sleep to eat were higher than those who sometimes woke up from sleep to eat something (Table 2; KW=9.698, p=0.008).

Nutritional self-efficacy scores of students who spend less than one hour a day with technological devices such as TV, computer, telephone, 1-2 hours or spending no time at all were found to higher than those spending more than 3 hours **(Table 3; KW=11.761, p=0.019)**, while the nutritional attitude scores of those who spend 1-2 hours a day (Table 3; KW=20.441, p<0.001) and the nutritional behaviour scores of those who spend 1-2 hours a day (Table 3; KW=9.995, p=0.041) were found to be higher than those spending more than three hours a day with technological devices. Nutritional self-efficacy scores of students performing physical activity 3-4 times a week were higher than those not performing a physical activity at all; and nutritional self-efficacy scores of students performing physical activity every day were higher than those not performing at all and those performing physical activities 1-2 times per week **(Table 3**; KW=8.642, p=0.034).

Table 3: Distribution of students' physical activity characteristics according to Nutrition Self-Efficacy, Attitude and Behavior Scales

Physical activity characteristics	N	Nutrition self-efficacy	Nutrition attitude	Nutrition behavior
		Median (min-max)	Median (min-max)	Median (min-max)
TV., smartphone, tablet, etc. time spent				
Never	12	8.0 (1.0-15.0)a	14.5 (7.0-16.0)a	6.0 (-8.0-14.0)a
1-2 hours a day	117	7.0 (-10.0-14.0)b	13.0 (4.0-16.0)b	4.0 (-12.0-14.0)b
3 hours or more per day	43	4.0 (-9.0-13.0)c	12.0 (4.0-16.0)c	0.0 (-10.0-12.0)c
less than 1 hour per day	5	11.0 (5.0-14.0)d	14.0 (11.0-16.0)d	4.0 (-10.0-14.0)d
Only the weekend	7	5.0 (-13.0-13.0)e	13.0 (9.0-16.0)e	-2.0 (-6.0-12.0)e
Test value z/KW;p		KW= 11.761** p= 0.019	KW= 20.441** p=0.000	KW= 9.995** p=0.041
Post hoc		a>c;b>c;d>c	a>c;b>c	b>c
Frequency of physical activity				
I never do	19	5.0 (-9.0-11.0)a	13.0 (6.0-16.0)	-2.0 (-10.0-12.0)
1-2 per week	89	6.0 (-13.0-15.0)b	13.0 (5.0-16.0)	2.0 (-12.0-14.0)
3-4 per week	72	6.5 (-6.0-14.0)c	14.0 (4.0-16.0)	4.0 (-12.0-14.0)
Everyday	7	11.0 (0.0-14.0)d	14.0 (12.0-16.0)	4.0 (-2.0-12.0)
Test value z/KW;p		KW= 8.642** p= 0.034	KW= 5.676** p= 0.128	KW= 7.334** P=0.062
Post hoc		c>a;d>a;d>b		

*: Mann Whitney U; **:Kruskall-Wallis

There was a positive moderate level of correlation between nutritional self-efficacy and nutritional attitude (r=0.429), a positive moderate level of correlation between nutritional self-efficacy and nutritional behaviour (r=0.468), and a positive weak level of correlation between nutritional attitude and nutritional behaviour (r=0.311). All of these correlations were statistically significant (p<0.001; **Table 4**).

Table 4: Results of Spearman Correlation analysis between Nutrition Self-efficacy, Attitude and Behavior Scales

Spearman Correlation	Nutrition self-efficacy	Nutrition attitude	Nutrition behavior
Nutrition self-efficacy	1000	0.429*	0.468*
Nutrition attitude	0.429*	1000	0.311*
Nutrition behavior	0.468*	0.311*	1000

*: p<0.001

DISCUSSION

In this study, we aimed to investigate the relationship between nutritional self-efficacy, nutritional attitude and nutritional behaviour of students with overweight and obesity, and the levels of these elements according to some variables. Nutritional self-efficacy, nutritional attitude and nutritional behaviour are important for the individual to adopt and maintain healthy lifestyle habits such as healthy nutrition. The findings of this study confirm that behaviours that increase susceptibility to overweight or obesity such as fast food eating habits, time spent with technological tools such as TV, telephone, computer, frequency of physical activity, and the habit of snacking after dinner might affect nutritional self-efficacy, nutritional attitudes and nutritional behaviour levels. Since studies on the nutritional self-efficacy, nutritional attitude and nutritional behaviour levels of students with overweight and obesity are limited, discussion of our findings was performed in line with the findings, which do not have any distinction between overweight and obesity, presented in the literature. Self-efficacy refers to one's confidence in the ability to initiate and maintain a certain behaviour and is especially important in achieving weight control in

individuals with obesity (20). In this study, the nutritional self-efficacy scores of the students were above the moderate level. Similarly, it was found above moderate levels in two different studies (13, 14).

Attitude is the individual's positive or negative evaluation of behaviour. The attitude-behaviour relationship is noted to increase with the strength of the attitude. It has been emphasized that attitude should be considered an independent predictor of behaviour (21). Therefore, a positive nutrition attitude becomes important in terms of the emergence of positive nutritional behaviour. In line with this, it can be said that students have a positive nutritional attitude since their nutritional attitude scores are above the moderate level. In a study conducted by Haney and Bahar, in parallel with this study, nutritional attitude scores were found to be above the moderate level (19).

There is an important relationship between nutritional behaviours and weight gain. Changes in nutritional behaviour (such as increasing snack intake, reducing fruit and vegetable intake) have been shown to contribute significantly to weight gain during the transition from adolescence to young adulthood (22). Accordingly, positive nutritional behaviour can be considered as one of the key factors in achieving weight control. In this study, the nutritional behaviour mean score of the students was determined to be above the moderate level. In two other studies, nutritional behaviour scores were found to be above the moderate level in parallel with this study (12, 23).

Childhood obesity has been reported to be less common in girls due to biological differences such as changes in body composition and leptin levels at birth and cultural differences such as emphasis on being thin and maintaining physical appearance (24). In line with this information, female students' nutritional self-efficacy, attitudes and behaviours were expected to be more positive than male students. However, the nutrition self-efficacy, nutritional attitude and nutritional behaviour scores were determined not to show statistically significant differences in terms of gender and BMI classification (p>0.05). In the study of Karacabey and Angın, there was no significant difference found in nutritional self-efficacy in terms of gender and BMI classification of students of the same age group (13). This study is parallel to our study in terms of nutritional self-efficacy results.

Parents' nutritional habits and attitudes affect their children as well (25). A nutritional attitude providing weight control in the family is naturally expected to ensure that the child has a more positive nutritional attitude. In parallel with this information, in this study, students who did not have an overweight family member were found to have a more positive nutritional attitude.

The results of this study revealed that grade 5 students had higher self-efficacy, more positive nutritional attitudes and healthier nutritional habits compared to grade 7 students. In the study in which Yılmaz and Kocataş evaluated the nutritional behaviour of the students, the nutritional behaviour scores of the students between the ages of 10-12 were found to be higher than the students between the ages of 13-15. Although this finding was not the result of children with overweight and obesity, it is similar to our study in terms of nutritional behaviour (10). A decrease in the influence of parental control with an increase in age in students, and children showing more behaviours according to their peer environment can be cited as the reason for this result.

Meal frequency has been shown to be negatively correlated with childhood obesity in some studies and that high meal frequency can prevent obesity (26, 27). In this study, it was found that students with a meal frequency of 1-2 were found to show healthier nutritional behaviours than students with a meal frequency of 3-5. An increase in the frequency of meals has been reported to have beneficial effects such as improvement in serum insulin level and sensitivity, and weight reduction (28). In line with this information, having a higher frequency of meals appears as healthy eating behaviour. However, in our study, on the contrary, children with overweight obesity showed healthier nutritional habits with a decrease in their frequency of meals. This condition may be related to the content of the increased frequency of meals. The frequency of meals of the participants in our study may have increased with unhealthy nutritional contents such as junk food and fast food.

The reason for the low nutritional behaviour scores of the students with a higher frequency of meals can be attributed to this situation. Snacking with high calories after dinner appears as a nutritional behaviour that causes obesity (29). The nutritional behaviour score of the students not snacking after dinner in parallel with the meal frequency was higher. This result shows that students who do not snack have healthier nutritional habits.

Due to its high-calorie values, fast food consumption is a factor that increases susceptibility to overweight and obesity (10) and is a nutritional behaviour that children with overweight and obesity should avoid. Maintaining an unhealthy eating behaviour by turning it into a healthy behaviour is expressed as self-efficacy (20). The frequency of unhealthy behaviour becomes important in maintaining healthy behaviour. In other words, it is a necessity to reduce the frequency of unhealthy behaviour in order to maintain healthy behaviour. In our study, students who consume fast food products 1-2 times a month were found to have higher self-efficacy than those who consume 1-2 times a week and a higher nutritional attitude than those consuming fast food 3-4 times a week. Students with high nutritional self-efficacy and attitude can be said to have less frequency of unhealthy nutritional behaviours.

A sedentary lifestyle and frequency of physical activity have an important role in the emergence of overweight and obesity. As the time children spent with technological devices such as TV, telephone and computer increases, their physical activities decrease (30). Nutritional self-efficacy, nutritional attitude and behaviour of children change with the time they spent with technological devices such as TV, telephone and computer. Students spending less than an hour a day with these technological devices had higher nutritional self-efficacy, students not spending time at all had more positive nutritional attitudes, and students spending 1-2 hours a day had healthier nutritional habits. Students performing physical activity 3-4 times a week or every day demonstrated a high nutritional self-efficacy. In another study, an improvement in nutritional behaviour was determined with an

increase in the physical activity frequency (10). In another study, a positive relationship was found between students' nutritional behaviours and physical activity status (12). Although these are not the results of students with overweight and obesity, they are similar to our study in terms of positive nutritional behaviour change depending on the frequency of physical activity.

A positive relationship was revealed between nutritional self-efficacy and nutritional attitude and nutritional behaviour. According to this result, an increase in nutritional self-efficacy may lead to a positive nutritional attitude and an improvement in healthy nutritional habits. In another study in which the relationship between these three variables was investigated, as nutritional self-efficacy and nutritional attitude increased, healthy nutritional habits were found to increase (14). This result is in parallel with our study.

According to the results of this study, the nutritional self-efficacy, nutritional attitudes and nutritional behaviour levels of children with overweight and obesity were found to be above the moderate level. The frequency of meals, the habit of fast food eating, the habit of snacking after dinner, the time spent with devices such as TV, phone and computer, the frequency of physical activity are effective in nutritional self-efficacy, nutritional attitude and nutritional behaviour levels. Nutritional self-efficacy, nutritional attitude and nutritional behaviour of students are positively correlated.

In conclusion, positive nutrition attitude scores and healthy nutritional behaviour scores increase, as the nutritional self-efficacy scores of students with overweight and obesity increase. Students, who were in fifth grade, did not have any overweight members in their family, did not snack after dinner, had fast food 1-2 times a month, never spent time with technological devices and had more positive nutritional attitudes than other students. Students, who were in fifth grade, had fast food 1-2 times a month, spent less than an hour per day with technological devices, and engaged in physical activity every day demonstrated higher nutritional self-efficacy. Students, who were in fifth grade, had a meal frequency of 1-2, did not snack after dinner, woke up from sleep for eating, and

never spent time with technological devices and had healthier nutritional behaviours than other students. As a complementary part of preventive health services, studies should be carried out in school health services to increase and improve the levels of nutritional self-efficacy, nutritional attitude and nutritional behaviour of students with overweight and obesity.

Acknowledgment

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

COVID-19 PANDEMİ DÖNEMİNDE UZAKTAN EĞİTİM SİSTEMİNİN ANATOMİ EĞİTİMİ ÜZERİNE ETKİSİ

THE EFFECT OF THE DISTANCE EDUCATION SYSTEM DURING THE COVID-19 PANDEMIC PERIOD ON THE ANATOMY EDUCATION

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ÖZET

AMAÇ: Çalışmamızda, Covid-19 pandemi döneminde uzaktan eğitim ile anatomi dersi alan öğrencilerin karşılaştıkları zorlukların, uyum sağlayabilme yeteneklerinin, uzaktan eğitiminde avantaj ve dezavantajlarının ve öğrenme başarısı ile ilişkisinin araştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışmamıza Balıkesir Üniversitesi, Tıp Fakültesi 1., 2., 3. ve 4. sınıfta öğrenim gören toplam 560 öğrenci dahil edildi, ancak bu öğrencilerden 399'u (%71,25) çalışmaya katılmıştır. Katılımcılara literatür taranarak araştırmacılar tarafından geliştirilen geri bildirim formu ve psikometrik anket uygulandı. Veriler analiz edilip yorumlandı.

BULGULAR: Araştırmamıza katılan öğrencilerin yaş ortalaması 20,57±2,21 olarak bulundu. Ortalama sınav başarı puanları ise sırasıyla birinci sınıflarda 79,20±10,0, ikinci sınıflarda 62,30±19,16, üçüncü sınıflarda 52,45±14,64 ve dördüncü sınıflarda 57,48±15,30 olarak hesaplandı. Yapılan analiz sonucunda, çevrimiçi uzaktan eğitim alan birinci sınıf öğrencilerinin ortalama başarı puanının istatistiksel olarak anlamlı bir şekilde diğer gruplardan daha fazla olduğu tespit edildi. Araştırmamıza katılan öğrencilerin %45,9'u, Covid-19 pandemi sonrasında anatomi eğitiminin tamamen yüz yüze olması gerektiğini belirtirken, öğrencilerin %3,8'i ise tamamen uzaktan eğitim olarak verilmesini ifade etmişlerdir.

SONUÇ: Öğrencilerin çevrimiçi anatomi eğitiminde daha başarılı oldukları tespit edilse de öğrencilerin çoğunluğu, anatomi dersinin yüz yüze verilmesini tercih etmişlerdir. Uzaktan eğitime geçilmesini gerektiren durumlarda, anatomi eğitimi teorik derslerinin çevrimiçi olarak sürdürülmesinin ancak pratik derslerin yüz yüze olarak devam ettirilmesinin anatomi eğitiminin başarısına olumlu yönde katkı sağlayacağı kanaatindeyiz.

ANAHTAR KELİMELER: Anatomi, Covid-19, Uzaktan eğitim, Tıp eğitimi.

ABSTRACT

OBJECTIVE: In our study, it was aimed to investigate the difficulties faced by students who took the anatomy lesson with distance education during the Covid-19 pandemic period, their ability to adapt, the advantages-disadvantages of distance education, and its relationship with learning success.

MATERIAL AND METHODS: A total of 560 students studying in the 1st, 2nd, 3rd and 4th grades of Balıkesir University, Faculty of Medicine were included in our study, but 399 (71.25%) of these students participated in the study. A feedback form developed by the researchers and a psychometric questionnaire were applied to the participants by scanning the literature. The data were analyzed and interpreted.

RESULTS: The mean age of the students participating in our study was found to be 20.57±2.21. Mean exam success scores were calculated as 79.20±10.30 in first grades, 62.30±19.16 in second grades, 52.45±14.64 in third grades and 57.48±15.30 in fourth grades, respectively. As a result of the analysis, it was determined that the average achievement score of the first-year students who received online distance education was higher than the other groups in a statistically significant way. While 45.9% of the students participating in our research stated that the anatomy education should be face-to-face after the Covid-19 pandemic, 3.8% of the students stated that it should be given as distance education.

CONCLUSIONS: As a result of our study, although it was determined that the students were more successful in online anatomy education, the majority of the students preferred face-to-face anatomy lessons. In cases where distance education is required, we believe that carrying on the theoretical lessons of anatomy education online but carrying on the practical lessons face-to-face will contribute positively to the success of the anatomy education.

KEYWORDS: Anatomy, Covid-19, Distance education, Medical education.

GİRİŞ

Eğitim sisteminin en önemli unsurlarından biri olan öğrenci, eğitimin her aşamasında önemli roller üstlenmektedir. Eğitim amaçlarının ve müfredatlarının belirlenmesinde, verilen eğitimin değerlendirilmesi sürecinde, fakültenin yönetim sistemi gibi konularda uygun veri toplama araçları ile öğrenci görüşlerine başvurmak büyük öneme sahiptir (1, 2). Öğrencilere uygulanan yazılı ve sözlü sınavlardaki başarı testleri ile kazanılması hedeflenen ögeler değerlendirilirken, öğrenciden alınan geri bildirimler sayesinde eğitimin niteliğini ve kalitesini artıracak yeni düzenlemeler geliştirilmektedir. Zamanla öğretmen merkezli eğitim sistemi, öğrencinin esas olduğu öğrenci merkezli eğitim sistemine doğru yönelim göstermiştir. Öğrenci merkezli bu programların düzenlenme aşamasında öğrenci geri bildirimleri rehber niteliği taşımaktadır (3, 4).

Son yıllarda geleneksel tıp eğitiminde, öğrencilerin teorik bilgi birikimleri pratik uygulama becerilerinin önüne geçmeye başlamıştır. Tıp eğitiminin amacı, öğrencilerin bilgiyi sığ bir şekilde öğrenmelerinin yerine öğrenmiş oldukları bilgiyi pratik uygulamalarda kullanabilme becerisini ve tutumunu geliştirmektir (5). Bu kapsamda anatomi eğitimi hangi eğitim modeliyle verilirse verilsin asıl amaç, öğrencilerin almış oldukları anatomi eğitimini mesleki hayatlarında en iyi şekilde kullanabilmelerini sağlamaktır.

Covid-19 pandemisi, her alanı etkilediği gibi eğitim sistemi üzerinde de büyük değişikliklere sebep olmuştur. Salgını kontrol altına almak amacıyla, üniversitelerde yüz yüze eğitime ara verilmesi, uzaktan eğitime hızlı ve zorunlu bir şekilde geçiş yapılmasına neden olmuştur. Bu nedenle çalışmamızda, Covid-19 pandemi döneminde hızlı bir şekilde geçilen uzaktan eğitim modelinin anatomi eğitimine katkısı, sistemin avantaj ve dezavantajları ve pandemi sonrası dönemde anatomi eğitiminin nasıl olması gerektiğine dair öğrenci görüşlerinin değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM

Çalışma Grupları

Çalışmamıza, Balıkesir Üniversitesi Tıp Fakültesi'nde 2020-2021 eğitim-öğretim yılında öğrenim gören 1., 2., 3. ve 4. sınıf öğrencileri dahil edildi. Toplam 560 öğrenciden 399'u (%71,25) çalışmaya katıldı. Çalışma gruplarımızı oluşturan 1. sınıf öğrencileri çevrimiçi (online), 2. sınıf öğrencileri yüz yüze ve senkron, 3. sınıf öğrencileri yüz yüze ve asenkron ve 4. sınıf öğrencileri ise tamamen yüz yüze eğitim modeli ile anatomi eğitimi almışlardır.

Verilerin Toplanması

Araştırmaya katılan öğrencilere geri bildirim formu, uzaktan eğitim ile gerçekleştirilen anatomi eğitimi teorik ve pratik derslerine ilişkin başarı puanlama testi ve likert ölçek ile kapalı uçlu psikometrik anket uygulandı (Cronbach Alpha 0,887). Online olarak toplanan geri bildirimlerin güvenilirliğini arttırmak ve öğrencilerin kendilerini baskı altında kalmadan fikirlerini özgür bir şekilde ifade etmelerini sağlamak amacıyla anket formu üzerine ad, soyad ve öğrenci numaralarını yazmamaları istendi.

Etik Kurul

Çalışmamız için Balıkesir Üniversitesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulu'ndan onay alındı (2021/149).

İstatistiksel Analiz

Elde edilen veriler SPSS (Statistical Package for Social Sciences) 22,0 paket programına kaydedilip, analizler yapıldı. Shapiro-Wilk testi ile sürekli değişkenlerin normallik analizi yapıldı. Değişkenlerin normallik varsayımını sağlamadığı tespit edilip, tek değişkenli analizlerde Mann-Whitney U ve Kruskal Wallis H testleri kullanılırken $p < 0,05$ istatistiksel olarak anlamlı şeklinde değerlendirildi.

BULGULAR

Çalışmamıza katılan öğrencilerin yaş ortalaması $20,57 \pm 2,21$ yıl olarak tespit edildi. Çalışmamıza birinci sınıftan 121 öğrenci (%30,3), ikinci sınıftan 130 öğrenci (%32,6), üçüncü sınıftan 76 öğrenci (%19) ve dördüncü sınıftan 72 öğrenci (%18) katıldı **(Tablo 1)**. Araştırmamıza katılan 1., 2., 3. ve 4. sınıf öğrencilerin anatomi dersi sınav başarı ortalamaları sırasıyla $79,20 \pm 10,30$, $62,30 \pm 19,16$, $52,45 \pm 14,64$ ve $57,48 \pm 15,30$ puan olarak tespit edildi. Tüm sınıfların ortalaması ise $64,68 \pm 18,36$ olarak hesaplanmıştır. Sınav başarıları karşılaştırıldığında tamamen çevrimiçi eğitim alan birinci sınıf öğrencilerinin ortalama başarı puanının istatistiksel olarak anlamlı bir şekilde diğer gruplardan daha fazla olduğu tespit edildi ($p = 0,000007$) **(Tablo 2)**.

Tablo 1: Katılımcılara ait tanımlayıcı verileri

	n (kişi sayısı)	%
Cinsiyet		
Kadın	207	51,9
Erkek	192	48,1
Yaşanılan yer		
İl Merkezi	254	63,7
İlçe	93	23,3
Mahalle/Köy	47	11,8
Kasaba	5	1,3
Kim ile yaşıyorsunuz		
Yalnız yaşıyorum	43	10,8
Ailemle yaşıyorum	333	23,3
Arkadaşlarımla yaşıyorum	23	5,8
Sınıf tekrarı yapma durumu		
Sınıf Tekrarı Yapan	36	9,0
Sınıf Tekrarı Yapmayan	363	91,0

n:kişi sayısı, %: yüzde

Tablo 2: Öğrencilerin anatomi sınav başarısı ve anatomi derslerini aktif dinleme sürelerine ilişkin veriler

	Birinci sınıf Ort ± SS	İkinci sınıf Ort ± SS	Üçüncü sınıf Ort ± SS	Dördüncü sınıf Ort ± SS	p
Anatomi teorik derslerini aktif dinleme süresi (dakika)	28,74±10,07	36,07±16,26	29,21±10,10	31,86±10,66	p=0,000029[a] / p=0,747853[b] / p=0,042691[c] / p=0,001063[d] / p=0,004986[e] / p=0,122549[f]
Anatomi pratik derslerini aktif dinleme süresi (dakika)	29,01±10,36	35,12±14,71	36,51±14,42	40,25±26,02	p=0,000199[a] / p=0,000034[b] / p=0,000037[c] / p=0,508257[d] / p=0,074525[e] / p=0,278465[f]
Anatomi dersi sınav başarısı	79,20±10,30	62,30±19,16	52,45±14,64	57,48±15,30	p=0,000018[a] / p=0,000009[b] / p=0,000007[c] / p=0,000145[d] / p=0,068021[e] / p=0,042437[f]

a: birinci ve ikinci sınıf arasındaki istatistiksel fark, b: birinci ve üçüncü sınıf arasındaki istatistiksel fark, c: birinci ve dördüncü sınıf arasındaki istatistiksel fark, d: ikinci ve üçüncü sınıf arasındaki istatistiksel fark, e: ikinci ve dördüncü sınıf arasındaki istatistiksel fark, f: üçüncü ve dördüncü sınıf arasındaki istatistiksel fark

Öğrencilerin pandemi öncesinde ekran başında geçirdiği süre, birinci sınıfta ortalama 3,31±1,45, ikinci sınıfta 3,35±1,33 ve üçüncü sınıfta 3,66±1,62 saat olarak tespit edilirken, pandemi döneminde ekran başında geçirilen süre yaklaşık %50 artış oranıyla sırasıyla ortalama 7,22±2,69, 6,88±2,78 ve 7,74±3,23 saat olarak gözlendi. Anatomi eğitimini tamamen çevrimiçi alan birinci sınıf öğrencilerinin ekran başında geçirdiği sürenin diğer sınıflara göre anlamlı bir şekilde artış gösterdiği görüldü (p=0,000777). Birinci sınıflarda, ekran başında geçirilen süre uzun olmasına rağmen, online eğitim sırasında anatomi teorik ve pratik derslerini aktif dinleme süreleri ortalama 29 dakika olarak belirlenmiştir. Tamamen yüz yüze eğitimle anatomi dersi alan dördüncü sınıflarda ise, aktif dinleme süreleri ortalama 36 dakika olarak bulunmuştur. Aktif ders dinleme süresi açısından sınıflar arasında oluşan farkın istatistiksel olarak anlamlı olduğu tespit edildi (teorik; p=0,000050, pratik; p=0,000017) Tablo 2.

Uygulanan anket formuna göre, öğrencilerin %62,4'ü anatomi teorik derslerinin uzaktan eğitim yoluyla yapılmasından memnun olsalar da %36,1'i anatomi pratik derslerinin uzaktan eğitim yoluyla yapılması konusunda kararsız olduklarını belirtmişlerdir **(Tablo 3)**.

Tablo 3: Öğrencilerin anket sorularına verdikleri cevaplar ilişkin veriler

Anket soruları		Kesinlikle Katılıyorum	Katılıyorum	Kararsızım	Katılmıyorum	Kesinlikle Katılmıyorum
Çevrimiçi anatomi eğitimi kendi kendime ve istediğim zaman aralığında öğrenmemi sağlar	n	104	169	90	26	10
	%	26,1	42,4	22,6	6,5	2,5
Çevrimiçi anatomi aşırı bilgi yüklenmemi önler ve anlayamadığım konuya daha çok zaman ayırırım	n	95	143	111	42	8
	%	23,8	35,8	27,8	10,5	2,0
Çevrimiçi anatomi eğitimi zaman kazandırır ve tekrar etme sayımı artırır	n	120	172	75	21	11
	%	30,1	43,1	18,8	5,3	2,8
Anatomi teorik kısmını kayıtlı video ders notları ve slaytlarla öğrenebilirim	n	138	191	45	17	8
	%	34,6	47,9	11,3	4,3	2,0
Anatominin bazı konularında çevrimiçi kaynak bulmakta zorlanıyorum	n	35	139	110	87	28
	%	8,8	34,8	27,6	21,8	7,0
Almış olduğum anatomi eğitiminin mesleğim boyunca yeterli olacağını düşünüyorum	n	54	156	151	27	11
	%	13,5	39,1	37,8	6,8	2,8
Pratik eğitimlerin eksikliğinden endişeleniyorum	n	77	139	94	66	33
	%	19,3	32,3	23,6	16,5	8,3
Kadavrayla çalışmayı mesleğimde iyi olmak ve kendimi geliştirmek adına gereklidir	n	173	163	42	14	7
	%	43,4	40,9	10,5	3,5	1,8
Pratik derslerdeki eksikliğin gelecekteki işime yansıyacağını düşünmekteyim	n	88	148	96	39	28
	%	22,1	37,1	24,1	9,8	7,0
Kaydedilmiş diseksiyon videoları ve kadavraların dijital fotoğrafları anatomi pratiği için yeterlidir	n	32	96	166	64	41
	%	8,0	24,1	41,6	16,0	10,3
Çevrimiçi kayıtlı kadavra kaynakları gerçek kadavraların yerini tutabilir	n	31	52	129	108	79
	%	7,8	13,0	32,3	27,1	19,8
Pratik derslere aktif bir şekilde katılabiliyorum	n	76	168	100	43	12
	%	19,0	42,1	25,1	10,8	3,0
Laboratuvar ortamında pratik uygulamalara katılmak isterim	n	166	165	52	6	10
	%	41,6	41,4	13,0	1,5	2,5
Öğretim üyeleri ile dersleri özlüyorum	n	158	142	66	19	14
	%	39,6	35,6	16,5	4,8	3,5
Çevrimiçi anatomi eğitimi yüz yüze eğitimin ve laboratuvar derslerinin yerine geçemez	n	140	117	86	34	22
	%	35,1	29,3	21,6	8,5	5,5
Çevrimiçi eğitim geleceğimle ilgili beni endişelendiriyor	n	93	120	88	58	40
	%	23,3	30,1	22,1	14,5	10,0
Üniversite ve kampüs yaşamından uzak olmak sosyalleşmemi engelliyor	n	123	148	72	25	11
	%	30,8	37,1	18,0	6,3	7,8
Konuları akranlarımla tartışma imkânım olmadığı için iletişim kurma becerilerim gelişmiyor	n	101	134	84	47	33
	%	25,3	33,6	21,1	11,8	8,3
Uzaktan anatomi teorik eğitiminden memnunum	n	97	152	99	29	22
	%	24,3	38,1	24,8	7,3	5,5
Uzaktan anatomi pratik eğitiminden memnunum	n	45	110	144	59	41
	%	11,3	27,6	36,1	14,8	10,3
Çevrimiçi/yüz yüze derste öğretim üyeleri ile rahatça iletişim kurabiliyorum	n	81	171	102	33	12
	%	20,3	42,9	25,6	8,3	3,0
Öğretim üyelerinin çevrimiçi derslerdeki etkileşimi (interaktif ders işleme) yeterlidir	n	88	185	88	30	8
	%	22,1	46,4	22,1	7,5	2,0

n: kişi sayısı, %: yüzde

Öğrencilerden anatomi teorik ders sınavlarının zorluk derecesini değerlendirmeleri istendiğinde, 26 kişi sınavları çok zor, 203 kişi zor, 161 kişi orta, 5 kişi kolay ve 4 kişi çok kolay olarak belirtmiştir. Öğrencilerin Uzaktan eğitim ve yüz yüze aldıkları Anatomi derslerinin ne kadar etkili olduğuna ilişkin veriler **Tablo 4**'de gösterilmiştir.

Tablo 4: Uzaktan eğitim ve yüz yüze alınan Anatomi derslerinin etkisine ilişkin veriler

		Çok Etkili	Etkili	Kararsızım	Etkisiz
Uzaktan eğitim ile verilen Anatomi eğitiminin değerlendirilmesi					
Çevrimiçi (online) teorik ve pratik dersler	n	45	172	109	73
	%	11,3	43,1	27,3	18,3
Ders kayıt videoları	n	181	139	59	20
	%	45,4	34,8	14,8	5,0
Yüz yüze anatomi eğitim şeklini değerlendirme					
Teorik ve pratik dersler	n	194	121	32	52
	%	48,6	30,3	8,0	13,1

n: kişi sayısı, %: yüzde

Araştırmamıza katılan öğrencilere yöneltilen "Covid-19 pandemi sonrasında anatomi eğitimi nasıl olmalıdır" sorusuna; 183 kişi (%45,9) "Tamamen yüz yüze", 149 kişi (%37,3) "Anatomi teorik dersler uzaktan eğitim, pratik dersler yüz yüze", 4 kişi (%1) "Anatomi teorik dersler yüz yüze, pratik dersler uzaktan eğitim", 48 kişi (%12) "Anatomi ders konularına göre uzaktan ve

yüz yüze olarak bölünmeli (%50 yüz yüze + %50 uzaktan eğitim)" ve 15 kişi (%3,8) "Tamamen uzaktan eğitim" olarak yanıtlamıştır **(Tablo 5)**.

Tablo 5: Covid-19 pandemi sonrasında sınıflara göre anatomi eğitimi nasıl olmalıdır

	1. Sınıf n	2. Sınıf n	3. Sınıf n	4. Sınıf n
Tamamen yüz yüze	85	34	30	34
Anatomi teorik dersler uzaktan eğitim, pratik dersler yüz yüze	27	70	22	30
Anatomi teorik dersler yüz yüze, pratik dersler uzaktan eğitim	0	0	4	0
Anatomi ders konularına göre uzaktan ve yüz yüze olarak bölünmeli (%50 yüz yüze + %50 uzaktan eğitim)	4	20	18	6
Tamamen uzaktan eğitim	5	6	2	2
TOPLAM	**121**	**130**	**76**	**72**

n: kişi sayısı

TARTIŞMA

Tüm dünyayı etkisi altına alan Covid-19 pandemisi, eğitim dahil birçok alanı etkilediği gibi anatomi eğitimini de olumsuz etkilemiş, amfi ve laboratuvar eğitiminden "acil" bir şekilde çevrimiçi öğrenme ortamına geçişe neden olmuştur (6). Çevrimiçi anatomi eğitiminin en iyi şekilde verilmesi için öğrencilerden alınan geri bildirimler oldukça önemlidir. Pandemi döneminde öğrencilerden alınacak geri bildirimler sayesinde, çevrimiçi anatomi eğitiminin eksik yönleri giderilerek teorik ve pratik derslerinin daha iyi öğrenilmesi sağlanacaktır (7).

Mahdy'nin rapor ettiği verilere göre, Covid-19 pandemisine bağlı olarak öğrencilerin ekran başında geçirdikleri sürenin arttığını bildirmiştir (8). Benzer şekilde çalışmamız sonunda, öğrencilerin Covid-19 pandemi döneminde ekran başında geçirilen sürenin, pandemi öncesinde ekran başında geçirilen süre ile karşılaştırıldığında, sürenin yaklaşık 2 kat arttığı tespit edilmiştir.

Singal ve ark.'nın (7) 2020 yılında yaptıkları çalışmada öğrencilerin çevrimiçi yeterli kaynak bulmakta zorlandıklarını rapor etmiştir. Mahdy tarafından 2020 yılında yapılan çalışmada ise öğrencilerin, çevrimiçi çalışma materyali olarak çoğunlukla Taşınabilir Belge Formatındaki (PDF) sunumları kullandıklarını bildirilmiştir (8).

Çalışmamıza katılan öğrenciler, çevrimiçi çalışma materyali olarak çevrimiçi dersleri, ders sunumlarını, kayıtlı videoları, ders kitaplarını ve anatomi atlaslarını kullandıklarını belirtmişlerdir. Öğrencilerimizin çevrimiçi anatomi dersleri için çalışma materyali olarak birden fazla kaynak kullanmalarının, anatomi eğitiminin öğrenilmesinde olumlu etki yaptığı kanaatine varılmıştır.

Uzaktan eğitimin senkron (eş zamanlı) mu yoksa asenkron (eş zamanlı olmayan) mu daha verimli olacağı ile ilgili tartışmalar halen devam ederken, He ve ark.'nın (9) 2021 yılında sağlık bilimleri öğrencileri ile gerçekleştirmiş olduğu çalışmanın sonuçları incelendiğinde, senkron verilen tıp eğitimi ile asenkron verilen tıp eğitimi arasında anlamlı bir farkın olmadığı görülmektedir. Çalışmamızdaki örneklem değerlendirildiğinde, anatomi eğitimini yalnız asenkron olarak tamamlayan öğrenci grubu bulunmamaktadır. 2. sınıf öğrencileri anatomi eğitimini yüz yüze ve senkron olarak, 3. sınıf öğrencileri ise yüz yüze ve asenkron olarak tamamlamıştır. Çalışma sonunda elde edilen verilere 2. ve 3. sınıfların sınav başarıları arasındaki fark istatiksel olarak anlamlı bulunması, He ve ark.'nın (9) aksine, senkron verilen anatomi eğitimi ile asenkron verilen anatomi eğitimi arasında anlamlı bir fark olduğu ortaya konulmuştur.

Çevrimiçi anatomi eğitiminin öğrenciler üzerindeki dezavantajları ile birlikte, Covid-19 pandemisi nedeniyle mevcut anatomi öğrencilerinin geleceklerine yönelik sorunlar da gündeme gelmektedir. Shahrvini ve ark.'larına (10) göre çevrimiçi eğitimin, öğrencilerin klinik becerilerini kaybetmelerine ve laboratuvar derslerinin olumsuz yönde etkilenmesine neden olduğu bildirilmiştir. Elde edilen veriler doğrultusunda, çalışmamıza katılan öğrencilerin kadavrayla çalışmayı, mesleklerinde iyi olmak ve kendilerini geliştirmek adına gerekli gördüğü tespit edilmiştir. Kadavrasız eğitime maruz kalan öğrencilerin gelecek ve mesleki yeterlilikle ilgili kaygıları oluşmaktadır. Çalışmamıza katılan 399 öğrenciden %37,1'i çevrimiçi olarak almış oldukları anatomi eğitiminde, pratik derslerdeki eksikliğin gelecekteki işine yansıyacağını düşünmektedir. Bu da kadavranın, özellikle tıp fakültesinde hem lisans eğitiminin daha iyi anlaşılmasını hem de mezuniyet sonrasında mesleklerini daha iyi yapmaları için oldukça önemlidir.

Öğrenciler yüz yüze öğrenme esnasında; dinleme, okuma, izleme gibi pasif öğrenme stillerinin yanı sıra, anlaşılmayan noktaları birbirine anlatarak ve konu hakkında tartışarak aktif öğrenme yöntemlerini de kullanmaktadır. Literatürde, aktif öğrenme stilinin pasif öğrenme stiline göre daha verimli olduğunu rapor eden çalışmalar yer almaktadır (11). Mathiowetz ve ark.'nın (12) 2016 yılında yayımladıkları çalışmada, pratik derslerde kullanılan kadavra diseksiyonunun, çevrimiçi diseksiyon programlarına göre çok daha iyi öğrenme imkânı sağladığını bildirmiştir.

Çalışmaya benzer şekilde araştırmamıza katılan öğrencilerin %50'sinden fazlası, "çevrimiçi anatomi eğitimi yüz yüze eğitimin ve laboratuvar derslerinin yerine geçemez" sorusuna "katılıyorum" yanıtını vermesi, anatomi pratik eğitiminde yüz yüze eğitimin önemini vurgulamaktadır.

Yoo ve ark. (13) çevrimiçi sınıfın; öğrencilerin ders saatlerini ayarlaması, kendi kendine çalışma için daha çok zaman ayırması, ders materyallerine kolay erişim sağlaması ve tekrar tekrar kendi hızlarında çalışmasına izin vermesi sebebiyle öğrenciler tarafından daha çok tercih edildiğini bildirmiştir. McBrien ve ark. (14) çevrimiçi eş zamanlı oturumların akran-akran ve akran-eğitici etkileşimlerini arttıracağını vurgulamıştır. Shahrvini ve ark. (10) öğrencilerin çevrimiçi eğitimde en çok program esnekliğini ve önceden kaydedilen derslere erken erişebilme sayesinde kendi hızlarında öğrenmekten memnun olduklarını rapor etmiştir. Böylece öğrencilerin sosyal yaşamda aktif olabilmeleri için daha çok zamanlarının olacağına dikkat çekilmiştir. Ortadeveci ve ark.'nın (15) 2021 yılında yayımladıkları çalışmada ise, öğrencilerin uzaktan eğitimin zaman kazandırdığını düşünmediklerini belirtilmiştir. Çalışmamıza katılan öğrencilerin uzaktan anatomi eğitiminin avantajlarına rağmen yüz yüze eğitimin daha etkili olduğunu bildirmişlerdir.

Singal ve ark. (7) öğrenciler için kampüs hayatının çok önemli olduğunu bildirmiştir. Öyle ki öğrencilerin, üniversiteyi kampüs hayatından bağımsız düşünemediklerini ve kampüs ortamındaki eğitimlerine geri dönmeyi istediklerini ifade etmektedir. Çalışmaya benzer şekilde araştırmamıza katılan öğrencilerin %50'sinden fazlası, üniversite ve kampüs ortamından uzak kalmalarının, sosyalleşmelerini olumsuz yönde etkilediğini belirtmiştir. Öğrencilerin kampüs ortamını özledikleri, akran etkileşiminde bulunmak istedikleri ve daha önce hiç kampüs ortamında bulunmayan 1. sınıf öğrencilerinin kampüs ortamını merak ettikleri tespit edilmiştir. Çevrimiçi eğitimde, öğrenciler ile öğretim üyeleri arasındaki etkileşimin daha az olduğunu bildiren Yoo ve ark. (13) öğrencilerin çok az bir kısmının çevrimiçi derslerde sohbet penceresini açtığını veya soru/cevap bölümünü kullandığını bildirmiştir. Araştırmamıza katılan öğrencilerin büyük çoğunluğu konu ile ilgili sorularını öğre-

tim üyelerine rahatlıkla sorabildiklerini, öğretim üyeleriyle çevrimiçi/yüz yüze eğitimde ders esnasında ve ders dışında rahatlıkla iletişim kurabildiklerini ifade etmişlerdir. Bu doğrultuda elde edilen verilere göre, çalışmamızdaki öğrencilerin genel olarak hem yüz yüze eğitimde hem de çevrimiçi eğitimde öğretim üyelerine rahatça ulaşabildiği ve bu konuda herhangi bir problemlerinin olmadığı sonucuna varılmaktadır.

Yapılan bir çalışmada, çevrimiçi anatomi eğitimi alan öğrencilerin, yüz yüze anatomi eğitimi alan öğrencilerden daha başarılı oldukları tespit edilmiştir. Bunun nedeni, çevrimiçi derslerde kullanılan materyallerin hem çeşitliliğinin fazla olması hem de bu materyallerin bireye kendi kendine öğrenme fırsatının daha fazla sunulmasına bağlanmıştır (13). Bu çalışma, araştırmamızda değerlendirilen, anatomi eğitimini tamamen çevrimiçi olarak alan 1. sınıf öğrencilerinin başarı ortalamalarının diğer sınıflara göre daha fazla olması, benzer sonuçlar elde edilmesi açısından çalışmamızı destekler niteliktedir.

Alkhowailed ve ark.'nın (16) 2020 yılında yaptıkları çalışmada, öğrencilerin çevrimiçi teorik derslerden, amaçlanan öğrenme çıktılarının kazanılmasından ve eğitim faaliyetlerinin dijitalleşmesinden memnun olduklarını bildirmiştir.

Araştırmamızdaki öğrencilerin %38,1'i uzaktan anatomi teorik eğitiminden memnun olduğunu ifade ederken, %36,1'i uzaktan anatomi pratik eğitiminden memnun olma konusunda kararsız kaldığını belirtmiştir. Anatomi pratik eğitiminin üç boyutlu düşünmeyi gerektirmesi ve çevrimiçi eğitimin öğrencilerin laboratuvar ortamındaki çalışmalarının yerini doldurabileceği bir eğitim ortamı olmaması sebebiyle, uzaktan anatomi pratik eğitiminden memnun olma konusunda kararsızlık yaşandığı düşünülmektedir.

Çalışmamıza katılan öğrencilerden %43,1'i çevrimiçi olarak gerçekleştirilen anatomi teorik ve pratik eğitiminin etkili olduğunu ifade ederken, %45,4'ü ders kayıt videolarının çok daha etkili olduğunu belirtmiştir. Bu veriler ışığında öğrencilerin, kendi kendine, istedikleri hızda ve istedikleri zaman aralığında öğrenmeyi tercih ettikleri anlaşılmaktadır. Elde edilen veriler sonucunda, yüz yüze anatomi eğitiminin öğrencilerin büyük çoğunluğu tarafından etkili

olarak değerlendirilmesi, her ne kadar çevrimiçi derslerin daha etkili olduğunu ifade etseler de alışkın oldukları geleneksel yüz yüze eğitimden vazgeçemediklerini ortaya koymaktadır.

Covid-19 pandemisinin zorunlu kıldığı uzaktan eğitime karşı öğrencilerin, gelecekteki anatomi eğitimi hakkındaki düşüncelerinin değerlendirilmesi büyük önem taşımaktadır. Arı ve ark.'nın (17) 2003 yılında yayımlanan çalışmasında, öğrencilerin uygulamalı derslere katılmak istemedikleri ve kişisel çalışmayı tercih ettikleri rapor edilmiştir. Çalışmamıza katılım gösteren öğrencilere, "Covid-19 pandemi sonrasında anatomi eğitimi nasıl olmalıdır" sorusu yöneltildiğinde, öğrencilerin %45,9'u "tamamen yüz yüze anatomi eğitimi" yanıtını verirken, buna en yakın oranda olan %37,3'ü "anatomi teorik dersler uzaktan eğitim, pratik dersler yüz yüze eğitimi" tercih ettiğini ifade etmektedir.

Öğrenci geri bildirimleri, eğitici rolünün değerlendirilmesinde kilit taşı konumundadır. Bu yapıcı dönütler sayesinde, eğitim sistemi yeniden düzenlenerek öğrenciye sunulmaktadır. Çalışmamızda, Covid-19 pandemisi sebebiyle "acil" bir şekilde çevrimiçi olarak gerçekleştirilen anatomi eğitimine ilişkin öğrencilerden alınan bu bilgilerin, ilerleyen dönemlerde anatomi eğitiminde yapılacak olan düzenlemelerde önemli katkılar sağlayacağı kanaatindeyiz.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

COVID-19 PANDEMİSİ SÜRECİNDE HEMİPLEJİ HASTALARINDA FONKSİYONELLİK, DEPRESYON VE YAŞAM KALİTESİNİN DEĞERLENDİRİLMESİ

EVALUATION OF FUNCTIONALITY, DEPRESSION AND QUALITY OF LIFE IN HEMIPLEGIC PATIENTS DURING COVID-19 PANDEMIC

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ÖZET

AMAÇ: Bu çalışmada amaç, iskemik veya hemorajik inmeye bağlı hemipleji tanısı ile takipli hastalarda COVİD-19 pandemisi sırasında fonksiyonellik, duygu-durum ve yaşam kalitesindeki değişiklikleri araştırmaktır.

GEREÇ VE YÖNTEM: COVID-19 pandemi döneminden önce inmeye bağlı hemipleji tanısı ile 30 seans rehabilitasyon tedavisi alan 83 hasta (ortalama yaş 62.0±6.43 yıl) çalışmaya dahil edildi. Katılımcıların yaş, cinsiyet, vücut kitle indeksi (VKİ), inme süresi, inme tipi, etkilenen taraf ve eğitim düzeyi ile ilgili veriler kaydedildi. Tüm değerlendirmeler COVID-19 pandemisinden önce yapıldı ve pandeminin başlamasından sonraki ilk yılda tekrarlandı. Hastaların fonksiyonel durumları Fonksiyonel Bağımsızlık Ölçütü (FIM) ile, depresyon düzeyleri Beck Depresyon Envanteri (BDI) kullanılarak, yaşam kaliteleri İnmeye Özgü Yaşam Kalitesi Ölçeği (SS-QOL) ile değerlendirildi.

BULGULAR: COVID-19 öncesi ve pandeminin 1. yılında değerlendirilen hastaların FIM toplam puanlarında istatistiksel olarak anlamlı fark saptandı (91.32±15.94 ve 87.15±15.60, p<0.001). COVID-19 öncesi ve pandeminin 1. yılında hastaların FIM öz bakım skorları sırasıyla 27.45±6.62 ve 25.27±7.08, FIM sfinkter kontrol skorları sırasıyla 10.10±2.56 ve 9.39±2.87, FIM transfer puanları sırasıyla 14.67±3.36 ve 13.61±3.54, FIM sosyal algı puanları sırasıyla 18.40±1.86 ve 17.67±1.93 olarak saptandı (p<0.001). BDI skoru pandemi öncesi 10.06±3.18 ve pandeminin 1. yılında 13.66±3.04, SS-QOL skorları pandemi öncesi 136.48±29.63 ve birinci yıl değerlendirmesinde 133.63±29.63 idi. (p<0.001).

SONUÇ: COVID-19 pandemisi kronik hemiplejili hastalarda hem takip hem de rehabilitasyon tedavisinde gecikmelere neden olmuştur. Rehabilitasyon tedavisinden yoksun kalma ve sosyal izolasyon hastaların fonksiyonelliğini, yaşam kalitesini ve duygu durumunu etkilenmiştir.

ANAHTAR KELİMELER: COVID-19 virüs, Hemipleji, Depresyon, Yaşam kalitesi.

ABSTRACT

OBJECTIVE: The aim of this study was to investigate the changes of the functionality, mood and life quality of patients diagnosed with hemiplegia due to an ischemic or hemorrhagic stroke during the COVID-19 pandemic.

MATERIAL AND METHODS: A total of 83 patients (mean age, 62.0±6.43 years) diagnosed with hemiplegia due to stroke, who received 30 sessions of rehabilitation therapy, before the COVID-19 pandemic, were included in this study. Data regarding the participants' age, gender, body mass index (BMI), duration of stroke, stroke type, affected side, and education level were recorded. All the assessments were undertaken before the COVID-19 pandemic and repeated at the first year after the beginning of the pandemic. The functional status of the patients was evaluated with the Functional Independence Measure (FIM). The depression levels of the participants were evaluated using the Beck Depression Inventory (BDI). The life quality of the participants was evaluated using the Stroke-Specific Quality of Life Scale (SS-QOL).

RESULTS: There were significant differences in the FIM total scores of the patients evaluated before and during COVID-19 (91.32±15.94 and 87.15±15.60, respectively, p<0.001). When the FIM domain scores were evaluated before COVID-19 and at the first-year control during COVID-19, the FIM self-care scores were 27.45±6.62 and 25.27±7.08, respectively, the FIM sphincter control scores were 10.10±2.56 and 9.39±2.87, respectively, the FIM transfers scores were 14.67±3.36 and 13.61±3.54, respectively, the FIM social cognition scores were 18.40±1.86 and 17.67±1.93 respectively (p<0.001). The BDI score was 10.06±3.18 before the pandemic and 13.66±3.04 at the first year of the pandemic, the SS-QOL scores was 136.48±29.63 before the pandemic and 133.63±29.63 at the first year evaluation (p<0.001).

CONCLUSIONS: The COVID-19 pandemic has caused delays in both follow-up and rehabilitation therapy in patients with chronic hemiplegia. The functionality, life quality and mood of the patients have been affected due to the lack of therapy and social isolation.

KEYWORDS: COVID-19 virus, hemiplegia, depression, quality of life.

INTRODUCTION

A new coronavirus called SARS-CoV-2 appeared in December, 2019 in Wuhan, People's Republic of China. The disease caused by this virus, coronavirus disease 2019 (COVID-19), was declared a global pandemic by the World Health Organization (WHO) on March 11, 2020. In many countries of the world, including Turkey, temporary curfews and physical distancing rules have been applied (1, 2). These new rules have affected individuals' participation in daily activities, such as community mobility and access to education, employment and healthcare (3).

WHO has expressed its concern about the psychosocial impacts of the pandemic on individuals and their mental health. During the pandemic, new measures such as quarantine and isolation have affected people's daily lives, habits and routines. These measures have led to an increase in loneliness, anxiety, depression, insomnia, or suicidal behavior (4).

The first case of COVID-19 in Turkey was detected on March 11, 2020. In order to prepare for the increasing number of COVID-19 cases, patients hospitalized due to other reasons were gradually discharged. Elective operations were postponed to reduce intensive care units. The Turkish Society of Physical Medicine and Rehabilitation published a consensus to reduce the infection rate in outpatient clinics, rehabilitation units, and inpatient rehabilitation services. In this guideline, it was recommended to postpone the doctor appointments of elderly patients and those with comorbidities posing a high risk of mortality due to COVID-19 (5).

Stroke is a common, serious and disabling health-care problem throughout the world (6). It is defined as the impairment of brain functions, which causes sudden and rapidly developing clinical symptoms lasting more than 24 hours or death. Stroke is an important health problem, which causes physical and psychological problems and can affect the patients' functionality, quality of life, participation in society. For this reason, the health changes of stroke patients are evaluated with functional and social as recommended in the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization. It is important to determine and measure the effectiveness of rehabilitation by focusing on the patient's physical structure, activities and participation. The rehabilitation program includes all efforts to maximize the physical, mental, social and professional accessibility of stroke patients (7 - 9). Stroke management, including early rehabilitation is crucial. Stroke rehabilitation and follow-up of stroke patients reduce the risk of death, accelerate hospital discharge, and reduce the burden on the health system (10, 11). However, the COVID-19 pandemic has severely limited access to rehabilitation for the patients with stroke-related hemiplegia.

Currently, many inpatients have been discharged from the hospital earlier than they should have been. However, it is important to continue inpatient or outpatient rehabilitation processes in order to reduce the long-term negative effects of the disease and achieve neuroplasticity (11 - 13).

The mood and functionality of hemiplegic patients, who could not have been included in the rehabilitation process for various reasons, such as new restrictions brought by the pandemic and limited access to healthcare services, may have been affected. The aim of this study was to reveal functionality, mood changes and quality of life in hemiplegic patients who could not have received rehabilitation therapy due to the pandemic conditions.

MATERIAL AND METHODS

This retrospective study was conducted between January 2020 and January 2021. A total of 83 patients diagnosed with hemiplegia due to stroke, who received 30 sessions of rehabilitation therapy just before the COVID-19 pandemic, were evaluated in the study. Patients whose Brunnstrom lower extremity stage were between 3 and 5 who were ambulated with an assistive device and over 18 years of age and had been diagnosed with hemiplegia at least six months earlier were included in the study. Patients who received rehabilitation therapy during the pandemic, those who had COVID-19 pneumonia, those with cognitive impairment and those with recurrent cerebrovascular disease were excluded from the study. Patients received 30 sessions of conventional physiotheraphy for 6 weeks, 60 minutes per day, 5 days of the week. The exercise program included upper and lower extremity range of motion, stret-

ching, strengthening exercises, occupational therapy and neural facilitation techniques in accordance with the functional levels of the patients. The basis of strengthening exercises is to strengthen, balance and stabilize the muscles on the affected side of the upper and lower extremities. In resistance exercises, exercises were performed with different colors of theraband according to the muscle strength of the patient. Data regarding the participants' age, gender, body mass index (BMI), duration of stroke, stroke type, affected side, and education level were recorded. All the assessments had been undertaken before the COVID-19 pandemic and were undertaken at the first year of the pandemic. The functional status of the patients was evaluated with Functional Independence Measure (FIM), which uses a scoring based on a seven-point scale (1: total assistance, 7: complete independence) in the categories of self-care, sphincter control, transfers, locomotion, communication and social cognition. In FIM, 13 items evaluate motor functions and five evaluate cognitive functions (14). The validity and reliability studies of the Turkish version of the scale were undertaken by Kucukdeveci et al. (15), who found it suitable to use in Turkish society. The depression levels of the participants were evaluated using the Beck Depression Inventory (BDI), which consists of 21 questions. Each question has a set of at least four possible responses (0-3), ranging in intensity. According to the total scores obtained, 0-9 is considered as normal, 10-19 is considered as mild depression, 20-30 is considered as moderate depression, and 31-63 is considered as severe depression. The validity and reliability of the Turkish version of BDI were proven by Hisli et al (16). The life quality levels of the participants were evaluated using the The Stroke-Specific Quality of Life Scale (SS-QOL), which consists of 49 questions in 12 different categories. Each item is evaluated with a 5-point Likert scale. The validity and reliability of the Turkish version of SS-QOL were proven by Hakverdioglu Yont G. et al (17).

The G.Power3.1 program was used to calculate the power, which was calculated using the baseline value of the FIM Total measurement of 91.32±15.94 and the values of 87.15±15.60 at the 1st year control of the pandemic, with an effect size of 0.26 and a significance level of 0.05 (95% confidence level). In the FIM Total measurement, the power value of the study was found to be 0.83 when 83 sample size and Wilcoxon Paired Two Sample Test were used to examine the differences between before pandemic and the first year of the pandemic.

Ethical Committee

Approval for the study was granted by the Clinical Research Ethics Committee of the Kutahya Health Science University (date/number: 11.11.2021/2021-15/29).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS, IBM, Armonk, NY, USA), version 24.0 was used for statistical analyses. Continuous variables were given as mean ± standard deviation values, and categorical variables as numbers (percentages). Frequency tables and descriptive statistics were used to interpret the findings. The conformity of the variables to the normal distribution was examined by visual (histogram and probability graphs) and analytical (Shapiro-Wilk test) methods. The paired-samples t-test was used for normal distributed data, and the Wilcoxon test for the non-normally distributed data. The significance value was accepted as $p<0.05$.

RESULTS

This study was completed with the participation of 83 hemiplegic patients, 43 female (51.8%) and 40 male (48.2%). **Table 1** presents the age, gender, body mass index, stroke duration, the cause of hemiplegia and education levels of the participants. There were significant differences in the FIM total scores, FIM self-care scores, FIM sphincter control scores, FIM transfers scores, FIM locomotion scores and the FIM social cognition of the patients evaluated before and at the first-year control during COVID-19 ($p<0.001$, $p<0.001$, $p<0.001$, $p<0.001$, $p=0.001$, $p<0.001$, respectively) **(Table 2)**. There was no statistically significant difference in the FIM communication scores of the patients evaluated before and at the first-year control during COVID-19. There were significant differences in the BDI and SS-QOL scores of the patients evaluated before and at the first-year control during COVID-19

(p<0.001, p<0.001, respectively) **(Table 3)**.

Table 1: Demographic characteristics of the group

	(Mean ± SD) (n= 83)	Min-Max (n= 83)
Age (years)	62±6.43	37-75
BMI (kg/m²)	27.38±3.99	20.10-39.30
Chronicity (months)	47.57±31.57	12-132
	n (n= 83)	% (n= 83)
Type of stroke		
Ischemic	76	91.6
Hemorrhagic	7	8.4
Affected side		
Right	46	55.4
Left	37	44.6
Gender		
Female	43	51.8
Male	40	48.2
Education		
Illiterate	12	14.5
Literate	5	6.0
Primary school	52	62.7
High school	5	6.0
University	9	10.8

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

Table 2: Changes in outcomes from the baseline to the first-year follow-up evaluation

	Mean ± SD (n=83)	Min-Max (n=83)	z	p
FIM self-care, baseline	27.45±6,62	28 (15-37)	-6.540	<0.001
FIM self-care, first year	25.27±7.08	26 (11-36)		
FIM sphincter control baseline	10.10±2.56	11 (4-12)	-4.452	<0.001
FIM sphincter control, first year	9.39±2.87	10 (3-12)		
FIM transfers, baseline	14.67±3.36	16 (6-18)	-5.114	<0.001
FIM transfers, first year	13.61±3.54	15 (6-18)		
FIM locomotion, baseline	10.33±3.09	12 (3-12)	-3.217	0.001
FIM locomotion, first year	10.15±3.27	12 (2-12)		
FIM communication, baseline	12.36±1.21	12 (10-14)	0	1.000
FIM communication, first year	12.36±1.21	12 (10-14)		
FIM social cognition, baseline	18.40±1.86	18 (15-21)	-5.115	<0.001
FIM social cognition, first year	17.67±1.93	18 (15-21)		
FIM total, baseline	91.32±15.94	94 (51-113)	-6.728	<0.001
FIM total, first year	87.15±15.60	90 (51-109)		

FIM: Functional Independence Measure, z:Wilcoxon test, *p<0.05

Table 3: Changes in outcomes from the baseline to the first-year follow-up evaluation

	Mean ± SD (n=83)	Min-Max (n=83)	z	p
BDI, baseline	10.08±3.06	10 (5-16)	-6.663	<0.001
BDI, first year	13.66±3.04	14 (6-19)		
SS-QOL, baseline	136.48±29.63	130 (95-206)		
SS-QOL, first year	133.63±29.63	126 (93-207)	-7.896	< 0.001

BDI: Beck Depression Inventory, SS-QOL: Stroke-Specific Quality of Life Scale,z: Wilcoxon test, *p<0.05

DISCUSSION

The COVID-19 has affected the lifestyles and moods of both healthy people and patients across the world, including Turkey. The interruption of standard care, increasing information about COVID-19, fear of quarantine and social isolation have affected the mental and physical health of individuals (18). In our study, it was determined that the mood, functionality and life quality of the patients with chronic hemiplegia were also affected by the pandemic conditions. As in all chronic patients, access to rehabilitation was restricted in patients with hemiplegia due to emergence of COVID-19, and the subsequent declaration of the pandemic (19). Patients began to be discharged from the hospital earlier than expected (20). Significant decreases were observed in the rates of the diagnosis of acute stroke, and hospitalization rates were reduced by almost half compared to the previous year (21). This may be attributed to the decrease in hospital admissions due to fear of COVID-19 although patients have stroke related symptoms.

In our study, the functionality of the patients with chronic hemiplegia who received neurological rehabilitation therapy was found decreased, which may result from the delay in both inpatient and outpatient treatments for a year. Another factor affecting this patient group may be their social isolation during the pandemic. Patients spent most of their time at home and avoided hospital visits although they needed rehabilitation therapy. This may have affected their functionality and increased their depression scores. In a study, 134 chronic stroke patients were evaluated during the COVID-19 pandemic, their access to rehabilitation and other previous health problems they experienced were questioned. It was determined that 72.7% of 134 patients received rehabilitation treatment before the pandemic, only 3% received rehabilitation treatment during the pandemic. As a result, it was concluded that the rehabilitation processes of stroke patients were adversely affected during the COVID-19 pandemic (22).

In another study evaluating the life quality, depression and anxiety status of patients with chronic spinal cord injury during the COVID-19 (between June 2020 and November 2020) an increase was found in depression scores during the pandemic, similar to our study. However, the most important difference from our study is that the authors did not state whether the patient group received treatment. Unlike our study, no significant difference was found in the quality of life scale scores (23). In our study, a statistically significant difference was found in quality of life (stroke-spesific) scales during the pandemic compared to before pandemic. This may be because the quality of life scale used in the assessment in the previous study was not specific to the disease. The Evaluation of the stroke-specific quality of life scale is the superiority of our study, we think that the evaluation with the disease-specific quality of life during the pandemic will be more objective. In another study, in which 344 stroke patients were evalua-

ted before and during the COVID-19 pandemic, the patients were evaluated with 36-item Short Form Health Survey (SF-36), the Activities of Daily Living (ADL) scale, and the Questionnaire about the Process of Recovery (QPR). A significant difference was detected in the SF-36 (physical and mental component scores) of the patients evaluated before and during COVID-19. This was thought to be related to the improvements in patients' personal recovery experience and the treatments received. Unlike this study, our study included patients who did not receive any treatment during the pandemic, so the pandemic period may have had a negative impact on the life quality of these patients (24).

The restriction of patients' access to treatment during the pandemic has revealed the need for telerehabilitation, which can be carried out through video-conferencing, sensor and virtual reality technologies. It has been suggested that telerehabilitation services provided without in-person contact can actually strengthen the communication among the patient, caregiver and healthcare personnel, in addition to reducing the spread of the pandemic. It has also been emphasized that telerehabilitation can be an alternative option for individuals who have to stay at home for various reasons (25, 26). It can be thought that telerehabilitation applications may be even more important during the COVID-19. The common feature of the patients included in our study is that their treatment processes had been completed in the form of a 30-session neurological rehabilitation program just before the pandemic started. Patients who had a history of recurrent cerebrovascular disease, another systemic disease or COVID-19 was excluded from the study. The patient group was small because of, this reason, patients who received rehabilitation during the pandemic were excluded from the evaluation.

The other limitations of the study are its retrospective nature and absence of a control group. Restrictions applied during the COVID-19 pandemic have caused delays in the treatment and follow-up of patients with chronic diseases. In our study, we determined that rehabilitation restriction in patients with chronic hemiplegia affected not only their functional status but also their emotional state and quality of life.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

DİŞ HEKİMLERİNİN DİŞ ÇIKARMA JELLERİ İLE İLGİLİ YAKLAŞIMLARI VE BİLGİ DÜZEYLERİ

THE DENTISTS' ATTITUDES AND KNOWLEDGE LEVEL ABOUT TEETHING GELS

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ÖZET

AMAÇ: Çalışmanın amacı, bir grup Türk diş hekiminin diş çıkarma jelleri konusundaki yaklaşımlarını ve bilgi düzeylerini değerlendirmektir.

GEREÇ VE YÖNTEM: Bu kesitsel çalışma için, iletişim bilgilerine ulaşılabilen diş hekimlerine (n=1829) üç bölüm ve yirmi sorudan oluşan bir anket gönderilmiştir. Reçete edilen her diş çıkarma jelinin içeriği, dozu ve yan etkileri için ayrı kategoriler oluşturulmuştur. Reçete edilen tüm jeller dikkate alınarak, diş hekimlerinin bilgi düzeyinin yüzdesi hesaplanmıştır.

BULGULAR: Çalışmaya toplam 484 diş hekimi dahil edildi. Araştırmaya katılan diş hekimlerinin yaklaşık yarısı (%51,2) ayda en az bir diş çıkarma jeli reçete ettiğini bildirdi. En çok reçete edilen diş çıkarma jelleri lidokain bazlı jeller (%70,9) olurken, bunu hyaluronik asit bazlı (%61,4) ve bitkisel bazlı jeller (%36) izledi. Diş hekimlerinin diş çıkarma jellerinin etken maddesi, dozu ve yan etkileri hakkındaki bilgi düzeyi medyanları sırasıyla %50, %25 ve %20 olduğu bulundu. Meslekteki yılı fazla olan dişhekimleri, jellerin etken maddesi ve yan etkileri hakkında mesleğe yeni başlayanlara göre daha fazla bilgiye sahipti (p<0.05). Yaşları 20-30 arasında olan diş hekimleri jel dozajı konusunda daha fazla bilgiye sahipti (p<0.05). Pedodontistler ve oral cerrahların jellerin yan etkileri konusundaki bilgi düzeylerinin diğer branşlara göre daha yüksek olduğu bulundu. (p<0.05). Uzman olmayan diş hekimlerinin diş çıkarma jelleri hakkındaki bilgi düzeyleri, uzman diş hekimlerine göre anlamlı düzeyde daha düşüktü (p<0.05).

SONUÇ: Sonuç olarak, diş hekimlerinin diş çıkarma jelleri hakkında yetersiz bilgiye sahip olduğu bulunmuştur. Diş hekimlerinin, bu jellerin yanlış ve kontrolsüz kullanımını önleyebilmek için daha fazla eğitime ihtiyacı bulunmaktadır.

ANAHTAR KELİMELER: Diş hekimleri, Lidokain, Diş çıkarma jelleri, Diş sürmesi.

ABSTRACT

OBJECTIVE: The aim of the study was to evaluate a group of Turkish dentists' attitudes and level of knowledge about teething gels.

MATERIAL AND METHODS: For this cross-sectional study, a questionnaire consisting of three parts and twenty questions was sent to dentists (n=1829) whose contact information could be reached. Separate categories were created for ingredients, dosage, and side effects of each prescribed teething gel. The percentages of the knowledge level of the dentists were calculated considering all prescribed gels.

RESULTS: A total of 484 dentists were included in the study. Approximately half of the dentists (51.2%) participating in the study reported that they prescribed at least one teething gel per month. The most commonly prescribed teething gels were lidocaine-based gels (70.9%), followed by hyaluronic acid-based (61.4%) and herbal-based gels (36%). The medians of the knowledge level of dentists about active ingredients, dosage, and side effects of teething gels were 50%, 25%, and 20%, respectively. Dentists with more years in the profession have more knowledge about the active ingredient and side effects of gels than those who are newer in the profession (p<0.05). Dentists with the aged between 20-30 years had more knowledge about the dosage of gels (p<0.05). It was found that the knowledge level of pediatric dentists and oral surgeons about the side effects of gels was higher than other branches. (p<0.05). The knowledge level about teething gels of non-specialist dentists was significantly lower than specialists (p<0.05).

CONCLUSIONS: In conclusion, it was found that dentists had insufficient knowledge about teething gels. Dentists need more education to prevent misuse and uncontrolled use of these gels.

KEYWORDS: Dentists, Lidocaine, Teething gels, Tooth eruption.

INTRODUCTION

Teething gels can be used for various purposes such as treating oral aphthous ulcers, providing anti-inflammatory activity in periodontal diseases, and accelerating healing in the post-oral surgery period, as well as teething symptoms (1 - 4). There are numerous types of teething gels. These gels can contain local anesthetic agents such as lidocaine and benzocaine, analgesic substances such as choline salicylate, and substances in the basic structure of the body such as hyaluronic acid. Today, the increasing interest in healthy living has led to an increase in the demand for products with natural ingredients, so many natural-containing teething gels such as black mulberry, clove, aloe vera, peppermint, calendula or chamomile extracts have been introduced to the market (5). Especially, when using products that claim to be natural, there is a strong misconception that there are no side effects and no dosage adjustment is necessary. Information on the prospectuses of these products, which can be accessed without a prescription, is also missing. However, numerous studies and case reports regarding the side effects of these products have been found in the literature (4, 6, 7). Unconscious use of teething gels can cause severe consequences of a chemical burn, aspiration, methemoglobinemia, allergy, seizures, or cardiac arrest (8, 9).

Today, although there is not sufficient scientific evidence to support the effectiveness of teething gels, both parents and health professionals frequently preferred these products (5, 10). Wake et al. (10) reported that dentists, nurses, pharmacists, and pediatricians were widely recommended for teething gels. The rate of recommending the use of teething gels by healthcare professionals was 19.3% in a study (11). This rate was reported as 30% in another study considering pediatricians (12). These gels can be prescribed by health professionals, and they can also be sold without a prescription. In a study, it was reported that the majority of pharmacists still recommend a benzocaine-containing product incorrectly (13). When the parent surveys conducted in various countries are examined, it is found that the use of teething gels varies between 4.4% and 73.4% (14 - 18).

There are limited studies in the accessible literature focusing on teething gels (8, 19-22). To the best of the authors' knowledge, there is no study on the knowledge level of dentists about teething gels. The aim of the study is to evaluate a group of dentists' approaches and knowledge about teething gels.

MATERIAL AND METHODS

The study was a cross-sectional survey using an online researcher-made questionnaire on Google Forms to investigate the self-reported knowledge and attitudes of dentists about teething gels.

Participants were recruited from the population of qualified dentists working in Türkiye. E-mails from dentists were reached through various channels (Turkish Dental Association, government/private hospitals websites, university websites, and social media). The invitation to participate included information outlining the research and a link to the online questionnaire. The inclusion criteria were dentists who agreed to participate in the study via an online questionnaire link and who have prescribed teething gels at least once in the past year. The dentists who work in Türkiye (n=1829) and whose contact information was provided were invited to participate in the survey. The e-mail invitations were sent on 4th February 2022. A reminder was sent two weeks after the initial invitation. The questionnaire link was accessible to invited participants for two months and closed on 4th April 2022.

The questionnaire was written in the Turkish language. The questionnaire was self-constructed and piloted with a small group of dentists (n=20) before implementation and modified according to the feedback received. The pilot study applied to participants, including 8 specialist dentists, 8 research assistants from all branches, and 4 general dentists. In addition, supervision was received from a statistician and a pharmacologist for validity. Participants made comprehensive suggestions so that the con-

tent of the questionnaire reflects the purpose of the research. The content of the questionnaire was reviewed in line with these feedbacks.

The questionnaire comprises 3 parts and 20 questions in total. In the first part, there are 6 questions about the demographic characteristics of the participants, 10 questions in the second part that evaluate the practice and approaches of dentists about teething gels, and in the third part one self-reported question 'Which teething gels do you prescribed?', and according to this question answers, 3 questions that measure their knowledge level about content, dosage and side effects of each teething gels which they reported prescribing. A scoring system has been determined by the researchers. Separate categories have been created for the ingredients, dosage and side effects of each prescribed teething gel. One (1) point was given if they knew the active ingredient / dosage/side effect of each teething gel. Zero (0) point was given if they stated they did not know the active ingredient/dose/side effect of each teething gel or if the answers were wrong. For dentists' level of knowledge about all the teething gels they prescribed the overall total score constituted the denominator, the score obtained with the defined criteria is placed on the numerator and the "percent (%)" of the knowledge level of the dentist was calculated.

Ethical Committee

The Local Ethics Committee of the Faculty of Medicine (Afyonkarahisar Health Sciences University, approval no. 2022/2-213) approved the study.

Statistical Analysis

The data were tabulated on a Microsoft Excel spreadsheet and then imported into IBM SPSS Statistics Package Program (version 26; Inc., Chicago, USA). The demographic data of this study were tabularized in number and percentage. The Kolmogorov-Smirnov test was done for verifying the normality of the data distribution. Comparison of the knowledge scores between genders was done with independent samples Mann-Whitney U test, other subgroups were done with the Kruskal-Wallis H test. A significant level was considered as $p<0.05$.

RESULTS

A total of 484 dentists (286 female, 198 male), met the inclusion criteria and completed the questionnaire. Of the dentists who sent a questionnaire for the study, 53.1% (n=971) did not respond, 18.4% (n=336) reported that they did not prescribe any teething gel, and 2.1% (n=38) were excluded because they filled the forms incompletely. Most of the respondents were general dentists (34.7%) and pediatric dentists (24%). According to the working place of dentists, 56.6% of them work in a university hospital, 25% in private clinic\hospital, and 18.4% in government hospitals. The distribution of the participants according to their demographic characteristics is shown in **Table 1**.

Table1: Demographic status of participants

		Number (n)	Percentage (%)
Gender	Female	286	59.1
	Male	198	40.9
Age	20-30	300	62.0
	30-40	120	24.8
	>40	64	13.2
Year of profession	0-5 years	287	59.3
	5-10 years	111	22.9
	>10 years	86	17.8
Profession	Oral and maxillofacial radiology	15	3.1
	Oral and maxillofacial surgery	68	14.0
	General dentist	168	34.7
	Endodontics	11	2.3
	Orthodontics	21	4.3
	Pediatric Dentistry	116	24.0
	Periodontology	50	10.3
	Prosthetic Dentistry	10	2.1
	Restorative Dentistry	25	5.2
Specialty	Not specialist	188	38.8
	Specialist	136	28.1
	Research assistant	160	33.1
Work place	Government hospital	89	18.4
	Private clinic/ hospital	121	25.0
	University hospital	274	56.6

Attitudes of the dentists towards teething gels were shown in **Table 2**. Nearly half of the dentists (51.2%) stated that they prescribed teething gels once a month. The most prescribed teething gels were lidocaine-based gels (70.9%), followed by hyaluronic acid-based (61.4%) and herbal-based gels (36%). The active ingredients and dosage of these teething gels were shown in **Table 3**. In the study, 80.4% of the dentists stated they received no feedback from their patients after prescribing teething gels.

The answers of the dentists to the question 'Which teething gel or gels do you prefer?' varied between 1 to 6 different trademarks and

16.1% of the dentists choose one teething gel, 27.9% of dentists choose two, 29.8% of the dentists choose three, 16.1% of the dentists choose four, 7.6% of the dentists choose five, and 2.5% choose six different teething gels. For each selected teething gel, their active ingredients, dosage, and side effects were asked. The median knowledge level of the dentists about the active ingredient of teething gels was 50%, about dosage was 25%, and the side effects were 20%.

Dentists with more years in the profession have more knowledge about the active ingredient and side effects of gels than those who are newer in the profession (p<0.001). Dentists between the age of 20-30 years have more knowledge about the dosage of gels (p=0.001). It was found that the knowledge level of pediatric dentists and oral surgeons about the side effects of gels was higher than other professions (p<0.001). The knowledge level about teething gels of non-specialist dentists was significantly lower than specialists (p<0.05). The distribution of knowledge levels according to different subgroups is shown in **Table 4**.

Table 2: Attitudes of the dentists towards teething gels

Questions	Answers	Number of dentists (n)	Percentage %
Q1.How often do you prescribe teething gels?	Once a week	4	0.8
	Two or more times a week	1	0.2
	Once a month	248	51.2
	Two or more times a month	29	6
	Rarely (once or twice a year)	202	41.7
Q2. For which problem/problems do you prescribe teething gels?	Teething symptoms	316	65.3
	Oral ulcers	194	40.1
	Wound healing after oral surgery	39	8.1
Q3.What is your purpose in prescribing teethIng gels?	Reducing pain	304	62.8
	Reducing inflammation	211	43.6
	Promote wound healing	39	8.1
	Reducing swelling	25	5.2
	Reducing irritability	21	4.3
	Reducing saliva	5	1
	Reducing fever	5	1
	Reducing itching	3	0.6
Q4. What is the most important factor affecting your choice of a teething gel?	Active ingredient of the gel	274	56.6
	Patient's feedback	84	17.3
	Cost of the gel	82	16.9
	Advertisement of the gel	48	9.9
	Taste of the gel	22	4.5
Q5.Which source/sources do you use for teething gel prescription?	Pharma representatives	124	25.6
	Internet/social media promotions	122	25.2
	Scientific articles	101	20.9
	Colleague comments	87	18
	Meetings/ congresses	33	6.8
	Patient request	22	4.5
Q6.Which teething gel/gels do you prescribe?	Lidocaine-based gels	343	70.9
	Benzocaine-based gels	39	8.1
	Choline salicylate-based gels	96	19.8
	Hyaluronic acid-based gels	297	61.4
	Herbal-based gels	174	36
Q7.Do you inform your patients about the dosage of teething gel?	Always	61	12.6
	Often	83	17.1
	Occasionally	102	21.1
	Rarely	231	47.7
	Never	7	1.4
Q8.Do you inform your patients about the usage of teething gel?	Always	89	18.4
	Often	127	26.2
	Occasionally	65	13.4
	Rarely	199	41.1
	Never	4	0.8
Q9.Do you inform your patients about the side effects of teething gel?	Always	3	0.6
	Often	25	5.2
	Occasionally	37	7.6
	Rarely	227	46.9
	Never	192	39.7
Q10. How was the feedback of the patients you prescribed teething gel?	Positive feedback	78	16.1
	Negative feedback	17	3.5
	No feedback	389	80.4

Table 3: The active ingredients and dosage of different teething gels prescribed by the dentists in the study

Teething gel	Active ingredient	Dosage in prospectus
Calgel® teething gel (GlaxoSmithKline, UK)	Lidocaine-based teething gel	Apply gel as big as chickpeas. Do not apply repetitively for more than three hours. It should not be used no more than 6 times in a day.
Dentinox® teething gel (Abdi Ibrahim, TURKEY)	Lidocaine-based teething gel	Apply 2-3 times a day
Aftamed® teething gel (Bioplax Pharma, UK)	Hyaluronic-acid based teething gel	Apply 3-6 times a day
Gengigel® teething gel (Dentocare, UK)	Hyaluronic-acid based teething gel	Apply 3-6 times a day
Dencol® teething gel (Berko Pharma, TURKEY)	Choline-salicylate based teething gel	Apply 1 puff 4 times a day
Tetagil® teething granule (Medfors Pharma, TURKEY)	Herbal-based teething gel	It is recommended to use the granules in the sachet every two hours orally, up to a maximum of 6 sachets per day.
Jack N' Jill® teething gel (Jack N'Jill, AUSTRALIA)	Herbal-based teething gel	Apply 4 times daily

Table 4: Knowledge level of the dentists about teething gels

		KNOWLEDGE ABOUT ACTIVE INGREDIENT	P VALUE	KNOWLEDGE ABOUT DOSAGE	P VALUE	KNOWLEDGE ABOUT SIDE EFFECTS	P VALUE
GENDER	Female	66.7 (0 - 100)	<0.001	0 (0 - 100)	NS	0 (0 - 100)	0.004
	Male	33.3 (0 - 100)		33.3 (0 - 100)		29.2 (0 - 100)	
AGE	20-30	50 (0 - 100)ᵃ	0.003	25 (0 - 100)ᵃ	0.001	0 (0 - 100)ᵃ	<0.001
	30-40	50 (0 - 100)ᵃ		0 (0 - 100)ᵃ		20 (0 - 100)ᵃ	
	>40	75 (0 - 100)ᵇ		0 (0 - 100)ᵇ		50 (0 - 100)ᵇ	
YEAR OF PROFESSION	0-5	50 (0 - 100)ᵃ	<0.001	25 (0 - 100)ᵃ	0.001	0 (0 - 100)ᵃ	<0.001
	5-10	33.3 (0 - 100)ᵇ		0 (0 - 100)ᵇ		0 (0 - 100)ᵃ	
	>10	66.7 (0 - 100)ᶜ		0 (0 - 100)ᵇ		80 (0 - 100)ᵇ	
BRANCHES	Oral and maxillofacial radiology	0 (0 - 100)ᵃ	<0.001	0 (0 - 100)ᵃ	<0.001	0 (0 - 100)ᵃ	<0.001
	Oral and maxillofacial surgery	41.7 (0 - 100)ᵇ		33.3 (0 – 100)ᵃ		50 (0 - 100)ᵇ	
	General dentist	0 (0 - 100)ᵃ		0 (0 - 50)ᵃ		0 (0 - 100)ᵃ	
	Endodontics	40 (0 - 66.7)ᵃᵇ		0 (0 - 50)ᵃ		0 (0 - 50)ᵃ	
	Orthodontics	0 (0 - 50)ᵃ		0 (0 - 50)ᵃ		0 (0 - 50)ᵃ	
	Pediatric Dentistry	100 (0 - 100)ᵇ		50 (0 - 100)ᵇ		50 (0 - 75)ᵇ	
	Periodontology	66.7 (0 - 100)ᵇ		0 (0 - 100)ᵃ		0 (0 - 100)ᵃ	
	Prosthetic Dentistry	50 (0 - 100)ᵇ		50 (0 - 50)ᵇ		0 (0 - 100)ᵃ	
	Restorative Dentistry	33.3 (0 - 100)ᵃ		0 (0 - 40)ᵃ		0 (0 - 40)ᵃ	
SPECIALITY	Not specialist	33.3 (0 - 100)ᵃ	<0.001	0 (0 - 100)ᵃ	0.046	0 (0 - 83.3)ᵃ	<0.001
	Specialist	66.7 (0 - 100)ᵇ		33.3 (0 - 100)ᵇ		50 (0 - 100)ᵇ	
	Research assistant	50 (0 - 100)ᵇ		25 (0 - 100)ᵇ		33.3 (0 - 100)ᵇ	
WORK PLACE	University hospital	66.7 (0 - 100)ᵃ	0.024	25 (0 - 100)	NS	50 (0 - 100)ᵃ	<0.001
	Private clinic/ hospital	66.7 (0 - 100)ᵃ		0 (0 - 100)		33.3 (0 - 100)ᵃ	
	Government hospital	50 (0 - 100)ᵇ		25 (0 - 100)		0 (0 - 100)ᵇ	

NOTE: Kruskal-Wallis H test, NS: Non-significant (p>0.05), ᵃ˒ᵇ˒ᶜ: Each subscript letter denotes a subset of group categories whose column properties do not differ significantly from each other at the 0.05 level.

DISCUSSION

Teething gels can be used for various purposes, such as providing anesthesia, analgesia, sedation, or a combination of all of them. Teething gels can be used in the treatment of oral aphthae, and mucosal ulcers and in the healing process of mouth sores, as well as relieving teething symptoms (1-3, 23). In this study, 65.3%

of the dentists stated they used gels for teething symptoms, 40.1% for oral ulcers, and 8.1% for wound healing after oral surgery. Although warnings from the Food and Drug Administration (FDA) and American Academy of Pediatrics Dentistry (AAPD) about the unconscious use of gels, it was found that dentists preferred to prescribe them, especially for teething symptoms of babies (24, 25). Because of the limited number of studies on teething gels in the accessible literature, this study aimed to evaluate the current approaches and knowledge levels of dentists about teething gels (8, 19-22).

There are numerous types of teething gels. They may vary in terms of ingredients, taste, texture, and functional characteristics. In this study, 56.6% of the dentists reported they focused on the active ingredient of the teething gel while prescribing. The most prescribed teething gels were lidocaine-based gels (70.9%), followed by hyaluronic acid-based (61.4%) However, the median of the knowledge level of dentists about active ingredients of teething gels was 50%. The limited number of patients who consult dentists with teething complaints and the insufficient experience in pharmacological treatments can explain the result (26 - 28). In the present study, the level of knowledge about teething gels of non-specialist dentists was significantly lower than specialists and research assistants. Unfortunately, this result also shows the inadequacy of continuous dentistry education programs and not following up-to-date literature and new product information. As another result of the study, the knowledge of female dentists about the dosage and side effects of teething gels were found insufficient. It can be associated with the effect of advertisements or social media by female dentists only caring about the ingredient of teething gels. Teething gels can be sold without a prescription, and it has been reported that topical products can be applied to babies by parents for months or even years during this period (29). In most of the prospectus of these products, there is no sufficient information about the pharmacokinetic and pharmacodynamic properties, possible side effects, or appropriate

dosage. During the application of the gel into the oral cavity, it mixes rapidly with the saliva, and the risk of swallowing increases. Therefore, it is difficult to determine the correct dosage (8). Incorrect dosage is the most frequently reported type of medication error in pediatric patients. In addition, differences in children's weight, body surface area, and organ development may affect the metabolism and excretion of high-dose drug intake from the body. As children's renal, immune, and hepatic functions continue to develop, it causes younger children to tolerate drug dose errors less (30).

In the present study, the dosage information of teething gels was found to be insufficient (25%). In order to prevent life-threatening overdoses, manufacturers should provide detailed information about the dose, dentists should increase their knowledge about the dosage and convey this information to their patients. Besides that, in this study the decrease in drug dose information with increasing age and the fact that the dose information of non-specialists is less than that of specialists indicates it is necessary to update the existing information of dentists.

Although there is not enough evidence about the therapeutic effects of teething gels in previous studies, most of the authors emphasized the side effects of them (4, 7, 8, 31). Topical anesthetics can cause iatrogenic oral mucosal trauma, sensitivity, or choking. Ingestion of these gels also numbs the child's mucous membranes and increases the risk of aspiration. Aspirated anesthetic agents will be absorbed directly through the respiratory tract and circulate to the central nervous system without undergoing liver metabolism (25, 32, 33). Lidocaine-based teething gels, which were the most commonly prescribed teething gels among dentists in this study (70.9%), can cause paresthesia, hypotension, seizures, bradycardia, and cardiac arrest (8, 9). In 2011, FDA issued a warning to avoid using gels containing benzocaine, due to the risk of methemoglobinemia (34). In a study in England, it was determined that sucrose and alcohol can be found in teething gels and it was also reported that sucrose in gels may lead to the formation of caries, and the alcohol content may cause

developmental problems (6). Various pediatricians and pharmacists advocate avoiding choline salicylate-based teething gels because of the risk of Reye's syndrome, salicylate poisoning, chemical burn, congestive heart failure, and metabolic acidosis (5). Symptoms can appear after the first dose or after several uses of these gels (8). Despite serious side effects were reported in the previous studies, it was found that the knowledge level of the dentists about side effects of teething gels was quite inadequate in the present study (20%). This result can be associated with the fact that dentists mostly use the recommendations of pharmaceutical company representatives or online product advertisements as a source for gel selection. Scientific articles were used as a knowledge source by only 20.9% of the dentists. The fact that no feedback was received from most of the patients is thought to be one reason for not getting sufficient data about the effects of gels. Besides the insufficient knowledge of dentists about the side effects of gels, almost half of the dentists (46.9%) in the study stated that they rarely warn patients about this issue. These gels should be used under medical supervision, due to the risk of side effects, which can be serious although rare.

The limitation of the study was the sampling because the study group did not represent sufficient populations. In the study, only the knowledge level of a group of Turkish dentists who prescribed teething gels was discussed. However, these gels can be prescribed by other medical doctors or sold without a prescription. Therefore, a more sophisticated survey with a larger population size that includes other professions and multiple geographical areas is required. However, the study can serve as a baseline for future more extensive community-based research. In future studies, it will be more beneficial to include over-the-counter folkloric teething mixtures. In conclusion, the level of knowledge of dentists about teething gels is incomplete. There is a gap in the literature on the efficacy, appropriate dosage, cytotoxicity, genotoxicity, or allergy potential of teething gels. Dentists should have the education to change the misconceptions and uncontrolled use of the teething gels.

Using these gels should be limited and carefully monitored, drug interactions should be evaluated, and patients should be informed about the dosage. Especially, pediatric dentists and pediatricians who usually deal with young children should also convey the correct information about these gels, which can be accessed without a prescription, to the parents.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

TIP FAKÜLTESİ ÖĞRENCİLERİNDE SİBERKONDRİA, SAĞLIK ANKSİYETESİ VE İNTERNET BAĞIMLILIĞI DÜZEYLERİ

LEVELS OF CYBERCHONDRIA, HEALTH ANXIETY AND INTERNET ADDICTION IN MEDICAL FACULTY STUDENTS

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ÖZET

AMAÇ: Bu çalışmada tıp fakültesi öğrencilerinin siberkondria, sağlık kaygısı ve internet bağımlılığı düzeylerinin diğer fakülte öğrencileri ile karşılaştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM: Çalışmaya tıp fakültesinde eğitim gören 223 öğrenci ve diğer fakültelerde eğitim gören 211 öğrenci dahil edilmiştir. Hemşirelik vb. gibi sağlıkla ilgili fakültelerde okuyan öğrenciler çalışmaya dahil edilmemiştir. Tüm katılımcılara sosyo-demografik veri formu, Siberkondria Şiddet Ölçeği (SŞÖ), Sağlık Anksiyetesi Envanteri (SAE) ve Young İnternet Bağımlılığı Ölçeği (YİBÖ) uygulanmıştır.

BULGULAR: Tıp fakültesi öğrencilerinin yaş ortalaması (21.27±2.27 yıl) diğer fakülte öğrencilerinin yaş ortalaması ile (21.38±2.05 yıl) benzer bulundu (p=0.440). SAE puan ortalamaları tıp fakültesi öğrencilerinde diğer fakülte öğrencilerinden anlamlı olarak yüksek saptanmıştır (p=0.007). Her iki grupta YİBÖ ve SŞÖ puanları benzer saptanmıştır (sırayla; p=0.536, p=0.960). Pre-klinik sınıflardaki tıp fakültesi öğrencilerinde YİBÖ puanları ve SŞÖ puanları klinik sınıflardaki öğrencilerden yüksek saptanmıştır (sırayla; p=0.017, p<0.001). Tüm katılımcılarda yaş arttıkça YİBÖ puanları azalmıştır (r= -0.119, p=0.013).

SONUÇ: Tıp fakültesi öğrencilerinde sağlık kaygısının daha fazla olduğu söylenebilir. Ayrıca pre-klinik sınıflardaki tıp fakültesi öğrencilerinde siberkondria düzeyleri ve internet bağımlılığı düzeyleri klinik sınıflardan daha yüksektir. Hastalıklarla ilgili bilgilerin yoğun şekilde arttığı tıp fakültesi eğitiminde sağlık kaygısı ve siberkondria hakkında öğrencilerin farkındalık düzeylerinin arttırılmasını öneriyoruz.

ANAHTAR KELİMELER: İnternet, Tıp Fakültesi, Anksiyete, Siberkondria, Sağlık kaygısı.

ABSTRACT

OBJECTIVE: In this study, it was aimed to compare the levels of cyberchondria, health anxiety and internet addiction of medical faculty students with other faculty students.

MATERIAL AND METHODS: 223 students studying at the faculty of medicine and 211 students studying at other faculties were included in the study. Students studying in health-related faculties such as nursing etc. were not included in the study. Socio-demographic data form, Cyberchondria Severity Scale (CSS), Health Anxiety Inventory (HAI), and Young Internet Addiction Scale (YIAS) were administered to all participants.

RESULTS: The mean age of medical faculty students (21.27±2.27 years) was found to be similar to the mean age of other faculty students (21.38±2.05 years) (p=0.440). HAI mean scores were found to be significantly higher in medical faculty students than in other faculties (p=0.007). YIAS and CSS scores were found to be similar in both groups (respectively; p=0.536, p=0.960). YIAS scores and CSS scores of medical faculty students in pre-clinical classes were higher than those in clinical classes (respectively; p=0.017, p<0.001). As the age increased in all participants, the YIAS scores decreased (r= -0.119, p=0.013).

CONCLUSIONS: It can be said that health anxiety is higher in medical faculty students. In addition, cyberchondria levels and internet addiction levels are higher in medical school students in pre-clinical classes than in clinical classes. We suggest that the awareness levels of students about health anxiety and cyberchondria should be increased in medical school education, where the knowledge about diseases increases intensively.

KEYWORDS: Internet, Medical Faculty, Anxiety, Cyberchondria, Health anxiety.

INTRODUCTION

Medical school students are under many stresses, such as a long and challenging education, academic pressure, and difficulties in clinical practice (1). For all these reasons, it is reported that medical school students experience more depression and anxiety compared to their peers (2). It has been reported that health anxiety is also high among medical faculty students. In a study conducted with 270 medical faculty students, health anxiety was reported in 17% of the participants (3). Medical students are more likely to associate the signs and symptoms of medical illness with their body sensations therefore, more likely to develop health anxiety. It is interpreted as a condition caused by excessive exposure to medical information (4, 5).

Cyberchondria is excessive or repetitive online health-related information seeking associated with increased health anxiety (6). Medical faculty students are exposed to more medical information that can increase susceptibility to cyberchondria, especially in the early years of medical education (7). Although studies report a relatively high prevalence of cyberchondria among medical faculty students, cyberchondria in this group has not been adequately studied (8). The literature also reported a relationship between cyberchondria and health anxiety (9). It is reported that internet addiction is also high among medical faculty students. A meta-analysis reported that the prevalence of internet addiction among medical faculty students was approximately five times higher than the general population (10). It is also known that there are relationships between internet addiction and health anxiety, as well as internet addiction and cyberchondria (11, 12).

In this study, we aimed to investigate the difference in health anxiety, cyberchondria, and internet addiction levels between medical school students and other faculty students.

MATERIAL AND METHODS

Sample

We contacted the student representatives of each faculty face-to-face and reached the students who agreed to participate in the study via messaging programs using their phone numbers.

Since the faculty representative directed the students who accepted to participate, the department they studied was known. We also talked to the students on the phone and confirmed the faculty they were studying. Other departments included in the study are the faculty of law, the faculty of sports sciences, and the faculty of communication. The total number of students in these departments is around 3000. The number of students in the faculty of medicine is approximately 1500. Our study is a cross-sectional type and was conducted between November 1, 2021, and April 1, 2022. Inclusion criteria for the study were being between the ages of 18-30, having voluntary participation in the study, having no history of psychiatric disease and chronic physical disease, and having internet access. Exclusion criteria for the study were being a health-related faculty-student (nursing faculty, faculty of health sciences, etc.) and receiving treatment for a disease. Socio-demographic data form, Young Internet Addiction Scale (YIAS) (13), Cyberchondria Severity Scale (CSS) (14), and Health Anxiety Inventory (HAI) (15) were administered to all participants. The surveys were created using Google Docs. We sent an introductory note explaining the purpose of the study in detail and an assurance note that the confidentiality of the data would be protected to all participants. A confirmation tab was added stating that participation in the study was on a voluntary basis, and online consent was obtained from those who voluntarily agreed to participate. Those who did not give consent could not have participated in the study. After obtaining informed consent, those who agreed to participate in the study were able to continue to fill out the scales. This survey was sent to the respondents via WhatsApp Messenger, an American free messaging software owned by Facebook Inc.

Ethical Committee

All stages of this study were carried out in accordance with the Declaration of Helsinki. Written ethics committee approval was obtained for our study from Akdeniz University Faculty of Medicine Clinical Research Ethics Committee with the decision number KAEK-729 on 13.10.2021.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) 23.0 program was used for statistical analysis. Categorical data have been given as numbers and percentages and continuous variables have been given as mean and standard deviation. The conformity of the data to the normal distribution was evaluated with the Kolmogorov-Smirnov test. The Mann-Whitney U Test was used as a non-parametric test to compare the numerical data of the two groups. Chi-square test was used to compare the categorical data. The relationship between the numerical data that did not conform to the normal distribution was evaluated with the Spearman correlation test. The statistical significance level (p-value) was accepted as 0.05 in the analyzes.

RESULTS

The mean age of medical faculty students was 21.27±2.27 years, and the mean age of students from other faculties was 21.38±2.05 years (p=0.440). All participants are single, and other socio-demographic data are summarized in **Table 1**.

Table 1: Comparison of the groups in terms of socio-demographic characteristics

		Medical School (n=223)		Other Faculties (n=211)		
		n	%	n	%	p
Gender	Male	93	41.7	65	30.8	0.018
	Female	130	58.3	146	69.2	
Life style	Alone	55	24.7	32	15.2	0.015
	With family	65	29.1	86	40.8	
	With friends	33	14.8	23	10.9	
	Student hostel	70	31.4	70	33.1	
Medical school classes	Pre-clinical	122	54.7			
	Clinical	101	45.3			
Age (years) (mean±SD)		21.27±2.27		21.38±2.05		0.440

The comparison of medical school students and other faculty students in terms of internet usage time, CSS scores, YIAS scores, and HAI scores is summarized in **Table 2**.

Table 2: Comparison of the groups in terms of duration of internet use, cyberchondria, internet addiction, and health anxiety

	Medical School (n=223) (mean±SD)	Other Faculties (n=211) (mean±SD)	p
Young Internet Addiction Scale	32.12±16.21	30.44±14.30	0.536
Cyberchondria Severity Scale	43.98±21.77	43.27±21.64	0.960
Health Anxiety Inventory	18.52±7.58	16.46±7.40	0.007
Daily Internet Usage Time (hours)	4.87±2.62	5.18±3.23	0.784

The relationships between age, duration of internet use, CSS, YIAS, and HAI scores of all participants are summarized in **Table 3**.

Table 3: Relationships between age, duration of internet use, cyberchondria, internet addiction, and health anxiety in all participants

	Age	YIAS*	Internet time	CSS*	HAI*
Age		-0.119**	-0.019	-0.124**	0.011
YIAS*	-0.119**		0.280***	0.217***	0.114**
Internet time	-0.019	0.280***		0.050	0.095**
CSS*	-0.124**	0.217***	0.050		0.405***
HAI*	0.011	0.114**	0.095**	0.405***	

-All values are correlation coefficients.
*YIAS: Young Internet Addiction Scale, CSS: Cyberchondria Severity Scale, HAI: Health Anxiety Inventory
**p<0.05
***p<0.001

Medical faculty students were divided into two groups as pre-clinical period (1st, 2nd, and 3rd grade) (n=122) and clinical period (4th, 5th, and 6th grades) (n=101). The mean YIAS score was found to be significantly higher in the pre-clinical period (34.12±15.73) than in the clinical period (29.71±16.52) (p=0.017). The mean duration of internet use was similar in the pre-clinical period (4.99±2.79 hours) and in the clinical period (4.73±2.41 hours) (p=0.625). The mean CSS scores were found to be significantly higher in the pre-clinical period (47.98±19.67) than in the clinical period (39.14±23.26) (p<0.001). HAI mean scores were similar in the pre-clinical period (18.77±7.31) and in the clinical period (18.22±7.91) (p=0.694). In addition, CSS scores decreased significantly from grade 1 to grade 6 (r=-0.199, p=0.003). Men and women were compared among all participants. CSS, YIAS, and HAI scores were found similar between men and women (respectively; p=0.624, p=0.190, p=0.814).

DISCUSSION

In our study, health anxiety scores were higher in medical faculty students than students from other faculties, and no difference was found in cyberchondria and internet addiction scores. Cyberchondria and internet addiction scores of medical faculty students studying in the preclinical years were found higher than the students studying in the clinical years. Internet addiction scores decreased as age increased in all participants, and health anxiety scores increased as cyberchondria scores increased. Moreover, cyberchondria and health anxiety scores increased as internet addiction scores increased.

It is reported as medical students learn about diseases during their medical education, they experience health anxiety about them. In the literature, this is called "medical student syndro-

me" (16). In a study, health anxiety was reported to be slightly higher among medical students (17.4%) than those studying at non-medical faculties (15%), which was not statistically significant (17). In our study, health anxiety was significantly higher in medical faculty students than in other faculty students. Medical faculty students are constantly exposed to disease information due to their education. This exposure may cause them to associate even the slightest sensation in their body with illness and reciprocally increase the health anxiety of medical students.

Health anxiety was also investigated according to academic years, and different results were found. A study reported that the rate of health anxiety was 11.9% among 513 medical students, and the academic year did not have a significant effect (4). In another study, health anxiety was reported more in the preclinical years than in the clinical years (17). In our study, health anxiety was similar in between preclinical and clinical years. In medical faculty, students encounter various new information during the preclinical and clinical years and could associate them with bodily sensations. Therefore, it can be expected that health anxiety would be similar in the preclinical and clinical years.

In a study conducted with a total of 280 medical students during the pandemic, it was reported that 39% of the students had moderate cyberchondria, and 50% had severe cyberchondria (18). However, to the best of our knowledge, the literature lacks a study that compares medical faculty students with other faculty students in terms of cyberchondria. Our results showed no difference between medical faculty students and other faculty students regarding cyberchondria. In the literature, it is reported that cyberchondria is associated with health anxiety (9). In our study, health anxiety was higher in medical faculty students than in other faculty students, but cyberchondria levels were not higher. Cyberchondria is associated with distinguishing between reliable and unreliable online information sources. This situation could also be affected by the individual's education level, ability to process information, and technological knowledge (19).

Compared to other faculty students, health anxiety is high in medical school students, while cyberchondria is not and might be related to medical faculty students' ability to interpret online information correctly. In addition, the level of cyberchondria was higher in our study's preclinical years. The fact that medical information is less in the preclinical years compared to the clinical years may increase the risk of misinterpreting online information in the preclinical period.

In our study, internet addiction levels were similar in medical faculty and other faculty students, and internet addiction was higher in the preclinical years than in the clinical years. Furthermore, as age increased, internet addiction scores decreased. In a study conducted with 282 medical students, the prevalence of internet addiction was reported as 58.87% (mild: 51.42%, moderate: 7.45%) (20). In another study conducted with 148 medical school students, 7.86% of the students met the criteria for internet addiction (21). Internet addiction is a common problem among university students (22). The lack of difference between faculties in our study might be related to this situation. We think it is necessary to raise university students' awareness about internet addiction, regardless of the faculty. In our study, the increase in internet addiction with decreasing age is compatible with the literature (23).

The critical feature of our work is that this is the first study in the literature that evaluates cyberchondria, health anxiety, and internet addiction in medical faculty students. Our study's limitations are that it is a cross-sectional study based on self-report scales.

We can say that health anxiety is higher in medical faculty students compared to other faculties, and the levels of cyberchondria and internet addiction are similar to other faculties. Also, in the pre-clinical period, medical school students have higher levels of cyberchondria and internet addiction. We recommend conducting seminar programs that inform medical faculty students in terms of health anxiety. In addition, prospective studies with very large samples from different regions are needed on these issues.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

TRANSPLANT HEKİMLERİNİN KORKULU RÜYASI: KEMİK İLİĞİ VERİCİ ADAYLARININ DONASYONDAN VAZGEÇMESİ

A NIGHTMARE FOR TRANSPLANT PHYSICIANS: BONE MARROW DONOR CANDIDATES WITHDRAWING FROM THE DONATION PROCESS

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ÖZET

AMAÇ: Ülkemizde kök hücre nakli (HSCT) konusunda çok ilerlemeler kaydedilmesine rağmen, nakil vericisi gönüllülerinin sayısı hala istenilen düzeyde değildir. Bu çalışmada sağlık çalışanlarına, kök hücre nakli vericisi olma konusunda uzmanlar tarafından verilecek eğitimlerin, verici olma konusundaki düşüncelerine ve kararlarına etkilerinin değerlendirilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Kök hücre nakli konusunda önceden herhangi bir eğitim almamış olan, sağlık çalışanları çalışmaya dahil edildi. 11-12 Ocak 2018 tarihlerinde Türkiye Kök Hücre Koordinasyon Merkezi (TÜRKÖK) tarafından, katılımcılara yarım saatlik bir toplu eğitim verildi. Bu çalışmaya TÜRKÖK tarafından verilen eğitimlere katılan 274 sağlık çalışanı dahil edilmiştir. Katılımcıların sosyo-demografik özellikleri, eğitim öncesi ve sonrası kök hücre nakli konusundaki bilgi ve tutumlarını, bağışçı olma konusunda kendilerini motive eden ve engelleyen faktörleri tespit etmeye yönelik ön test ve son test uygulandı.

BULGULAR: Eğitim almadan önce verici olmayı düşünmeyen 95 katılımcının, verici olmak istememelerine en çok neden olan faktörler sağlık sistemine güvenmemeleri idi (%16.5), ağrıya neden olma endişesi (%15.4), kemik iliği vericisi olmanın sağlığı olumsuz etkilediği düşüncesiydi (%13.4). Eğitim sonrasında kök hücre nakli vericisi olmayı düşünenlerin (p:,0001), kök hücre nakli ile ilgili yeterli bilgiye sahip olduğunu düşünenlerin (p:,0001), kök hücre vericisi olmak için nereye başvurulması gerektiğini bildiğini düşünenlerin (p:,000), ülkemizde kök hücre nakli ile ilgili toplumun yeterince bilgilendirildiğini düşünenlerin (p:,0001) oranlarında istatistiksel olarak anlamlı artış saptandı. Katılımcıların %67.3'ü (171 kişi) tüm süreç sonuna kadar verici olma kararlılığının devam edeceğini belirtirken, %32.7'si (83 kişi) verici olmaktan vazgeçebileceğini belirtti.

SONUÇ: Sonuçlarımız bu tür eğitimlerinin yaygınlaşarak, özellikle kurumlarda verilmeye devam edilmesinin, ülkemizde konu ile ilgili farkındalığı artırıp, yanlış inanışları azaltarak, kök hücre vericisi gönüllüsü sayısının yeterli düzeye ulaşmasına çok önemli katkı sağlayacağını göstermektedir.

ANAHTAR KELİMELER: HSCT, Donör, Bilgi, Tutum, Eğitim.

ABSTRACT

OBJECTIVE: Although there have been remarkable developments regarding stem-cell transplantation (HSCT) in Turkey, but the number of people who would like to be stem cell donors is not yet at the desired level. The present study aimed to assess the effect of the training delivered by specialists on the thoughts and decisions of the health employees working in our center on being HSCT donors.

MATERIAL AND METHODS: Employees in the health sector who have not received any training in HSCT were included in the study. A half-hour of collective training for all participants was delivered by the General Directorate of Health Services Turkey Stem Cell Coordination Center (TÜRKÖK) on January 11-12, 2018. The present study included 274 health employees who attended the training delivered by TÜRKÖK. The pre-test and post-test were applied to determine the socio-demographic characteristics of the participants, their knowledge and attitudes about stem cell transplantation before and after the training, and the factors that motivate and prevent them from being a donor.

RESULTS: Among the 95 participants, who did not think about being a donor before receiving education, the factors that caused them to not want to be a donor the most were their distrust of the health system (16.5%), the worry of causing pain (15.4%), and the thought that being a bone marrow donor had a negative impact on health (13.4%). A statistically significant increase was found in the rate of those who think about becoming a stem cell transplant donor after education (p:,0001), those who think they have enough information about stem cell transplant (p:,0001), those who think they know where to apply to be a stem cell donor (p:,000) those who thought that the society was sufficiently informed about stem cell transplantation (p:,0001). While 67.3% (171 people) of the participants stated that their determination to be a donor would continue until the end of the whole process, 32.7% (83 people) stated that they could stop being a donor.

CONCLUSIONS: Our results show that continuing giving such trainings, especially in institutions, will contribute to the increase of the number of stem cell donor volunteers to a sufficient level by raising awareness on the subject and reducing false beliefs in our country.

KEYWORDS: HSCT, Donor, Knowledge, Attitude, Training.

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INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a life-saving treatment for several benign and malign hematologic diseases such as sickle cell anemia, severe thalassemia, Fanconi vanemia, aplastic anemia, severe combined immunodeficiency, lymphomas, and leukemias (1). Bone marrow transplantation (BMT), peripheral blood stem-cell transplantation (PBSCT), and umbilical cord blood are the three main procedures utilized in HSCT (2). A healthy hematopoietic stem cell source compatible with HLA (human-leukocyte-antigen) is the most important precondition for successful transplantation. In 70% of the cases that require HSCT, unrelated HLA-matched donors are required (3). For this reason, national donor screening banks have been established for the screening of unrelated HLA-matched donors around the world, especially in the developed countries. A stem cell donor pool and stem cell bank have been established in Turkey under the name of TÜRKÖK in collaboration with the Municipality of Health and Turkish Red Crescent. TÜRKÖK is a member of the Worldwide Network for Blood and Marrow Transplantation (WBMT) (4).

Although there have been significant developments in Turkey regarding bone marrow and stem-cell transplantation after the establishment of TÜRKÖK, the number of patients who require HSCT is much higher than the number of transplant donors, and it does not meet the need. In the literature, it has been reported that the training activities customized after the identification of the knowledge and attitude of people, as well as motivators and preventive factors affecting them, can be beneficial to increase the number of donors needed for bone marrow and stem cell transplantation (5). Health employees are viewed as guiding partners for the people in their environment regarding health decisions (6). Based on this fact, the present study aimed to contribute to increasing awareness in society, as well as to identify the motivation, opinions, knowledge levels, and attitudes of the health employees working at the Afyonkarahisar Health Sciences University Medical Faculty Hospital and the factors motivating them to be bone marrow and stem-cell transplantation donors. Assessing the impact of the trainings events delivered by related specialists on health employees' thoughts and decisions about being donors was also one of the aims of the study.

MATERIAL AND METHODS

Subjects and Approval

Among the health employees working in Afyonkarahisar Health Sciences University Medical Faculty Hospital who have not received any training on the subject of bone marrow and stem-cell transplantation, the employees who attended a half-hour collective training on January 11 - 12, 2018, delivered by TÜRKÖK and employees who stated permission for their answers to be used in the study on the training surveys before and after the training were included in the study. Health employees who have received training on bone marrow and stem-cell transplantation before and employees who did not let their survey answers to be used in the studies were excluded from the study.

Lecture and Testing

Preliminary test forms were prepared in accordance with the literature by the training nurses and the researchers of the study working in Afyonkarahisar Health Sciences University Medical Faculty Hospital and the forms were finalized with the recommendation of three specialists. These forms and the final forms prepared in the same manner were filled by the participants before and after the training. They were collected by the training nurse. Related forms were utilized as data collection tool after having been evaluated retrospectively by the researchers (7 - 13). There were five questions to identify the sociodemographic features of the participants, thirteen questions to identify their knowledge and attitude regarding bone marrow and stem-cell transplantation, two questions regarding factors which motivated them to be donors and prevented them from being donors, one question to increase awareness of bone marrow transplantation and being a do-

nor in society, and one question to identify if the answers given could be used for research and publication purposes within the pre-training form, which includes 22 questions in total. The answer key for the 13 questions which were to identify the participants' knowledge and attitude regarding bone marrow and stem-cell transplantation was prepared in "yes/no" questions. The answer key for the other questions was prepared as open-ended questions placing the most frequent answers given to the similar questions in the literature to the answer choices and adding "another" option. Ten of the twelve questions and answers on the post-training test form were the same as those used before the training. This was to measure the effect of the training they received on their knowledge, attitudes, and the motivating and preventive factors. One question in the test form after the training was prepared to assess how the participants who would like to be donors would decide if a compatible patient was found after their donor registration. The answer key for this question was prepared as an open-ended question because no similar question could be found in the literature. The last question on the test form after the training was prepared to identify if the participants would let their answers be used for the study and publication purposes.

Ethical Committee

The study was conducted with the approval of the Afyonkarahisar Health Sciences University Medical Faculty Ethics Committee dated 05.01.2018 and numbered 2018/1-25.

Statistical Analysis

Data were registered in the computer by using a licensed SPSS program, SPSS for Windows 20.0 package program (SPSS Inc. Chicago, IL, USA) and analyzed accordingly. Number and percentage were used for the discrete variables, and median values (minimum-maximum) were used for the continuous variables in the definitive statistics. McNemar tests were used in dependent variables and Chi-square tests were used in independent variables to identify whether there was a difference between the percentages of the survey answers given by the participants. All statistical evaluations were conducted two sided, and a P-value less than 0.05 was considered statistically significant.

RESULTS

The present study included 274 health employees who participated in the training delivered by TÜRKÖK and gave permission for their survey answers to be used in the studies. The study excluded 20 people who had received some kind of training on bone marrow and stem-cell transplantation, and 86 employees who did not let their survey answers be used in the studies. The participants' median age was 32.7 (minimum=22, maximum=55) with 32.8% (90) males and 67.2% (184) females. The thoughts of the participants regarding being bone marrow donors before the training was shown in Table 1 based on their sociodemographic features **(Table 1)**.

Table 1: The evaluation of the thoughts of the participants on being bone marrow transplantation donor before the training based on their sociodemographic features

Demographic features		Yes	No	Total
Gender				
	Female	110 (66%)	56 (34%)	166
	Male	41 (52%)	39 (48%)	80
Marital Status				
	Single	57 (64%)	31 (36%)	88
	Married	94 (60%)	64 (40%)	158
Education Level				
	Primary School	12 (66%)	6 (34%)	18
	Middle School	10 (50%)	10 (50%)	20
	High School	42 (56%)	32 (34%)	74
	College	87 (64%)	47 (36%)	134
Profession				
	Doctor	8 (72%)	3 (28%)	11
	Nurse	72 (66%)	33 (34%)	110
	Technician	17 (46%)	20 (54%)	37
	Health Officer	14 (78%)	4 (28%)	18
	Medical Secretary	14 (50%)	14 (50%)	28
	Administrative Staff	18 (58%)	16 (42%)	37
	Security	8 (62%)	5 (38%)	13

Accordingly,14.6% (37) of the participants donated blood regularly, 5.1% (14) of them had a family member, relative or friend who was a bone marrow donor, 2.6% (7) of them had a family member, relative or friend who needed bone marrow transplantation. The opinions on being bone marrow donors for the specific groups have been shared below statistically:

The opinions of 37 people who donated blood regularly were shown in **Figure 1**, the opinions of 14 people who had a bone marrow donor family member, relative or friend and the opinions of 7 people who had a family member, relative or friend in need of bone marrow transplantati-

on, based on the test results before the training **(Figure 1)**.
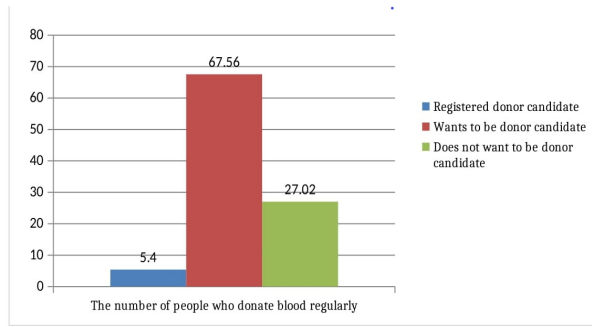
Figure 1: The thoughts of participants who donate blood regularly on being bone marrow donor before the training

While the distribution of the factors motivating participants who considered being bone marrow donors was shared in Figure 2 based on their answers in the test form before the training, the distribution of the factors preventing involuntary participants was shared in Figure 3 **(Figure 2, 3)**.

Figure 2: The Factors Affecting the Consideration of Being Bone Marrow Donor in a Positive Way
•Helping a Person 79.2
•The Thought of Saving Life 81.1
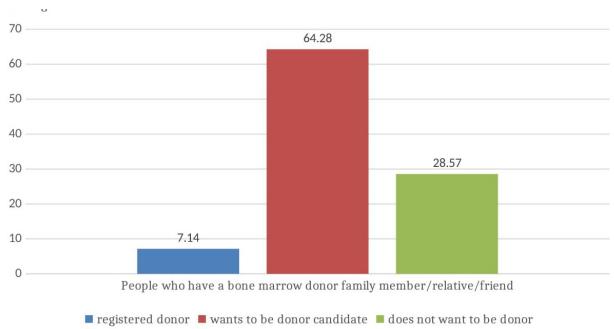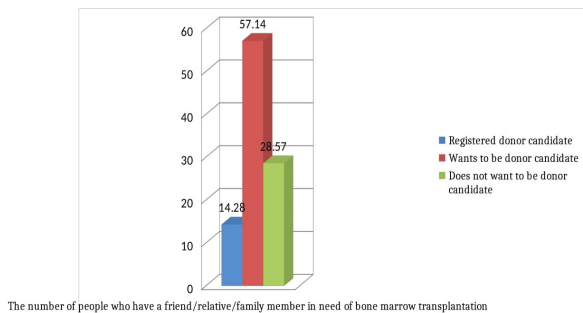•Family's/Friends'/Relatives' Need for Help 22
•Recommendation of a Friend 4.4
•Media 7.5
•Bone Marrow Transplantation Saves Life 70.4
•Other Reasons 5.7
From the people who are bone marrow donor candidates and whom would like to be donor candidates

Figure 3: The Factors affecting the Consideration of Being Bone Marrow Donor in a Negative Way
•Being bone marrow donor affecting health in a negative way 34.3
•Concern it can cause pain 39.4
•Not acceptable for religion 13.1
•The family's disapproval of it 11.1
•The cost of being bone marrow donor 5.1
•The thought it can be a financial burden 7.1
•Not believing in the health system 42.4
•Other reasons 24.2

According to this data, the most encouraging factor for the 151 participants who considered being donors before the training was the thought of saving lives (50.8%; 129 people). The second most frequent (49.6%; 126 people) factor was the thought of helping people, and the third most frequent factor was considering it as a life-saving intervention (44.1%; 112 people). The reason why 95 participants who did not consider being donors before the training was distrust in the health system (16.5 %; 42 people). The second most frequent opinion (15.4%; 39 people) was the concern that it could cause pain, and the third most frequent opinion (13.4%; 34 people) was that being a bone marrow donor affecting health in a negative way. The evaluation of the answers given to the same questions before and after the training has been shown in **Table 2** .

Table 2: The evaluation of the participants' answers to the same questions before and after the training

Questions	Before Lecture	After Lecture	P value
1) Do you think that you have sufficient information about the bone marrow transplantation?			
Yes	11 (4.3%)	215 (84.6%)	**0,0001**
No	243 (95.7%)	39 (%15.4)	
2) Do you know how bone marrow transplantation is conducted?			
Yes	59 (23.2%)	223 (87.8%)	**0,0001**
No	195 (76.8%)	31 (12.2%)	
3) Do you know where to apply to be bone marrow donor?			
Yes	57 (22.4%)	232 (91.3%)	**0,0001**
No	197 (77.6%)	22 (8.7%)	
4) Do you think that the bone marrow transplantation is acceptable for religion?			
Yes	216 (85%)	229 (90.2%)	0,085
No	38 (15%)	25 (9.8%)	
5) Do you think that your health will be affected in a negative way after you donate bone marrow when you become bone marrow donor and a compatible patient is found?			
Yes	35 (13.8%)	44 (17.3%)	0,289
No	219 (86.2%)	210 (82.2%)	
6) If you become a bone marrow donor and a compatible patient is found, do you think that the bone marrow transplantation process will be financial burden for you?			
Yes	29 (11.4%)	25 (9.8%)	0,618
No	225 (88.6%)	229 (90.2%)	
7) Will your family's, friends' and relatives' attitude be effective in your decision about being a bone marrow donor?			
Yes	107 (%42.1)	104 (%40.9)	0,801
No	147 (%57.9)	150 (%59.1)	
8) Do you think that, society in Turkey is being informed enough about bone marrow transplantation?			
Yes	14 (%5.5)	52 (%20.5)	**0,0001**
No	240 (%94.5)	202 (%79.5)	
9) Do you think that giving training for institutions will lead to raising awareness of our society on bone marrow transplantation and being bone marrow donor?			
Yes	145 (%57.1)	182 (%71.7)	**0,0001**
No	109 (%42.9)	72 (%28.3)	

According to the evaluation, a statistically significant change was identified in the rates of people in the stated groups at the end of the training: The rate of people considering being bone marrow donors went from 37.4% to 75.8% (p=000), people who thought they had sufficient information regarding bone marrow transplantation went from 4.3 % to 84.6% (p=0,000), people who thought they knew how bone mar-

row transplantation was conducted went from 23.2% to 87.8% (p=0,000), people who thought they knew where to apply if they wanted to be bone marrow donors went from 22.4% to 91.3% (p=0,000), people who thought the community was being sufficiently informed in Turkey went from 5.5% to 20.5% (p=0,000), and people who thought the best method to increase awareness regarding being a bone marrow donor in the community is delivering training for the organizations went from 57.1% to 71.7% (p=0,000). No statistically significant change in the number of people who considered bone marrow transplantation not acceptable because of religious reasons, thought being a bone marrow donor might affect health in a negative way, thought that the process of bone marrow collection could bring financial burden and believed the attitude of families, friends or relatives had an impact on their decision of being bone marrow donor was identified. After the participants' donation registrations were completed, the distribution of their answers on how their decisions might be affected when a patient who was matching them and in need of a transplant was found was analyzed based on their sociodemographic features **(Table 3)**.

Table 3: The decisiveness of the participants on being donors when their donor registrations are completed, a compatible patient in need of transplantation is found

Demographic feature	Yes	No	Total
Will you be donor if a compatible patient is found whom you can be donor for after your donor registration is completed?	171 (67.3%)	83 (32.7%)	254 (100)
Features of the people who stated they could quit being donors after their donor registrations are completed, and a compatible patient is identified for them			
Gender			
Female		47 (56.6%)	
Male		36 (43.4%)	
Marital Status			
Single		27 (32.5%)	
Married		56 (67.5%)	
Education Level			
Primary School		7 (8.4%)	
Middle School		7 (8.4%)	
High School		26 (31.3%)	
College		43 (51.8%)	
Profession			
Doctor		2 (2.4%)	
Nurse		36 (43.4%)	
Technician		17 (20.5%)	
Medical Secretary		5 (6%)	
Health Officer		5 (6%)	
Administrative Staff		2 (2.4%)	
Other Health Staff		16 (19.3%)	
The reasons of people who stated they could withdraw from the donation process			
Religious reasons		9.6% of them (8 people)	
People who think that it can affect the donor's health in a negative way		20.5% of them (17 people)	
People who think that it can create financial burden for the donor		12% of them (10 people)	
People who think that their family/friends will have a negative effect in their decisions		48.2% of them (40 people)	

Of the participants, 67.3% (171 people) stated that their decisiveness regarding being a donor would continue until the end of the whole process, 32.7% (83 people) stated they could possibly quit being a donor. People who stated they could quit did not write their reasons even though an open-ended answer was requested. Of the respondents who stated they could quit the process, 43.4% (36 people) were males and 56.6% (47 people) were females. Of the participants, 67.5% (56 people) were married, and 32.5% (27 people) were single. About the educational background, 8.4% (7 people) were primary school graduates, 8.4% (7 people) were middle school graduates, %31.3 (26 people) were high school graduates and 51.8% (43 people) were university graduates. Of the participants, 43.4% (36 people) were nurses, 6% (5 people) were medical secretaries, 19.3% (16 people) were from the other professions (9 cleaning personnel, 1 chef, 3 kitchen staff, 3 security staff), 2.4% (2 people) were doctors, 20.5% (17 people) were technicians, 6% (5 people) were health officers, 2.4% (2 people) were administrative staff. Of the participants, 9.6% (8 people) stated that bone marrow transplantation would not be proper for religious reasons, 20.5% (17 people) stated it could affect health in a negative way, 12% (10) stated that the recovery process of bone marrow transplantation could be a burden financially, and 48.2% (40) stated that their, families', friends', or relatives' attitude could be effective in their decisions.

DISCUSSION

Health employees, especially doctors, are regarded as behavioral role models in society, especially in the issues of health. However, not only doctors but also other health employees can lead the community primarily in matters of health. According to the data of European Group for Blood and Marrow Transplant (EBMT) which many transplant centers are members in Turkey, the number of donors who are not relatives is not at the desired level yet and it does not meet the need. It is believed that the main

reason for this is because there is not enough awareness and knowledge of the topic in Turkey yet (14). Our study's target audience included not only doctors, but all health employees, based on our hypothesis that it would raise awareness about the topic in our society more quickly and to the desired level. The knowledge level of our target audience regarding being bone marrow donors was evaluated with a survey form. Then it was ensured they got a half hour visual training in a lecture hall. Then, the effects of the training on their knowledge, attitude, and decision to be donors were assessed. There have been studies in Turkey assessing the knowledge of medical faculty students (15) and the knowledge of cancer patients or people having cancer patients in their families (16) regarding being bone marrow transplantation donors. However, we have not come across any study in the literature assessing the knowledge level of people regarding being bone marrow donors involving all hospital employees. In the TÜRKÖK project, the aim was to inform, especially blood donors as the target audience, and raise awareness so that the bone marrow candidate pool expands. While 2 (5.4%) of the 37 participants who donated blood regularly were registered as donor candidates, 25 (67.56%) of them were considering being donors according to the test results before the training. In the study in which Narayanan et al. (17) evaluated the knowledge, attitude and behaviors of the medical faculty students about being bone marrow donors, it was reported that 56% of students who were previously blood product donors were registered as candidate donors. Hazzazi et al. (1) reported that 36% of the students who were previously blood product donors were registered as donor candidates. Suluhan et al.(18) reported that no donor from the 100 donors who donated regularly was registered as donor candidate, and 47% of them were considering being donor candidates. It was reported that the people who donated regularly were more motivated to be donors in the study conducted by Galenos et al.(10). This finding is in line with the results of our study. Our study demonstrates that the selection of primarily blood donors as the target audience for the TÜRKÖK project was the correct approach.

The present study found that those who had a family member, friend, or relative who was a bone marrow donor or who needed a bone marrow transplant were more motivated to be donors and were more sensitive to the issue. In the study Bagcivan et al. conducted, it was reported that the stem-cell transplantation awareness of cancer patients and their families were higher than the awareness of patients, and their families, who had a disease other than cancer. When health employees were evaluated, the groups with the highest involuntary rate were as follows: the middle school graduates (based on their educational background), technicians (based on their profession), married couples (based on their marital status), and males (based on their gender). These groups did not consider being donors with the highest involuntary rate. Factors leading to this condition can be analyzed with the studies focused on these groups and the training events can be customized accordingly. It may also contribute increasing the number of people who would consider being bone marrow donor candidates. Our study, in parallel with the previous studies, showed that people who had a higher education level were more motivated to be bone marrow donors (11, 18 - 20). While men were more motivated to be bone marrow donors in the study conducted by Suluhan et al. (18), in the study conducted by Onitilo et al. (11) women were more motivated to be bone marrow donors. The results of the study of Onitilo et al. were similar to the results of our study. In the study conducted by Narayanan et al. (17) majority of the bone marrow donor registrations were reported to be females.

The following were the reasons given by research participants who stated that they did not consider becoming bone marrow donors in a pre-TÜRKÖK survey: The health system is not trusted, the concern that it can be painful, and the thought of being a bone marrow donor affect health in a negative way. In a study conducted with medical students in Minnesota, USA, the most reported concerns regarding being a bone marrow donor were the thought that the process could be painful, considering it as a time consuming process (time commitment), long-term adverse effects and concerns regarding financial cost (17). In a study with medical students in Saudi Arabia, refraining from long-term costs, considering it a time consuming process (time commitment) and the concern that the process would be painful were the most frequent concerns stated (1). In a study conducted in South Carolina, USA, fe-

aring pain, having health problems, considering it not convenient and distrust in the health system were the most frequent concerns (11). In another study, conducted in South Carolina, the most frequent reasons were reported as worrying about costs, not having the opportunity, other reasons and fear of the pain (19). In a study in Hong Kong involving people from the public between the ages of 18-60, the most frequent reasons were reported as health problems, fearing of the pain, insufficient level of knowledge, families not giving permission and distrust in the health system (20).

Focusing on the concerns of public regarding being a donor in the training events can be effective to change the thoughts of people from negative to positive. Donors may need to rest for 7-10 days after the process and this can cause financial loss for both donors and employers (21). It has been reported that there has been a significant increase in the number of donors thanks to the leave and/or tax reduction practices for the donors and employers (22) in many states in the USA. We think that in addition to training events informing public on the HSCT, preparing certificates of appreciation/honor which will increase respectability in the society and supporting both the donor and employer financially (tax reduction) can contribute to increasing the number of donors in Turkey. In the present study, the number of people who considered being a bone marrow donor after the training, the number of people who thought they had enough information regarding bone marrow transplantation, the number of people who thought they knew how bone marrow transplantation was conducted, the number of people who thought they knew where to apply to be a bone marrow donor and the number of people who thought society was being informed sufficiently in Turkey and the number of people who thought the best method to increase awareness in the public regarding being a bone marrow donor would be through training programs for institutions, significantly increased after the training statistically. These data show that the training delivered by TÜRKÖK achieved its objective and the awareness of the participants increased. In a study (15) conducted in Turkey, it has been reported that the knowledge and awareness level of students regarding stem cell donation, stem cell banking, and/or

the number of stem cell donors in Turkey, and the number of people who would like to donate blood and stem cells have significantly increased statistically compared with the pre-training period according to the tests filled in by the medical and law faculty students after the training. In a study (23) conducted in Korea with nursing students in which nursing students' knowledge, attitude regarding HSCT and motivation for being donors were assessed before and after the training, it has been reported that the students' knowledge, attitude (p <0.001) regarding HSCT and motivation (p=0,06) for being donors significantly increased statistically according to the tests performed in the second week after the training. It has also been reported that the registration rate (p=0.039) for the HSCT statistically, significantly increased 14 weeks after the training. The identification of statistical, significant increase in the number of people who believe that the best method to increase awareness in the society is delivering training for the institutions shows that continuation of the training events will contribute to increasing the number of bone marrow donors in society and awareness on the subject significantly.

A high percentage of the participants (32.7%, 83 people) stated that they might quit being donors when a proper patient was found after considering being donors and having been registered as donors. People who stated they could quit the process did not write their reasons even though an open-ended answer was requested from them. Since this condition can lead to significant problems after a donor is found and the transplantation process is started, studies researching the cause of the condition and solutions are needed urgently. It has been identified that the 48.2% of the participants (40 people) who stated they could quit the process (even if they were registered) upon a donor was found were the ones who thought that the attitude of families, friends, or relatives was instrumental in their decision to be donors. When there is a compatible patient for a donor candidate, the involvement of the families, friends, or relatives of the patients in the training by the will of the donor shall reduce the risk of donors leaving the process and it can reduce negativities during the transplant process. According to the data the Head of the Municipality of Health, the General

Directorate of the Health Services Blood, Organ, Tissue Transplant Services Office, shared in his presentation in the health authority session in the 11th National Bone Marrow Transplantation and Stem Cell Treatments Congress, 12.87% percent of compatible donors withdrew from the process in the period from the date TÜRKÖK was established to March 2nd, 2019 (472/3666). It has been reported that 66.7% of the people left the process because of individual reasons. It has been reported that the major reason for this situation is involvement of inappropriate people in the system such as people who cannot accept donorship, who do not have a developed sense of donorship culture. Of the people who quit the process, 27.5% did this because of the family pressure. This supported the findings in our study. This group consisted of mainly females. Other less prevalent reasons for quitting included a willingness to get to know the patient, financial expectations, skepticism in the system, refusal to accept the method of transplantation, and general discontent.

There has been only one study in Turkey assessing the motivation to be a donor and the knowledge and attitude change regarding HSCT after the delivery of training on HSCT, conducted by Kaya et al. (15). We believe that the awareness regarding the subject will increase and false beliefs will decrease in Turkey thanks to these studies and the TÜRKÖK training events will become widespread and continue to be delivered, especially in the institutions. We believe that all these developments will contribute to the number of bone marrow donors reaching a sufficient level. When there is a compatible patient found for a donor candidate, the involvement of the families, friends, or relatives of the patients in the training by the will of the donor will reduce the risk of donor's leaving the process and it can reduce the negativities during the transplant process for this reason. Involvement of people who regularly donate blood in the system and conducting a face-to-face and questions&answers meeting with visual aids with the participation of educated and experienced transplant doctors and people whom the donor would be requested when there is a match can lead to significant decreases in the rate of withdrawal.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

ERİŞKİN HASTALARIN İNFLUENZA, PNÖMOKOK, HERPES ZOSTER VE TETANOS AŞILARI HAKKINDA TUTUM VE DAVRANIŞLARININ DEĞERLENDİRİLMESİ: TEK MERKEZLİ ANKET ÇALIŞMASI

EVALUATION OF ADULT PATIENTS' ATTITUDES AND BEHAVIORS ABOUT INFLUENZA, PNEUMOCOCCAL, HERPES ZOSTER AND TETANUS VACCINES: A SINGLE-CENTER SURVEY STUDY

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ÖZET

AMAÇ: Erişkin aşılaması, koruyucu sağlık hizmetlerinin anahtar bileşenidir. Bu çalışmanın amacı, aile hekimliği polikliniklerine başvuran hastaların erişkin aşıları ve aşılama oranları hakkındaki bilgilerini değerlendirmektir.

GEREÇ VE YÖNTEM: Çalışmaya toplam 442 hasta dahil edildi. Hastaların demografik ve klinik özellikleri değerlendirildi. Hastaların influenza, pnömoni, herpes zoster ve tetanos aşı durumları ve erişkin aşıları hakkındaki bilgi düzeyleri sorgulandı.

BULGULAR: Hastaların ortanca yaşı 42 (min-maks: 18-97) olup 227'si (%51,4) kadındı. Tetanos için aşılama oranları %32,6, influenza için %21,7, pnömokok aşısı için %3,6 ve herpes zoster için %2,5 olarak bulundu. Komorbiditesi olan hastaların aşılanma oranları beklenenden daha düşük bulundu. Geriatrik hastalarda pnömokok aşılama oranı %2,8, tetanos aşılama oranı %19,7, influenza aşılama oranı %33,8'idi. 65 yaş üstü hiçbir hasta herpes zoster aşı yaptırmamıştı. Üniversite mezunlarında herpes zoster, pnömokok ve tetanos aşısı yaptıranların oranı daha yüksekti. Hastaların aşı yaptırmama nedenleri arasında yan etki korkusu (%20), aşıya ulaşma zorluğu (%6), aşı fiyatlarının yüksekliği yer alırken (%1), hastaların %16'sı aşının yararlarına inanmadığını belirtti.

SONUÇ: Çalışma grubumuzda erişkin bağışıklama hızı beklenen seviyenin altındadır ve bu oranı artırmak için hastaların erişkin aşıları konusunda bilinçlendirilmesi önemlidir.

ANAHTAR KELİMELER: Koruyucu hekimlik, Aşılama, İnsan İnfluenzası, Tetanos.

ABSTRACT

OBJECTIVE: The key component of preventive health care is adult immunization. The aim of this study was to assess the patients' knowledge about adult vaccination and the vaccination rates of patients admitted to the family medicine outpatient clinics.

MATERIAL AND METHODS: A total of 442 patients were included in the study. Patient demographic and clinic characteristics were evaluated. Patients' vaccination status with influenza, pneumococcal vaccine, herpes zoster, and tetanus and their knowledge levels about adult vaccines were questioned.

RESULTS: The median age of the patients was 42 (min-max: 18-97) and 227 (51.4%) of them were female. Vaccination rates were found 32.6% for tetanus, 21.7% for influenza, 3.6% for pneumococcal, and 2.5% for herpes zoster. Patients with co-morbidities vaccination rates were found to be very low. The pneumococcal vaccination rate was 2.8%, the tetanus vaccination rate was 19.7% , and the influenza vaccination rate was 33.8% in geriatric patients. No patient older than 65 has ever received the zona vaccination. The rate of patients who had herpes zoster, pneumococcal vaccine, and tetanus vaccine was higher among university graduates. Fear of side effects (20%), difficulty in accessing the vaccine (6%), high vaccination prices (1%) were among the reasons why patients did not have vaccinated, and 16% of the patients stated that they did not believe in the benefits of vaccine.

CONCLUSIONS: In conclusion, we are still far below the desired levels of adult vaccination in our study population, and it is important to increase patients awareness of adult immunizations.

KEYWORDS: Preventive medicine, Vaccination, Influenza, Tetanus.

INTRODUCTION

Vaccination, the most effective method to prevent infectious diseases, is the leading preventive health care service. While significant improvements have been achieved in childhood vaccination both in our country and around the world, adult immunization rates are still insufficient (1).

According to the vaccination program published by the Centers for Disease Control and Prevention (CDC) in 2021, it is recommended to inoculate adults against influenza, diphtheria, tetanus, pertussis, measles, rubella, mumps, herpes zoster, chickenpox, human papilloma virus, pneumococcus, Hepatitis A, Hepatitis B, meningococcus, and haemophilus influenza type B. Vaccination is also recommended for geriatric patients, pregnant women, healthcare professionals, and the followed-up patients due to some diseases, including immunosuppression, HIV, asplenia, end-stage renal disease, heart and lung diseases, alcoholism, chronic liver disease, and diabetes mellitus (2). Updated in 2016, adult immunization guidelines of the Turkish Infectious Diseases and Clinical Microbiology Specialist Association for vaccination have made similar proposals (1).

The geriatric population is increasing both in the world and in our country. According to data released by the Turkish Statistical Institute, the population over the age of 65 has increased by 21.9% in the last five years and reached approximately 7 million and 550 thousand in 2019 (3). Infectious diseases result in more serious health conditions in older adults. Moreover, the *dependence on others* to perform *daily activities*, frailty, and mortality increases with advancing age (4). Age related dysregulation in the immune system is called immunosenescence. It is associated with an increase in infectious diseases in older patients, as well as a decrease in vaccine response and low antibody titres in older adults after vaccination (5). Older adults constitute an important target group for adult vaccination programs.

Among the reasons why adult vaccination rates are under the desired target, patient and health system related factors, as well as socioeconomic problems can be taken into account. Some of the most important problems are that healthcare professionals have insufficient knowledge about adult vaccination and do not recommend it for adult patients (6).

In a study conducted in our country in which 200 physicians were included, 45.5% of the physicians did not think that they gave the necessary importance to adult vaccination in their daily practice (7).

In the present study, we aimed to investigate the patients' knowledge about adult vaccination and the vaccination rates of patients admitted to the family medicine outpatient clinics.

MATERIAL AND METHODS

Study Population

Every patient who applied to a family medicine outpatient clinic between November 15, 2017 and November 15, 2018, was informed about the study. A total of 442 patients over the age of 18 who participated in the study voluntarily and did not have a disease that would prevent them from answering the questions were included.

Data Collection

Data on the vaccine awareness and patients' vaccination rates were collected by a face to face questionnaire method. A standardized questionnaire was developed for the survey based on data in the literature. Six questions about the patients' level of adult vaccination knowledge were asked after assessing the patients' sociodemographic and clinical characteristics in the questionnaire form. 1. Have you heard of influenza, herpes zoster, tetanus, and pneumococcal vaccines for adults? 2. Have you ever been recommended these vaccinations in your adult life? 3. Have you ever been vaccinated in your adult life? 4. Where did you get the information about the vaccines? 5. Do you think immunizations are beneficial? 6. If you have not been vaccinated, what is your reason for not getting vaccinated? **(Appendix-1).**

Ethical Committee

Ethics committee approval for the study was obtained by the local (Taksim Training and Research Hospital Ethics Committee number: 94/Date:15.11.2017). All patients signed a document of informed consent.

Statistical Analysis

In the power analysis, the awareness of the vaccine obtained from studies was determined to be 32% (7,8). At least 335 cases with a margin of error of 5% were included in the study. To strengthen the validity of the study, the questionnaire was continued to be applied even after the target number was reached until the scheduled last day of the study. They were expressed as mean ± standard deviation for variables with a normal distribution, as median (minimum-maximum) for variables with non-normal distribution, and as percentage (%) for categorical variables. For values that did not conform to the normal distribution, the Mann Whitney U test or the Kruskall Wallis test were used, depending on the number of groups. A chi-square test was used to compare categorical variables. The results were considered statistically significant for p<0.05. The IBM SPSS 23 program was utilized for data analysis.

RESULTS

Four hundred forty two patients were included in the study. The median age of the patients was 42 (min-max: 18-97) and 227 (51.4%) of them were female. 306 of the patients (69.2%) were married. In terms of their education levels, 32 (7.2%) patients were illiterate, 77 (17.4%) were primary school graduates, 60 (12.6%) were secondary school graduates, 74 (16.7%) were high school graduates and, 199 (45%) were university graduates. 197 (44.6%) of those included in the study lived in the city centre. The median number of household members was 3 (0-11).

A total of 164 (37.1%) study participants had chronic illnesses for which vaccination would be recommended or had high-risk occupations such as healthcare workers, people who work in childhood education and care, caregivers, staff of nursing homes, and long-term care facilities for people of any age. Of the patients included

in the study, 47 (10.6%) had diabetes mellitus (DM), 29 (6.6%) had chronic obstructive pulmonary disease (COPD), 27 (6.1%) had congestive heart failure, 15 (3.5%) had chronic kidney disease, 7 (1.6%) had haematological diseases, 6 (1.4%) underwent immunosuppressive treatment, 2 (0.5%) had chronic liver disease and 2 (0.5%) were followed up patients due to alcohol abuse. The clinical and socio-demographic data of the patients are demonstrated in **Table**1.

Table 1: Clinical and socio-demographic data of the patients

Parameter	n=442
Age	42 (18-97)
Gender (Female %)	227 (51.4%)
Marital status	
Married	306 (69.2%)
Single	128 (29%)
Divorced	8 (1.8%)
Education level	
Illiterate	32 (7.2%)
Primary school	77 (17.4%)
Middle School	60 (12.6%)
High school	74 (16.7%)
University	199 (45%)
Income (Monthly)	
<1500 TL	114 (25.8%)
1,501-2,500 TL	95 (21.5%)
2,501-3,500 TL	104 (23.5%)
>3,500 TL	92 (20.8%)
Living place	
Provincial center	197 (44.6%)
District	99 (22.4%)
Village	146 (33%)
Risk factor *	164 (37.1%)
Co-morbidities	
Diabetes Mellitus	47 (10.6%)
Chronic Obstructive Pulmonary Disease	29 (6.6%)
Congestive heart failure	27 (6.1%)
Chronic Kidney Disease	15 (3.5%)
Haematological Disease	7 (1.6%)
Immunosuppressive treatment	6 (1.4%)
Chronic Liver Disease	2 (0.5%)
Alcohol abuse	2 (0.5%)

* Risk factors = to have a chronic illness (Diabetes Mellitus, Chronic Obstructive Pulmonary Disease, Congestive heart failure, Chronic Kidney Disease, Haematological Disease, Immunosuppressive treatment, ,Chronic Liver Disease, Alcohol abuse) or high-risk occupations (healthcare workers, people who work in childhood education and care, carers, staff of nursing homes, and long-term care facilities for people of any age)TL=Turkish Lira

Table 2 summarizes the patients' levels of knowledge of adult vaccines, whether they have heard of tetanus, herpes zoster, influenza, and pneumococcal vaccines; whether these were recommended to them, and their level of immunization.

Table 2: Patients' level of knowledge about adult vaccinations

|	Heard of adult vaccines	Recommended adult vaccines	Received adult vaccines
Tetanus	399 (90.3%)	196 (44.3%)	144 (32.6%)
Pneumococcal vaccine	361 (81.7%)	88 (19.9%)	16 (3.6%)
Herpes zoster	376 (85.1%)	104 (23.5%)	11 (2.5%)
Influenza	404 (91.4%)	189 (42.8%)	96 (21.7%)

Two hundred and sixty four (59.7%) patients obtained information about adult vaccines from healthcare professionals, 93(21%) from the internet or printed and visual media, and 74 (16.7%) from their relatives. The patient group, who had previously been recommended to have tetanus, pneumococcal vaccine, herpes zoster (p<0.001), and influenza (p=0.004) vaccines, were informed about adult vaccination mainly by healthcare professionals. The younger (p=0.028) and the patient group employed in high risk occupations (p=0.012), as well as the patient group for whom adult immunization was recommended (p=0.028), also received information about vaccines from healthcare professionals **(Table 3)**.

Table 3: Methods of obtaining information about vaccination

Where did you get information about vaccination?	Health Professional	The Internet or printed and visual media	Relatives	p
	n = 264 (59.7%)	n= 93 (21%)	n=74 (16.7%)	
Age (median, min-max)	40 (20-95)	50 (22-97)	43.5 (18-90)	0.028
Gender (Female)	142 (64.5%)	48 (21.8%)	30 (13.7%)	0.130
High-risk occupations	32 (82.1%)	2 (5.1%)	5 (12.8%)	0.012
Vaccine recommended group	106 (67.5%)	23 (14.6%)	28 (17.9%)	0.028
Tetanus vaccine recommended	143 (%73)	27 (13.7%)	26 (13.3%)	<0.001
Tetanus vaccine received	101 (70.1%)	26 (18.1%)	17(11.8%)	0.022
Influenza vaccine recommended	129 (68.3%)	27 (14.3%)	33 (17.4%)	0.004
Influenza vaccine received	61 (63.5%)	20 (15.7%)	15 (20.8%)	0.857
Pneumococcus vaccine recommended	76 (86.4%)	2 (2.2%)	10 (11.4%)	<0.001
Pneumococcus vaccine received	13 (81.3%)	0 (0%)	3 (18.7%)	0.048
Herpes zoster vaccine recommended	85 (81.7%)	7 (6.8%)	12 (11.5%)	<0.001
Herpes zoster vaccine received	10 (90.9%)	1 (10.1%)	0 (0%)	0.150

While almost 85% of the patients had an opinion that vaccines were beneficial, 16% of them stated that they did not believe in the benefits of vaccines. Although adult vaccination was recommended for patients, fear of side effects (20%), difficulty in accessing the vaccine due to logistic reasons (6%), high vaccination prices (1%) and prefer not to indicate (57%) were listed as reasons for not having adult vaccination **(Figure 1)**.
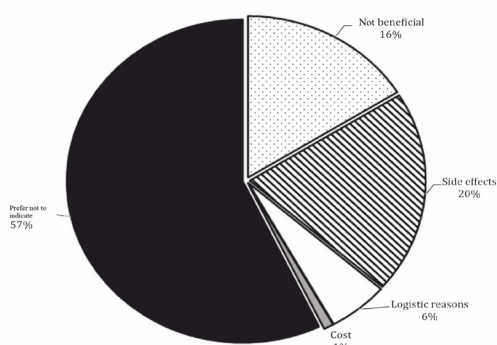
Figure 1: Vaccine hesitancy reasons

Although 376 of the patients (85.1%) stated that they were aware of the herpes zoster vaccine, it was recommended for 104 (23.5%) patients. However, only 11 (2.5%) patients had the herpes zoster vaccine. All of the patients who had the herpes zoster vaccine were university graduates (p = 0.015). 139 (77.7%) patients over the age of 50 were aware of the herpes zoster vaccine, while 40 (22.3%) patients were not (p<0.001). Of the patients involved in the study, 361 (81.7%) were aware of the pneumococcal vaccine, 88 patients (19.9%) were recommended vaccination, and 16 patients (3.6%) had pneumococcal vaccine. While 152 (92.7%) of 164 patients with an indication of pneumococcal vaccine did not get vaccinated, 12 (7.3%) patients were vaccinated (p=0.002). Of 361 patients who were aware of the pneumococcal vaccine, 30.2% (n=109) lived in the village, 22.7% (n= 82) and 47.1% (n=170) lived in the city centre (p=0.021). In addition, 50.4% (n=182) of the patients who were aware of the pneumococcal vaccine were university graduates, 17.5% (n=63) were high school graduates, 27.4% (n=99) were primary school graduates and; 4.7% (n=17) were illiterate (p<0.001). Pneumococcal vaccine was recommended for 4 (66.7%) of 6 immunosuppressive patients (p=0.016), but only one patient had pneumococcal vaccine.

91.4% of the patients (n=404) were aware of the influenza vaccine. While vaccination was recommended for 42.8% (n=189), only 21.7% (n=96) of the patients had influenza vaccine. The rate of influenza vaccination was lower in those with a monthly income of 1500 Turkish Lira (TL) or less than the other groups (16.7% vs. 83.3%, p=0.039).

A total of 399 (90.3%) patients were aware of the tetanus vaccine, 44.3% (n=196) were recommended to be vaccinated before, and 32.6% (n=144) patients had the tetanus vaccine. Similar to the influenza vaccine, the vaccination rate for tetanus was statistically lower in the patient group with the lowest monthly income compared to the other groups (p 0.001). The rate of patients who had the tetanus vaccine was higher among university graduates compared to other groups (61.1% vs. 38.9%; p0.001). While 130 (35%) of 144 patients who had the tetanus vaccine were under 65 years old, 14 (19.7%) were 65 years old or over (p=0.012).

Seventy-one of the study participants are 65 years of age or older. When patients over 65 are evaluated separately, individuals who knew about the tetanus [53 (74.6%) vs 18 (25.4%), p<0.001], herpes zoster [52 (73.2%) vs 19 (26.8%), p=0.002], influenza [58 (81.7 %) vs 13 (18.3%), p=0.001], and pneumococcal vaccine [46 (64.8%) vs 25 (35.2%), p<0.001] were higher than those who did not. Only 2 (2.8%) of 71 patients had pneumococcal vaccine, while 24 patients (33.8%) had influenza vaccine (p = 0.007), 14 patients (19.7%) had tetanus vaccine (p=0.012). No patient older than 65 has ever received the zona vaccination.

When the patients were evaluated according to their comorbidities, it was observed that only 1 (2.1%) of 47 patients followed-up for DM received pneumococcal vaccine (p=0.562) and 19 patients (40.4%) had influenza vaccine (p = 0.001). Of the patients with CHF, 4 (14.8%) had the pneumococcal vaccine, while 23 (85.2%) did not (p=0.012) and 11 (40.7%) had the influenza vaccine, while 16 (59.3%) did not (p=0.013). In the patient group with COPD, 6 patients received the pneumococcal vaccine (p<0.001) and 13 patients had the influenza vaccine (p=0.002). Vaccination rates were found to be very low in patients followed up for CKD. While none of the 15 patients received pneumococcal vaccine, only 2 patients had influenza vaccine. Two patients with chronic liver disease had influenza vaccine but not pneumococcal vaccine **(Table 4)**.

Table 4: Comparison of Pneumococcus and influenza vaccine in terms of their co-morbidities

Co-morbidity	Pneumococcus vaccine			Influenza vaccine		
	Received (n,%)	Not received (n,%)	p	Received (n,%)	Not received (n,%)	p
DM	1 (2.1%)	46 (97.9%)	0.562	19 (40.4%)	28 (59.6%)	0.001
CHF	4 (14.8%)	23 (85.2%)	0.012	11 (40.7%)	16 (59.3%)	0.013
COPD	6 (20.7%)	23 (79.3%)	<0.001	13 (44.8%)	16 (55.2%)	0.002
CKD	-	15 (100%)	-	2 (13.3%)	13 (86.7%)	0.540
Chronic liver disease	-	2 (100%)	-	2 (100%)	-	-
> 65 years old	2 (2.8%)	69 (97.2%)	0.693	24 (33.8%)	47 (66.2%)	0.007

* DM: Diabetes mellitus, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease, CKD: Chronic kidney disease

DISCUSSION

In our study, vaccination rates were found to be very low in patients over the age of 18 admitted to family medicine clinics. Although 85% of the patients believed that vaccines were beneficial, they did not have the vaccine due to side effects, inability to access the vaccine, and cost.

In a study involving patients aged 18-64 years admitted to internal medicine outpatient clinics in our country, the adult vaccination rate was found to be 36.1%. Similar to our study, tetanus vaccination was performed most frequently in the study (23%) (6). In another study evaluating tetanus seropositivity, it was observed that tetanus seropositivity was 95.2%, 84.4%, and 57.3% in participants aged 21-39, 40-49 and over 50 years old, respectively (9). High awareness of tetanus vaccination in pregnant women, routine vaccination before military service, and post-exposure prophylaxis are among the reasons why tetanus is the most common adult vaccine. In a study conducted on inpatients, 26.6% of the patients stated that they had the tetanus vaccine. Similar to our study, awareness and vaccination rates were higher among well-educated patients in comparison to those with low education (10). In a study conducted in 2015, the rate of tetanus vaccination was found to be 61% for those aged 19-49, 72.2% for those aged 50-64, and 81.4% for those over 65 years old. In contrast to this study, our study found that tetanus immunization rates were much lower in the patient population over 65. This difference may be the result of the fact that adult vaccines do not contain sufficient records, and vaccination is not recommended for routine health care (11). In a study evaluating the patient groups with vaccine indication, the proportion of patients who received diphtheria-tetanus vaccination in the last 10 years similar to our study was 29.9% (95% CI: 20.2-41.5) for Type 2 DM and 26.5% (95% CI: 21-32.8) for solid organ transplantation, 37.7% (95% CI: 27.1-49.5) for CHF, and 34.1% (95% CI: 27.1-41.8) for COPD (12).

Influenza is still an important cause of mortality and morbidity worldwide. Annual influenza vaccination is recommended for patients over the age of 65, pregnant women, and immunosuppressed patients, as well as for patients with metabolic diseases such as chronic heart dise-

ase, chronic kidney disease, chronic liver disease, chronic neurological disease, DM, morbid obesity and respiratory system diseases, including COPD, asthma, and cystic fibrosis, and for healthcare professionals (13). In a study carried out in Turkey, the influenza vaccination rate was determined to be 20%. Although there was no statistical difference between the educational levels of the patients and vaccination rates, a positive correlation was observed between health literacy, especially about disease prevention, and vaccination rates (14). In our study, the rate of influenza vaccination was found to be 21.7%, and no statistical difference was found between educational levels and vaccine administration.

In a different study, the vaccination rate was 40%, and it was found that vaccination rates increased as education levels improved (15). One of the key aspects in removing barriers to adult immunization is education. Patients of all education levels should be offered adult immunization in a way that allows them to understand it and confidently address their concerns. It's possible that the lack of adequate information provided by medical staff contributed to the low and consistent rates of influenza vaccination in our study across all educational levels. In a study involving geriatric patients in Turkey, the influenza vaccination rate was found to be 44.4%. In order to improve vaccination in older patients, it has been recommended to expand the information about vaccination and facilitate vaccine access, considering the sociocultural differences, with the efforts of healthcare professionals, family, friends, and communication tools (16). In another study, influenza vaccination was observed more frequently in patient group over 65 years of age and those with at least one risk factor and a chronic disease. Similar to our study, the reasons for not getting the influenza vaccine were reported as follows: not catching the flu frequently, fear of side effects, concerns about the effectiveness of the vaccine, and the belief that the vaccine causes flu (17). In pneumococcal vaccination, the 13-valent conjugated pneumococcal vaccine (PCV13 [Prevnar 13, Pfizer, Inc.]) and the 23-valent polysaccharide pneumococcal vaccine (PPSV23 [Pneumovax 23, Merck and Co., Inc.]) were used because they are the ones that are available in our country. Considering that the

disease burden would be reduced with the increase of PCV 13 vaccination in children, in 2019 the Advisory Committee on Vaccination Practices (ACIP) advised that PCV 13 vaccination be performed with shared clinical decision-making for individuals aged 65 years old who did not have immunosuppressive, cerebrospinal fluid (CSF) leakage and cochlear implants as well as who had never had PCV13 before (18). In our study, the rate of pneumococcal vaccination including PCV 13 and PPSV 23 was 3.6%. In a study conducted in France, the pneumococcal vaccination rate between April 2013 and April 2017 was determined to be 4%. The rate was 12% in HIV-infected patients and 2% in patients followed up for DM (19). TEMD Vaccination Study shows that for patients with type 2 diabetes mellitus, pneumococcal vaccination rates were 7%, and the reason for this minimal difference from the current study may be that the patients applied to the family medicine outpatient or endocrine clinics (20). Although the pneumococcal vaccine is known to reduce the disease burden, pneumococcal vaccination rates in adults are lower compared to other routine vaccines (21). In our study, the frequency of awareness of the pneumococcal vaccine was higher among university graduates compared to people with lower education. In a study conducted by Mutlu H et al., as the education level increased, the pneumococcal vaccination rate and vaccine awareness increased in patients over 65 years of age (22). In our study, the herpes zoster vaccine had the lowest vaccination rate. It is recommended for people over 50 years old to reduce the risk of herpes zoster and post herpetic neuralgia. There are two types of this vaccine: recombinant zoster vaccine (RZV, Shingrix) administered in two doses and live zoster vaccine (ZVL, Zostavax) administered in a single dose. There is only a live zoster virus vaccine in Turkey, but since July 1, 2020, this vaccine is not available in the United States (23). Kızmaz M. et al. found that the rate of vaccination with herpes zoster was found to be 1.8% in patients over 65 years of age (24). In a study evaluating the efficacy of live zoster vaccine in Australia, the efficacy of the vaccine was 63.5% (95% CI: 47.5-74.6%) in the first year, while this rate was regressed to 48.2% (95% CI: 30–61.7%) in the second year (25). In addition, the effectiveness of the recombinant zoster vaccine was found

to be 85.5% (95% CI: 83.5-87.3) (26). The lack of recombinant zoster vaccine in our country and the high cost of live zoster vaccine are the most important reasons for the low vaccination rates.

The major reason for patients those did not accept vaccination even though they had been told is that they "prefer not to indicate ". This does not include reasons like cost, side effects, or logistic problems. Participants may have been hesitant to declare that they do not believe in vaccines, or they may have held other unsupported beliefs. Increasing answer alternatives when planning a study might decrease the burden of "other reasons" as a response. In another study, vaccination hesitancy reasons were concerns about industrial profiteering, preference for natural immunity, thinking about whether they will not get ill, and a low sense of shared community responsibility (27).

This could be accepted as a limitation of our study. One of the other limitation of our study is that it is a cross-sectional study conducted in a single centre. Moreover, we got information about the vaccination of patients from them, but we could not check it over a registry system. We primarily evaluated the vaccination rates for influenza, pneumococcal vaccine, tetanus, and herpes zoster. Our study did not include all vaccines recommended for adult vaccination. It is among the strengths of our study that it revealed the vaccine awareness in our country and evaluated all vaccine recommended groups and the geriatric patient group separately.

As a result, we are still far below the desired levels of adult vaccination in our study group. It should be considered that adult vaccination is the most effective way to prevent diseases. As a result, it is critical to raise patient and healthcare professional awareness of on this issue.

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APPENDIX-1

Vaccination Questionnaire

1. Age:
2. Gender: Female☐   Male ☐
3. Marital status: Married ☐ Single ☐ Divorced ☐
4. Monthly income: ☐   0-1500 Turkish lira(TL)
   - ☐   1501-2500 TL
   - ☐   2501-3500 TL
   - ☐ 3500+ TL
5. Occupation:
   - High-risk occupations
   - Healthcare workers ☐
   - People who work in childhood education and care ☐
   - Caregiver ☐
   - Staff of nursing homes, and long-term care facilities ☐
6. Educational degree: Illiterate ☐ Primary school ☐ Secondary school ☐ High school ☐ University ☐
7. Living in: Urban ☐ Rural ☐
8. Household members:

Vaccination	9. Have you heard of these vaccines for adults?	10. Have you ever been recommended these vaccination in your adult life?	11. Have you ever been vaccinated in your adult life?
Tetanus			
Pneumococcal vaccine			
Herpes zoster			
Influenza			

12. Where did you get the information about the vaccines?
   - Internet or printed and visual medial ☐
   - Friends or relatives ☐
   - Healthcare professionals ☐

13. Do you think immunizations are beneficial?   Yes ☐   No ☐

14. If you have not been vaccinated, what is your reason for not getting vaccinated?
   - Fear of side effects ☐
   - Difficulty in accessing the vaccine due to logistic reasons ☐
   - High vaccination prices ☐
   - Prefer not to indicate ☐

15. Do you have any chronical medical condition?

	Diabetes mellitus
	Chronic obstructive pulmonary disease or Bronchial Asthma
	Underwent immunosuppressive treatment
	Congestive heart failure
	Haematological diseases
	Chronic liver disease
	Chronic kidney disease
	Alcoholism
	Asplenia

ARAŞTIRMA YAZISI / RESEARCH ARTICLE

ÇOCUKLARDA SARS-COV-2 ENFEKSİYONUNDA İMMÜNOGLOBULİNLER HASTALIK ŞİDDETİ VE HASTANEDE YATIŞ SÜRESİNE ETKİLİ MİYDİ ?

WAS IMMUNOGLOBULINS EFFECTIVE IN DISEASE SEVERITY AND LENGTH OF HOSPITAL STAY IN CHILDREN WITH THE INFECTION OF SARS-COV-2 ?

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ÖZET

AMAÇ: Hastaneye yatış gerektiren ciddi hastalığı olan çocuklarda başvuru sırasındaki immünoglobulin düzeylerinin hastalık şiddeti, SARS-CoV-2 RT-PCR testinin negatifleşmesine kadar geçen süre ve hastanede kalış süresi ile ilişkili olup olmadığını araştırdık.

GEREÇ VE YÖNTEM: Hastaneye yatırılan ve COVID-19 tedavisi gören kırk dört pediatrik hasta dahil edildi. Hastalar değerlendirme kolaylığı açısından hafif-orta (n=35) ve ağır hastalığı olanlar (n=9) olarak iki gruba ayrıldı. İmmünoglobulin düzeylerinin hastalık şiddeti, SARS-CoV-2 RT-PCR testi negatifleşmesine kadar geçen süre ve hastanede kalış süresi ile ilişkisi incelendi.

BULGULAR: Çalışma popülasyonunun ortanca (min-maks) yaşı 13 (1-18) olup, 25'i (%56,8) kız ve 19'u (%43,2) erkekten oluşmaktadır. Hafif-orta hastalığı olan çocukların %89.2'sinde (n=33) IgG seviyeleri normaldi ve %5.7'sinde (n=2) yükselmişti. Ağır hastalığı olan hastaların %44.4'ünde (n=4) IgG seviyeleri normaldi ve %55.6'sında (n=5) yükselmişti. IgG düzeyleri açısından gruplar arasında anlamlı fark bulundu (p=0,002). IgG düzeyinin hastanede kalış süresi ve SARS-CoV-2 RT-PCR testi negatifleşmesine kadar geçen süre ile ilişkisi incelendiğinde, SARS-CoV-2 RT-PCR test negatifleşmesine kadar geçen süre ile Ig G düzeyi arasında anlamlı bir ilişki gözlenmedi (p=0.096, z=1.667). Ancak Ig G düzeyi yüksek olan hastalarda hastanede kalış süresi anlamlı olarak daha uzundu (p=0.096, p=0.002).

SONUÇ: Normalden yüksek endojen IgG seviyeleri, COVID-19 nedeniyle hastaneye yatırılan çocuklarda ciddi hastalık gelişimi ve uzun süreli hastanede kalış süresi ile bağımsız olarak ilişkili olabilir.

ANAHTAR KELİMELER: COVID-19, Çocuk, İmmünoglobulinler.

ABSTRACT

OBJECTIVE: We investigated whether immunoglobulin levels on admission are associated with disease severity, time to negativization of SARS-CoV-2 RT-PCR test, and length of hospital stay in children with severe illness requiring hospitalization.

MATERIAL AND METHODS: Forty-four pediatric patients hospitalized and treated for COVID-19 were included. The patients were divided into two groups as those with mild-to-moderate (n=35) and those with severe disease (n=9) for ease of evaluation. The relationship of immunoglobulin levels with disease severity, time to SARS-CoV-2 RT-PCR test negativization and length of hospital stay was examined.

RESULTS: The study population had a median (min-max) age of 13 (1-18) years and consisted of 25 (56.8%) girls and 19 (43.2%) boys. IgG levels were normal in 89.2% (n=33) and elevated in 5.7% (n=2) of the children with mild-to-moderate disease. Among patients with severe disease, IgG levels were normal in 44.4% (n=4) and elevated in 55.6% (n=5). A significant difference was found between the groups in terms of IgG levels (p=0.002). When the relationship of IgG level with length of hospital stay and time to SARS-CoV-2 RT-PCR test negativization was investigated, no significant correlation was observed between time to SARS-CoV-2 RT-PCR test negativization and Ig G level (p=0.096, z=1.667). However, the length of hospital stay was significantly longer in patients with elevated IgG levels (p=0.096, p=0.002).

CONCLUSIONS: Higher-than-normal endogenous IgG levels may be independently associated with the development of severe illness and prolonged hospital stay in children hospitalized for COVID-19.

KEYWORDS: COVID-19, Children, Immunoglobulins.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). While most of the infected children do not show any symptoms or experience mild symptoms, severe clinical manifestations may develop especially in children with an underlying chronic disease. Currently, no specific treatment with demonstrated effectiveness is available for COVID-19 (1). In general, the severity of an infection depends on the virulence of the pathogen involved and the immunological response of the host. Although an active immune response is required to eliminate pathogens, uncontrolled host immune responses can cause damage in healthy cells and tissues, consequently determining the disease outcome. There is ongoing debate on the pathophysiology of COVID-19 and high pathogenicity of the virus. In the adult population, cytokine release syndrome and lymphopenia have been identified as hallmarks of severe COVID-19, which indicate increased systemic inflammatory response (2). Immunoglobulins (Ig) produced by plasma cells act as a critical component of the overall immune response and are mainly involved in the recognition, neutralization, opsonization and direct lysis of the pathogens. They also have anti-inflammatory and immunomodulatory properties. There is little information about the changes in serum Ig levels in patients with COVID-19. To the best of our knowledge, the effects of Ig levels on the length of hospital stay and the time to negativization of SARS-CoV-2 polymerase chain reaction (PCR) test in COVID-19 patients are unknown (3 - 8). For these reasons, we sought to investigate whether Ig levels (IgG, IgM and IgA) measured shortly after admission affect the disease severity, length of hospital stay and time to SARS-CoV-2 PCR test negativization in pediatric patients with mild-to-moderate or severe COVID-19 requiring hospitalization.

MATERIAL AND METHODS

This single-center, retrospective, cross-sectional study included pediatric patients with mild-to-moderate or severe COVID-19 who were hospitalized and followed at the Pediatric Infectious Diseases clinic of a tertiary care hospital between 01.04.2020 and 01.03.2022 whose Ig levels were available. Initially, 246 hospitalized pediatric patients were recruited for the study. Subsequently, a total of 202 children with pre-existing immune deficiency syndromes and/or with no Ig measurements available were excluded. Ultimately, the study was conducted with 44 children. All children had been fully vaccinated in accordance with the national immunization schedule of the Republic of Turkey. For all participants, the diagnosis of COVID-19 was confirmed by detection of SARS-CoV-2 in combined oropharyngeal and nasopharyngeal swabs using real-time reverse transcription PCR (RT-PCR) test. The pediatric cases were divided into two groups as those with mild-to-moderate disease and those with severe disease to facilitate assessment. Patients with significant tachypnea on admission and/or at any time during hospitalization, those needing oxygen support >2 L/min and respiratory support with continuous positive airway pressure (CPAP), those who were intubated and/or required intensive care support were included in the severe disease group. Clinical classification of the study patients was performed according to the COVID-19 (SARS CoV-2 infection) guidelines issued by Republic of Turkey Ministry of Health General Directorate of Public Health updated on 06.01.2022 (9). The need for hospitalization was determined individually for each patient based on their clinical condition and in line with the recommendations set forth in the national COVID-19 Guidelines of Turkey, which were periodically updated in the early stages of the pandemic. Even patients with a mild clinical course were hospitalized because in the early phase of the pandemic, there were recommendations to isolate and follow these patients at the hospital due to greater uncertainties at that time.

Age, sex, time to RT-PCR test negativization and length of hospital stay were retrieved from patient files retrospectively. Among laboratory parameters, white blood cell (WBC) and platelet (PLT) counts, hemoglobin level, and lymphocyte and neutrophil counts were noted. IgG, IgM and IgA levels were evaluated

according to age and recorded as decreased, normal or increased. The Nelson Textbook of Pediatrics, 20th Edition was used as a guide to determine the reference ranges of Ig levels (10).

Ethical Committee

This study was approved by the Institutional Ethics Review Committee of University of Adıyaman Turkey, (decision no: 5-15, date: 24.05.2022).

Statistical Analysis

Statistical analyses were conducted to determine the impact of disease severity on laboratory parameters and the relationship of immunoglobulin levels with length of hospital stay and time to PCR negativization. Descriptive statistics were summarized as means and standard deviation (minimum-maximum) for continuous variables and numbers (n) and percentages (%) for categorical variables. The normality of data distribution was checked with Kolmogorov-Smirnov for continuous variables. The results were analyzed using independent samples t-test or Mann Whitney U test depending on the outcome of the normality test. Fisher's exact test and chi-square test were used for categorical variables. All statistical analyses were performed using SPSS software, version 23.0 (IBM Corp., Armonk, NY), and the level of significance was set at $p < 0.05$.

RESULTS

The study sample had a median (min-max) age of 13 (1-18) years and consisted of 25 (56.8%) girls and 19 (43.2%) boys. 79.5% (n=35) of the participants had mild-to-moderate disease and 20.5% (n=9) had severe disease. Four patients with severe COVID-19 had additional chronic conditions, including Down's syndrome (n=2), atrial septal defect not causing heart failure and epilepsy (n=1 each). During follow-up, two patients required intensive care but all patients were discharged with full recovery after receiving appropriate treatment. The study groups did not differ significantly in terms of demographic characteristics, which are presented in **Table 1** by disease severity. The length of hospital stay [median (min-max)] was 6 (5-8) days in patients with mild-to-moderate disease and

11 (7-16) days in patients with severe disease, with significantly longer hospitalization observed for severe patients ($p < 0.001$, z=4.615). The time to negativization of SARS-CoV-2 RT-PCR test [median (min-max)] was 6 (4-8) days in patients with mild-to-moderate disease and 6 (5-13) days for patients with severe disease, with severely ill patients showing significantly longer time to PCR negativization (p=0.026, z=2.228). Data on routine laboratory parameters and immunoglobulin values are summarized in Table 1. Severely ill patients were found to have a significantly lower lymphocyte count (p=0.008, z=2.662) and significantly higher prevalence of elevated IgG levels (p=0.002). Other laboratory findings were similar between the groups.

When the relation of IgG level with the length of hospital stay and time to SARS-CoV-2 RT-PCR test was examined, no significant association was found between time to SARS-CoV-2 RT-PCR test negativization [median (min –max), normal IgG group: 6 (4-8) days, elevated IgG group: 7 (5-13) days] and IgG level (p=0.096, z=1.667). However, the length of hospital stay [median (min –max), normal IgG group: 6 (5-12) days, elevated IgG group: 11 (6-16) days] was significantly longer in patients with elevated IgG levels (p=0.096, p=0.002).

Table 1: Demographic and laboratory data of the study groups by disease severity

Parameters (mean ± SD)	Mild-to-moderate disease (n=35)	Severe disease (n=9)	p
Age, years	11.69 ± 5.14	12.77 ± 4.89	0.365
Sex, n (%)			
• Female	21 (60%)	4 (44.4%)	0.401
• Male	14 (40%)	5 (55.6%)	
Hemoglobin (g/dL)	13.19 ± 1.27	14.13 ± 1.59	0.091
Platelet count (10^3/uL)	255.0 ± 70.0	212.0 ± 68.0	0.180
White blood cell count (10^3/uL)	6.877 ± 2.341	5.325 ± 2.780	0.120
Lymphocyte count (10^3/uL)	2.749 ± 1.965	1.521 ± 5.87	**0.008**
Polymorphonuclear leukocytes (10^3/uL)	3.347 ± 1.446	4.782 ± 4.013	0.141
IgA, n (%)			
• Normal	32 (91.4%)	9 (100%)	0.494
• Increased	3 (8.6%)	0 (0%)	
IgG, n (%)			
• Normal	33 (89.2%)	4 (44.4%)	0.002
• Increased	2 (5.7%)	5 (55.6%)	
IgM, n (%)			
• Normal	33 (94.3%)	8 (88.9%)	0.506
• Increased	2 (5.7%)	1 (11.1%)	

DISCUSSION

To the best of our knowledge, this is the first study examining the association of Ig (IgG, IgM and IgA) levels with the length of hospi-

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tal stay and time to SARS-CoV-2 PCR negativization in pediatric patients. We found that the children with severe disease had higher IgG levels than children with mild-to-moderate disease and children with higher IgG levels had a longer duration of hospitalization. Higher IgG levels emerged as an independent predictor of prolonged hospitalization and the development of severe disease. However, IgM and IgA levels were within normal range in patients with mild-to-moderate disease and severely ill patients, and therefore, their relations with time to SARS-CoV-2 PCR were not analyzed. The aforementioned findings suggest that higher IgG levels can be used to predict disease severity and length of hospital stay.

Since the early reports on COVID-19, several prognostic factors have been increasingly cited in the literature including hematologic, cardiac, renal, inflammatory and coagulation biomarkers as well as demographic characteristics and comorbidities (11). In line with previous reports, in our study, lymphopenia and the presence of comorbidities were correlated with the development of severe COVID-19 manifestations. Contrastingly, relationships of sex and neutrophilia with severe disease as reported in the literature, could not be demonstrated in our study. As a matter of fact, only a limited number of studies have focused on serum Ig levels in relation to the severity of COVID-19 and clinical outcome. However, these studies have reported conflicting results. In a study by Qin et al., decrease was found only in IgM levels in patients with severe COVID-19, with no differences in other Ig levels (12). Marcos-Jiménez et al. reported that IgG levels on admission were not different between patients with severe COVID-19 and normal healthy individuals but when the disease severity was considered, IgG levels were lower in severely ill patients (4). Hasan Ali et al. showed increased IgA levels in patients with severe COVID-19 compared to those with mild and moderate disease but there was no marked difference in IgG levels (13). Zhao et al. investigated the correlation between mortality and Ig levels in COVID-19 and demonstrated elevated IgG, IgA and IgE concentrations in non-survivors versus survivors, with no difference in IgM levels

(8). It is noteworthy that all studies were conducted in adult population and studies examining Ig levels in pediatric population are lacking.

Our study included children with mild-to-moderate disease or severe disease as well as children whose condition worsened and required intensive care despite being classified as severely ill. Although the current study had a retrospective design, we are aware that many uncertainties around COVID-19 management at the beginning of the pandemic have prompted clinicians to tread carefully. In an attempt to identify parameters that can predict disease prognosis, Ig levels were measured within 48 hours of admission in a portion of hospitalized children. Early assessment of immunoglobulins ensured that Ig levels remained unchanged by other pathogens causing coinfection or drugs administered. Patients with immunodeficiencies and/or IgG deficiency diagnosed with COVID-19 were shown to a more severe disease course and a higher mortality rate (14). In contrast, in our study, Ig levels were not lower than normal in any of the patients in both groups. This may be due to the exclusion of children with immunodeficiencies from the current study. There may be other mechanisms that could explain this finding, which are currently unknown.

Innate and adaptive immune responses vary depending on the severity of COVID-19 manifestations and are correlated with clinical outcome. More specifically, the severe form of COVID-19 has been linked to a dysfunctional innate immune response coupled with aberrant adaptive immunity including inadequate type I interferon response. In adaptive immunity, differential T-cell and B-cell responses have been found in patients with severe disease compared to those with mild disease (15 - 18). Irrespective of the mechanisms, IgG is a key component of humoral immunity and its presence is crucial for host defense against pathogens. IgG is the most abundant Ig and mediates many beneficial immunologic functions (3).

In contrast to adult studies, elevated IgG levels were observed in severely ill children in our study. Additionally, it was shown with the present study that children with increased IgG levels

developed clinically severe illness and required prolonged hospitalization but were discharged with full recovery. This may be the reason why children are often less affected by SARS-CoV-2 infection as a result of some unknown mechanisms mediated by immunoglobulins.

Some limitations should be noted for this study. First, the study had a retrospective design and the sample size was relatively small. Secondly, this was a single-center study. Further studies with large numbers of cases are warranted to demonstrate the generalizability of our findings. Finally, Ig measurements were obtained only once (on admission) for each patient. Serial Ig analyses can better describe the course of IgG over time.

Higher-than-normal endogenous IgG levels may be associated with the development of severe illness and prolonged hospital stay in pediatric patients hospitalized for COVID-19.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

SIÇANLARDA KARACİĞER VE ÇİZGİLİ KAS BİLGİSAYARLI TOMOGRAFİ ATENÜASYONLARI İLE POST-MORTEM İNTERVAL TAYİNİ

POST-MORTEM INTERVAL ESTIMATION BASED ON LIVER AND STRIATED MUSCLE COMPUTED TOMOGRAPHY ATTENUATIONS IN RATS

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ÖZET

AMAÇ: Post-mortem interval (PMI) tayinini hedefleyen ölüm sonrası bilgisayarlı tomografik çalışmalara ilgi artmaktadır. Literatürde çoğu çalışma, kontrolsüz veya nispeten daha az kontrollü bir durumda yürütülmüştür. Bu çalışma, sıkı kontrollü çevresel koşullar altında PMI tahmininde karaciğer ve çizgili kasların bilgisayarlı tomografi atenüasyonlarının kullanılabilirliğini araştırmaktadır.

GEREÇ VE YÖNTEM: 30 Wistar Albino sıçanın ölümden sonraki ilk 30 dakikada ve post-mortem 12, 24, 36, 48, 72, 96, 120, 144 ve 168. saatte bilgisayarlı tomografi görüntüleri alındı. 0,12 cm² ilgi alanında karaciğerin lateral lobları ve paraspinal kasın tekrarlayan atenüasyonları kaydedildi.

BULGULAR: Karaciğer ve paraspinal kasların atenüasyon değerleri, ölümden 12 saat sonra daha yüksek bulundu. Hem erkek (p=0,01) hem de dişi sıçanlarda (p=0,01) otopsiden 30 dakika sonra elde edilen görüntüler ile otopsiden 12 saat sonra elde edilen görüntüler arasında anlamlı fark gözlendi. PMI tayini için karaciğer ve kas dokusu için farklı atenüasyon eşik değerleri belirlendi."

SONUÇ: Önerilen model ile karaciğer ve çizgili kasların atenüasyon değerlerinin kullanımı, PMI tayini için faydalı bulunmuştur. Atenüasyonun eşik değerleri, özellikle karaciğer için, PMI sınırlandırılmasında kullanılabileceği anlaşılmıştır.

ANAHTAR KELİMELER: Post-mortem interval tayini, Post-mortem bilgisayarlı tomografi, Karaciğer atenüasyonu, Kas atenüasyonu .

ABSTRACT

OBJECTIVE: The interest on post-mortem computed tomographic studies targeting post-mortem interval (PMI) estimations is increasing. Most studies have been conducted in an uncontrolled or relatively less controlled condition. However, this study investigates the usefulness of computed tomography attenuations of the liver and striated muscles in PMI estimation under strictly controlled environmental conditions.

MATERIAL AND METHODS: Post-mortem computed tomography images of 30 Wistar Albino rats were obtained in the first 30 min after death and 12, 24, 36, 48, 72, 96, 120, 144 and 168-hours following death. Repeated attenuations of both the lateral lobes of the liver and paraspinal muscle were recorded in 0.12-cm² regions of interest.

RESULTS: The attenuation values of the liver and paraspinal muscles were higher 12-hour post-mortem. A significant difference was observed between the images obtained 30 minutes post-mortem and those obtained 12 hours post-mortem in both male (p=0.01) and female rats (p=0.01). Different cut-off attenuation values for the liver and muscle tissue were determined to estimate the post-mortem interval.

CONCLUSIONS: The use of attenuation values of the liver and striated muscles with the proposed model was found to be beneficial for the determination of PMI. The cut-off values of attenuation, especially for the liver, can be used in the delimitation of the post-mortem interval.

KEYWORDS: Post-mortem interval estimation, Post-mortem computed tomography, Liver attenuation, Muscle attenuation.

INTRODUCTION

For many decades, post-mortem interval (PMI) estimation has been a frequently studied topic in forensic sciences. Scientists from various disciplines have described several PMI estimation methods. However, there is still no universally valid method to estimate PMI in a certain manner (1, 2).

Post-mortem radiological methods have been gradually developing following the 'Virtopsy project', which was announced by a team led by Thali et al. (3). Based on this encouraging inspiration, forensic scientists have shown an increasing effort toward post-mortem radiological studies to establish a post-mortem diagnosis or determine PMI. Among these radiological studies, a few dealt with PMI estimation (4 – 7), whereas most were dedicated to enlightening the radiological characteristics of post-mortem changes compared with antemortem data (8 – 17). However, some studies were conducted under relatively controlled conditions, while some were performed in a relatively open and slightly controlled environment, which potentially exposed the study material, the cadavers, to numerous variables such as insect activity, humidity, heat and cold. The following questions led to this study: 'What is the pattern of post-mortem liver or striated muscle computed tomography (CT) attenuation changes under strictly controlled environmental conditions?' and 'How useful is this for PMI estimation in comparison to previous studies conducted in open or relatively uncontrolled environment?' Therefore, our team prepared a longitudinal design that can provide a close environment in which temperature and humidity are both controlled.

As the basic study point of this paper, the attenuation value measures the ability of an incident energy beam to penetrate a material. It is the quantity of the beam, such as sound waves and X-rays, weakened by the material while passing through. In routine radiological screening applications, CT attenuation values are revealed based on a linear density scale, as 'Hounsfield units' (HU), which is calculated by the following formula:

$$HU = 1000 \times ((\mu tissue - \mu water) / \mu water)$$
(μ stands for CT linear attenuation coefficient)

This study investigates the use of CT attenuation of the liver and striated muscle in estimating PMIs and reveals the relationship between post-mortem attenuation values of the liver and striated muscles on CT images in rat models.

MATERIAL AND METHODS

The Design of the Study

Thirty healthy Wistar albino rats (15 males and 15 females) with an age of 22 weeks were euthanised using CO_2 inhalation in the beginning of the study. Wistar albino rats were chosen because of their relatively similar enzymatic systems to humans in both striated muscles and liver tissue. The rats were weighed just after death, and the mean weight was 351.9 g (standard deviation (SD) = 12.9) for female rats and 401.1 g (SD = 12.6) for male rats. All rat cadavers were fixed in the supine position to minimise the effect of post-mortem lividity on the right (RLL) and left (LLL) lateral lobes of the liver. The rat cadavers were kept in a strictly controlled environment in a Microtest® MIT 120 test cabin (ELECTROMATIC Equipment Co., Inc., Cedarhurst, NY, USA). The temperature and relative humidity were set to 23°C and 40% respectively. The actual temperature and humidity values were measured once every 30 minutes using the automatic internal measurement device in the test cabin. The mean cabin temperature and relative humidity were 23.1°C ± 0.6°C and 40.7% ± 2.4% respectively, during the whole procedure.

CT Protocol

CT was used in this study because of its frequent use in post-mortem imaging as a cheaper, faster and easily accessible radiological screening method. The first CT scans of all animals were conducted 30 minutes post-mortem and follow-up scans were performed at 12-, 24-, 36-, 48-, 72-, 96-, 120-, 144- and 168-hours following death. CT scans were performed using a 16-row channel CT device with a 1-mm detector collimation. The cadavers were scanned in the axial plane, and images were reconstructed using the filter back projection method in an H10f filter and 1.5-mm slice thickness. The image matrix was 512×512. The attenuation values (in HU) of the RLL and LLL of the liver and paraspinal muscles (PSM) were measured in 0.12-cm² regions of interest

(ROIs) by two blinded radiologists (a certified radiologist with 25-year experience and a trainee with four-year experience). The 0.12-cm² ROIs are the largest homogenous parenchymal areas without any main vasculature and bile ducts in the liver and a homogenous tissue site of the left paraspinal muscle between the L1 and L3 sections of the rats in this study. Three ROIs were selected from the most appropriate central parts of the RLL and LLL without the main vasculature and bile duct of the cadavers; similarly, three ROIs were selected from the left paraspinal muscle. The averages of the three acquired ROIs of the same site were calculated. Therefore, three ROIs (averages of the main ones) (two from the liver and one from the paraspinal muscles) were selected for each rat.

Ethical Committee

Ethics approval was obtained from Animal Experimentations Local Ethics Board of Hacettepe University (decision number: 2016/29). The study was carried out in accordance with the principles of "Guide for the Care and Use of Laboratory Animals".

Statistical Analysis

Statistical Package for the Social Sciences (version 24; IBM Corp., Armonk, NY, USA) was used for statistical analysis. Descriptive statistics were performed for the general properties of rat cadavers. An analysis of variance (ANOVA) was used to identify the correlations between attenuation values of different time zones and receiver operative characteristics to determine cut-off values. This point was the peak of timeline for steady changes in attenuation values.

Inter-observer and intra-observer reliability and repeatability of attenuation values were assessed using unweighted and linear-weighted kappa (κ) statistics, given that the attenuation value is ordinal. The agreement rate and 95% Wilson score confidence interval (CI) were revealed. P values of <0.05 were used to indicate statistical significance. The κ values were interpreted as follows: κ < 0.20: poor agreement; κ = 0.21–0.40: fair agreement; κ = 0.41–0.60: moderate agreement; κ = 0.61–0.80: good agreement and κ = 0.81–1.00: very good agreement.

RESULTS

Liver Attenuation Values

All attenuation values were measured from the RLL and LLL using areas free from putrefactive gases and vascular formations until the 72nd hour images. However, there was not enough area to get 0.12-cm2 ROIs without putrefactive signs in the 96th hour liver images. 'Swiss cheese' signs were seen on all liver images obtained 72 hours post-mortem with minor intact areas. Statistical analysis was performed on the mean values of the RLL and LLL since no significant differences were found between the RLL and LLL of each rat (p = 0.69). All liver attenuation values were significantly higher than that obtained 30 minutes post-mortem in rat cadavers. The liver attenuation values increased with an increasing PMI **(Figure 1)**.
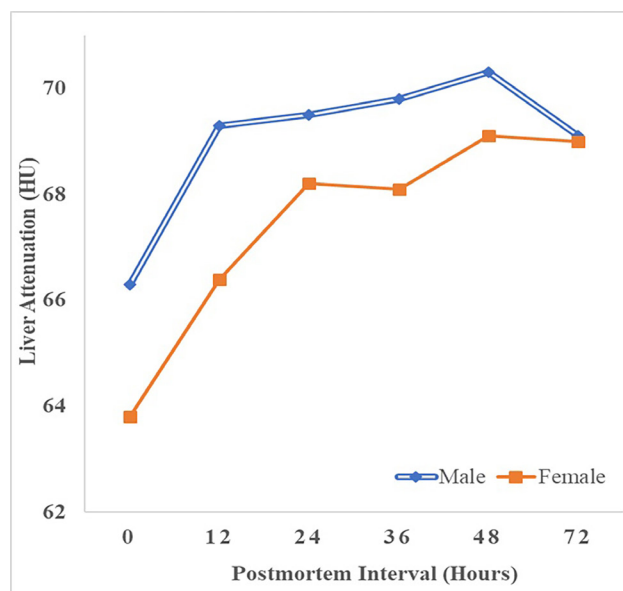
Figure1: Change of mean liver attenuations with time in male and female cadavers (HU: Hounsfield Unit, F: female, M: male)

The most significant difference was observed between the images obtained 30 minutes post-mortem and those obtained 12 hours post-mortem in both male (p = 0.01) and female (p = 0.01) rats respectively. Female cadavers showed significantly higher liver attenuation values, except in the images obtained 24-, 48- and 72-hours post-mortem. Receiver Operating Characteristics (ROC) analysis was performed to determine cut-off values to estimate PMI. Cut-off values of all male and female cadavers for 12th hour PMI are shown in **Table 1**.

Table1: Mean liver attenuation cut-off values of all individuals, male cadavers and female cadavers for 12-hour postmortem interval.

	Cut-off value	Sensitivity	Specificity	ROC AUC*
All cadavers	67.25 HU	80%	83.3%	87%
Female cadavers	65 HU	96%	73.3%	90.4%
Male cadavers	68.25 HU	81.3%	80%	86.8%

* ROC AUC: Area under the curve of receive operative characteristics

This point was the peak of timeline for steady changes in attenuation values, after which comparison of attenuation values become unreliable. The PSM attenuation values increased after death, as well. However, these values differed between different time points without showing any linear pattern **(Figure 2)**.

Figure 2: Change of PSM attenuations with time in male and female cadavers (HU: Hounsfield Unit, F: female, M: male)

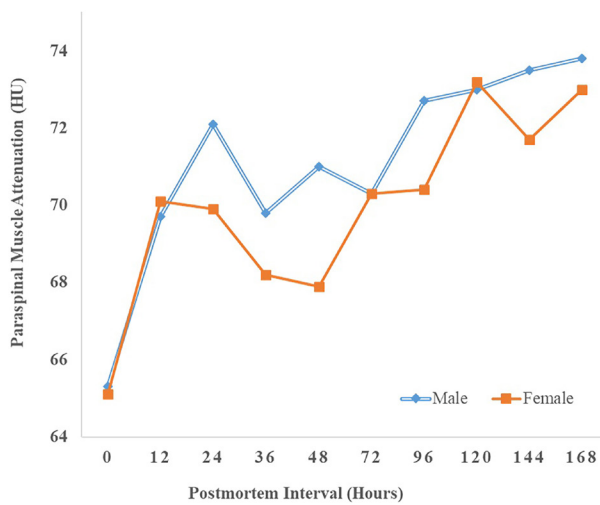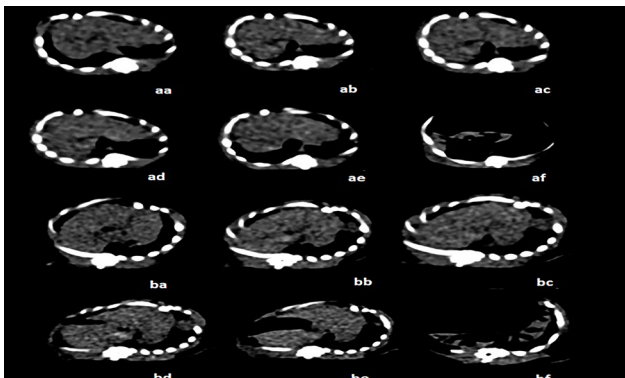Among mean liver attenuation values, PSM attenuation values showed the most significant increase in the first 12 hours post-mortem in both male (p = 0.01) and female (p = 0.01) rats. Liver CT images obtained 0–72 hours post-mortem are shown in Figure 3 **(Figure 3)**.

Figure 2: Postmortem Liver CT Scan Images for 0-72 hours (aa-af: Female rats, aa: 0 h, ab:12 h, ac: 24 h, ad: 36 h, ae:48 h, af: 72 h) (ba-bf: Male rats, ba: 0 h, bb:12 h, bc: 24 h, bd: 36 h, be:48 h, bf: 72 h)

PSM Attenuation Values

The PSM attenuation cut-off values of all cadavers for 12-hour PMI are shown in **Table 2**.

Table 2: PSM attenuation cut-off values of all individuals, male cadavers and female cadavers for 12-hour postmortem interval

	Cut-off value	Sensitivity	Specificity	ROC AUC*
All cadavers	68.5 HU	75.6%	86.7%	89.7%
Female cadavers	68.5 HU	81.5%	93.3%	84.6%
Male cadavers	67.5 HU	84.4%	73.3%	94.7%

* ROC AUC: Area under the curve of receive operative characteristics

After this point, changes in attenuation values of PSM were relatively unstable.

Inter- and Intra-Observer Agreement

Weighted kappa statistics indicated a high level of agreement for the inter- and intra-observer agreement, reliability and repeatability of the ROI choice and CT attenuation measurements **(Table 3)**.

Table 3: Inter- and intra-observer agreement

	Inter-observer Agreement			Intra-observer Agreement		
	RLL	LLL	PSM	RLL	LLL	PSM
n	90	90	90	90	90	90
Kappa (±se)	0.801±0.045	0.795±0.051	0.833±0.046	0.831±0.019	0.823±0.019	0.838±0.019
W. Kappa (±se)	0.861±0.035	0.856±0.037	0.903±0.030	0.892±0.012	0.893±0.023	0.892±0.013
Agreement Rate (%)	94.3	94.0	94.1	98.0	97.8	98.5
(95% CI)	80.9-93.4	77.4-91.7	80.7-94.0	85.1-90.2	84.5-90.0	85.9-91.2
p-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

n: number of measurements, se: Standard error, W: Weighted, CI: Confidence Interval of Wilson Score

DISCUSSION

In this study, there was an increase in attenuation values of the liver and striated muscles for both male and female rats with increasing PMI, except in CT images obtained at 72 hours post-mortem. The increase in the attenuation values has been attributed to post-mortem autolytic changes of tissues and protein degradation, which occur spontaneously in early post-mortem phases (18, 19). There was a slight decrease in attenuation values of the liver of our subjects at 72 hours post-mortem, which may be related to intra-parenchymal gas formation and increased bacterial succession. Our experimental model was designed to protect the RLL and LLL from post-mortem lividity as much as possible by placing and fixing the rats in the supine position during the procedure. On the other hand, this model caused the PSM to be affected by post-mortem lividity, a common post-mortem change, as a consequence of blood displa-

cement by gravity. Therefore, the PSM attenuation values decreased between 12- and 36-hours post-mortem1, which might be attributed to the post-mortem change secondary to lividity. PMI estimation based on radiological changes is a relatively new topic in the field. However, there are many studies in the last few years investigating the value of post-mortem CT changes in PMI estimation (4, 6, 8). The thyroid (4), heart (7, 9, 10), cardiothoracic index (8), muscle (11), liver (12), spleen (13), bone (14), brain (15), central nervous system (15, 16), lung (17), aorta (20) and surrenal glands (21) were studied to understand the changes during post-mortem processes in the literature. A summary of review of the related literature is presented in Table 4 **(Table 4)**.

Table 4: A summary of literature review regarding PMI and certain postmortem

Tissue	Finding	Target	Reference
Thyroid	Attenuation decrease on postmortem CT	Postmortem Change	(7)
Brain	Increase in both White and gray matter attenuations with loss of differentiation between gray and white matter	Postmortem Change	(15)
Heart and great vessels	Partial increase in attenuation of dependent areas and differentiated fluid levels in vessels due to postmortem hypostasis	Postmortem Change	(4, 9, 10, 21)
Spleen	Attenuation increase on postmortem CT	Postmortem Change	(13)
Lung	Hyper attenuated dependent areas due to postmortem hypostasis	Postmortem Change	(17)
Striated Muscle	Attenuation increase on postmortem CT	Postmortem Change	(11)
Liver	No significant change by increased postmortem interval	PMI	(25)
Vitreous	Attenuation increase in correlation with postmortem interval	PMI	(22)
Cerebrospinal Fluid	Attenuation increase in correlation with postmortem interval	PMI	(22)

To the best of our knowledge, this is the first study dealing with the relationship of the liver and striated muscle attenuation values and PMI estimation in a strictly controlled environment using a rat model. In a longitudinal post-mortem CT study from Japan (20), the widest and narrowest diameters of the aorta were scaled, and the ratio of these two diameters were investigated as a method of determining PMI, which is found to be useful.

This finding is parallel to the structural changes caused by post-mortem decomposition processes, as shown in this study. The radiodensities of the cerebrospinal fluid and vitreous humour were studied by Koopmanschap et al. (22). It has been stated that the attenuation values of the

cerebrospinal fluid and vitreous humour was associated with PMI (16, 22). Since these biological fluids are preserved in a relatively closed environment, they are exposed to environmental conditions in a later stage compared with the liver. Therefore, i/n contrast to tissues relatively resistant to autolysis and putrefaction as suggested by the findings of this study, CT attenuation of the liver in the first 12 hours post-mortem seems to be more appropriate to be used. Okuma et al. (11) investigated the use of striated muscle attenuations in determining PMI in 33 human cadavers in a non-controlled environment within 20 hours of maximum PMI. Similar to the findings of this study, they showed a significant difference between antemortem and post-mortem striated muscle attenuations; however, in contrast to our findings, there was no strong correlation between striated muscle attenuation values and PMI in their study (11). This difference might be attributed to a wide spectrum of variables in human cadavers, such as the subjects' antemortem diseases, level of lividity, muscle mass and body mass index differences. This study revealed a correlation between PSM attenuation values and PMI, which might be attributed to the established stable environmental conditions and the use of a standard experimental rat model. In a preliminary study investigating a multi-factor methodology to estimate PMI with post-mortem CT features (23), they described morphological changes on post-mortem rabbit liver images. According to their study, they recorded the stages of post-mortem liver changes as stable, peripheral gas accumulation, liver shrinkage and separation due to intra-parenchymal gas formations. However, all these stages ended in less than 96 hours in this study, whereas it took 196 hours in Wang et al.'s study (23), which might be attributed to the differences in subjects and liver masses. Iwamoto et al. revealed that post-mortem changes of intestinal gas and portal venous gas volumes can be used for PMI estimation. Furthermore, they observed that the rate of post-mortem portal venous gas increased steeply from the 72nd hour

of post-mortem period. However, in contrast to our study, they did not examine the effects of environmental factors (24). In addition to our findings, the literature shows that the organs' minor structural decomposition due to enzymatic autolysis or bacterial decay results in changes in the CT attenuation values, which might be used in the estimation of early PMI. However, gross decomposition with excess gas formation takes longer, which makes its assessment more valuable in PMI estimation in 72 hours after death. Fischer et al. (25) also investigated post-mortem liver attenuation changes longitudinally in five human subjects in an uncontrolled environment. In contrast to this study, Fischer et al. (25) revealed no significant changes in liver tissue attenuation values in relation to PMI. This difference may be caused by the small number of cases and relatively uncontrolled conditions (e.g., age, sex and environmental conditions, such as humidity and temperature) in their study. In this study, the overall gender-related differences in CT attenuation levels of the liver and striated muscle were attributed to the ante-mortem characteristics of these tissues, such as weight differences, lipid metabolism and glycolysis/gluconeogenesis differences caused by the various activities of liver enzymes and female sex-hormones, and higher mitochondrial mass and oxidative/phosphorylative capacities of the female rats' striated muscle; however, as a limitation of this study, potential molecular mechanisms behind gender-related differences could not be identified (26 – 28). As another limitation of this study, a control group exposed to uncontrolled normal environmental conditions was not added since there were related data in the literature (11, 12, 25). Since excessive heat, cold and humidity strongly interfere with post-mortem decomposition processes, such as autolysis, bacterial or insect activity and decay of tissue, CT attenuation values might be extremely different from those achieved in this study. This study involved rats, which is the most important limitation, to achieve a standard model; therefore, the obtained results would not represent human subjects and cannot be directly compared with those of human studies. However, gathering a larger cohort of human subjects and providing strictly controlled conditions for such examinations on humans were impossible.

Our experimental model was designed to protect the RLL and LLL from post-mortem lividity as much as possible by placing and fixing the rats in the supine position during the procedure, which unfortunately caused the PSM to be affected by post-mortem lividity. Additionally, because of a lack of similar studies, some referred articles described general comparisons between antemortem and post-mortem findings, instead of time-dependent changes after death.

The presented model suggests that a combination of liver and striated muscle attenuation values can be used as an additional and alternative method to estimate PMI at early post-mortem stages, particularly up to the first 12 hours post-mortem. Furthermore, the male and female subjects might reveal potentially different values due to gender-related differences, which suggest the importance of including subjects of both genders in such studies. In this respect, there is a strong need for further studies examining several groups of male and female human subjects under different controlled environmental conditions to determine the relationship of age, body mass index and environmental conditions with post-mortem changes in CT attenuation values of the liver and muscle.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

"COVID-19 İÇİN EVDE KAL" HAYATININ ÖĞRENCİLERİN KAYGI DÜZEYLERİ VE YEME DAVRANIŞLARINA ETKİSİ

THE EFFECT OF "STAY HOME FOR COVID-19" LIFE ON STUDENTS ANXIETY LEVELS AND EATING BEHAVIORS

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ÖZET

AMAÇ: Bu çalışma COVİD-19 pandemisinde uygulanan karantina sürecinin bireylerin kaygı düzeyleri ve yeme davranışlarına etkisini belirlemek için yapılmıştır.

GEREÇ VE YÖNTEM: Çalışma bir üniversitenin sağlık bölümünde okuyan öğrenciler ile kesitsel tipte yapılmıştır. Çalışmaya 510 öğrenci katılmıştır. Veriler sosyodemografik anket formu, Üç Faktörlü Yeme Anketi (TFEQ) ve Yaygın Anksiyete Bozukluğu Testi (YAB-7) kullanılarak toplanmıştır.

BULGULAR: Çalışmaya katılan öğrencilerin yaş ortalaması 21.82±4.45, %21.4'ü erkek, %78.6'sı kadındır. Evde kalınan süre zarfında bireyler daha fazla ev yemeği tükettiğini ve sağlıklı beslendiğini sıklıkla ifade etmiştir. Araştırmada öğrencilerin yaşları ile TFEQ alt boyutu olan kontrolsüz yemek yeme ve duygusal yemek yeme arasında anlamlı bir korelasyon saptanmıştır. Öğrencilerin Yaygın Anksiyete Bozukluğu Ölçeğinden aldıkları puan ortalaması 8.73±5.80 olarak bulunmuştur. Ayrıca anksiyete düzeyleri derecelendirildiğinde ise %25.9'unun hafif anksiyete, %35.5'inin orta derece anksiyete, %21.8'inin yüksek anksiyete ve %17.8'inin ciddi anksiyete yaşadığı saptanmıştır. Yaygın anksiyete grupları ile TFEQ toplam puanları ve TFEQ alt gruplarına ait puanları karşılaştırılmış olup yaygın anksiyete gruplarından hafif anksiyetesi olan kişilerin TFEQ toplam puanı 38,03 ± 10,57 iken orta seviyede anksiyetesi olanların 41,65 ± 10,74 yüksek anksiyetesi olanların 45,22 ± 8,58 ve ciddi anksiyetesi olanların ise 41,97 ± 11,62 olarak belirlenmiştir.

SONUÇ: Bu çalışma, pandemiden kaynaklı ülke çapında uygulanan karantina sırasında, üniversite öğrencilerinin önemli bir bölümünün yeme davranışlarında değişimler ve anksiyete bozukluğu yaşadığını ortaya koymaktadır. Toplum sağlığını korumak için alınan karantina önlemleri özellikle hafif şişman ve şişman grupta yeme bozukluklarının arttığını göstermiştir.

ANAHTAR KELİMELER: COVİD 19, Karantina, Yeme bozukluğu, Kontrolsüz yeme, Anksiyete.

ABSTRACT

OBJECTIVE: This study was conducted to determine the effect of the quarantine process applied in the COVID-19 pandemic on the anxiety levels and eating behaviors of individuals.

MATERIAL AND METHODS: The study was made in a cross-sectional type with students studying in the health department of a university. 510 students participated in the study. Data were collected using a sociodemographic questionnaire, the Three-Factor Eating Questionnaire (TFEQ), and the Generalized Anxiety Disorder Test (GAD-7).

RESULTS: The mean age of the students participating in the study was 21.82±4.45, 21.4% were male and 78.6% were female. During the stay at home, individuals frequently stated that they consume more home-cooked food and eat healthy. In the study, a significant correlation was found between the ages of the students and the TFEQ sub-dimension, uncontrolled eating and emotional eating. The mean score of the students from the Generalized Anxiety Disorder Scale was found to be 8.73±5.80. In addition, when their anxiety levels were graded, it was found that 25.9% had mild anxiety, 35.5% had moderate anxiety, 21.8% had high anxiety and 17.8% had severe anxiety. The general anxiety groups and TFEQ total scores and the scores of the TFEQ subgroups were compared and the TFEQ total score of the generalized anxiety groups was 38.03 ± 10.57, while those with moderate anxiety were 41.65 ± 10.74 and those with high anxiety were 45.22. ± 8.58 and those with severe anxiety were determined as 41.97 ± 11.62.

CONCLUSIONS: This study reveals that a significant portion of university students experienced changes in eating behaviors and anxiety disorders during the nationwide quarantine caused by the pandemic. Quarantine measures taken to protect public health have shown that eating disorders have increased especially in the overweight and obese group.

KEYWORDS: COVID-19, Quarantine, Eating disorder, Uncontrolled eating, Anxiety.

INTRODUCTION

The new Coronavirus disease (Covid-19) emerged in Wuhan, China in December 2019 and spread all over the world in a short time. This disease is a severe acute respiratory syndrome caused by SARS coronavirus 2 (SARS-CoV-2) (1). Due to the increasing cases in different international locations in addition to China, on January 30, 2020, the World Health Organization (WHO) Emergency Committee declared this disease as a global health emergency, a pandemic. During this period, important practices were implemented to combat the pandemic. The most important of these practices, which are important for public health, is quarantine. The droplet contamination feature of COVID-19 particularly has made it mandatory to implement quarantine measures in many areas.

Quarantine measures significantly affect lifestyle, and consequently, health-affecting risks associated with sedentary behavior, smoking, and sleeping habits can arise (2). Individuals with reduced physical activity and limited access to groceries started to stock up on food during the quarantine period. And it was reported that ready-to-eat foods, junk food and snacks, and highly processed food products are started to be consumed more. However, recent research has indicated that consumption of fresh foods, especially fruit, vegetables, and fish decreased. Furthermore, psychological and emotional responses to the COVID-19 pandemic also increase the risk of uncontrolled eating behaviors (1, 3, 4).

Nutrition and food choices are affected by many factors including genetic, physiological, psychological, social, and cultural. Emotional state not only affects the type, quantity, and quality of food consumed but also affects subsequent food choices. Depending on one's emotional state or their own characteristics, the relationship between eating and emotions may vary (5). Research has shown that emotional coping strategies or stress avoidance behavior can lead to unhealthy eating behaviors such as meal skipping (6). Emotional eating is believed to be a response to a stressful situation. Exposure to high levels of stress, especially after a natural disaster can affect eating behaviors. In a 2-year study involving 105 middle-aged women, the pre- and post-earthquake eating behaviors of women were examined and the results revealed that a correlation exists between high stress and eating behavior. Earthquake-related high levels of stress reduced healthy eating behaviors (vegetable eating, breakfast eating) (7).

The COVID-19 pandemic is accompanied by many challenging stress factors. Some of these are fear of getting sick or losing a family member, losing job, financial insecurity, and quarantine measures. Studies have shown that these stressors significantly increase anxiety in people (8). Generalized anxiety disorder (GAD) is a chronic and very common disorder characterized by uncontrollable excessive worry, chronic anxiety, and tension (9). Generally, GAD is accompanied by a series of physical findings that cause significant impairments in daily social and occupational functioning (10).

GAD is common both in communities and across healthcare settings. A study conducted in the United States showed that the lifetime prevalence of GAD ranged from 5.1% to 11.9% (11, 12). In a review study on epidemiological studies in Europe, the 12-month prevalence of anxiety ranged from 1.7-3.4%, and the lifetime prevalence ranged from 4.3% to 5.9% (13, 14).

Many studies examining the emotional state and uncontrolled eating behaviors have shown that there is a positive or negative relationship between emotional states and food intake (1). Emotional and uncontrolled eating behaviors are important risk factors for recurrent weight gain. Accordingly, the current study presents the examination of anxiety among college students caused by the quarantine measures implemented during the pandemic and its relation to eating habits and eating behaviors.

MATERIAL AND METHODS

Sample

The study was intended to include 756 students enrolled in the health departments of a university in 2021. A cross-sectional study was designed and a sample selection procedure was not performed. The consent forms were sent to all students via email and those who agreed to participate in the study were asked to fill out the online forms. 246 students who did not accept

to participate in the study and filled the questionnaires incompletely were not included in the study. A total of 510 students who completely filled out the forms participated in the study.

Data Collection Tools

The data for this study were collected from February to April 2021 using a 13-item sociodemographic data sheet prepared by the authors, the Three-Factor Eating Questionnaire (TFEQ), and the Generalized Anxiety Disorder Scale-7 (GAD-7).

The sociodemographic data sheet measures the sociodemographic characteristics of the participants such as age, gender, meal skipping status, body mass index (BMI), and sleep duration. *Three-Factor Eating Questionnaire* (TFEQ) was developed by Stunkard and Messick and further revised by Karlsson et al. (15). The questionnaire was adopted into the Turkish language by Kıraç et al and the authors also verified the validity and reliability of the Turkish version questionnaire (16). The choices in questions 1 to 13 are from 4 to 1 from top to bottom, the choices between questions 14 and 17 are from 1 to 4 from top to bottom, and in question 18, choices 1 and 2 are 1, 3 and 4. 19 choices Options 2, 5 and 6 are scored as 3, 7 and 8 are scored as 4 points.

Factor-1: It consists of questions 1-7-13-14 and 17 and measures the level of uncontrolled eating (loss of control of excessive food intake and a tendency to eat more than normal due to subjective thoughts against hunger).

Factor-2: It consists of questions 3, 6 and 10 and measures the emotional eating (insufficiency against emotional symptoms) levels of individuals.

Factor-3: It consists of questions 2-11-12-15-16 and 18 and measures the degree of conscious eating restriction (consciously restricting food intake in order to keep body weight under control or to increase body weight loss).

Factor-4: It consists of questions 4-5-8 and 9. and it was determined that it measures the levels of sensitivity to hunger (difficulty of controlling the level of eating when hunger is felt).

Emotional eating behavior increases as the uncontrolled eating score, emotional eating score and hunger sensitivity score increas. As the conscious eating restriction score increases, emotional eating behavior decreases.

Generalized Anxiety Disorder Scale-7 (GAD-7) was developed by Spitzer et al and is a 4-point Likert scale (17). This 7-item self-report scale was developed according to DSM-IV-TR criteria and measures generalized anxiety disorder within two weeks. The scale was adopted into the Turkish language by Konkan et al and the validity and reliability of the Turkish version were confirmed (18). A total GAD-7 score of 0-4 indicates mild, 5-9 moderate, 10-14 high, and 15-21 severe anxiety disorder (16).

Ethical Committee

Ethical permission to conduct the study was obtained from Amasya University (dated 06/01/2021 and numbered 2021/30) and permission from the relevant administrative institution was also received (dated 15/06/2020 and numbered E.11290). Plus, informed consents were obtained from the students who agreed to participate in the study.

Statistical Analysis

The data collected in this study were examined by SPSS 25.0 for Windows (Statistical Package for Social Sciences). Discontinuous variables were examined using frequency analysis and continuous variables using descriptive statistics. In the frequency analysis, numbers (n) and percentages (%) of the discontinuous variables were examined. And the descriptive statistics were reported using numbers (n) and percentages (%), arithmetic mean±standard deviation, min. and max. values of continuous variables. An independent sample t-test was performed for comparing numerical data between two independent groups. For examining data that met non-parametric test conditions; the Mann-Whitney U test was conducted to compare two independent groups and the Kruskal-Wallis test for more than two groups. In the analyses, $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of the participant students was 21.82±4.45 years. The participants were 21.4% males and 78.6% females. The sociodemographic and descriptive characteristics of the students are given in **Table 1**. Also, the mean daily sleep duration of the students was 8.34±1.67 hours.

Table 1: Sociodemographic characteristics and descriptive statistics of the participants

Characteristics	Number (n)	Percentage (%)
Gender		
Female	401	78.6
Male	109	21.4
Smoking		
Never smoked	360	70.6
Smoked but quitted	63	12.4
Still smoking	87	17.1
Alcohol drinking		
Never drank	411	80.6
Drank but quitted	49	9.6
Still drinking	50	9.8
BMI classification		
Underweight (18.5 and below)	75	14.7
Normal (18.6-24.9)	325	63.7
Overweight (25.0-29.9)	95	18.6
Obese (30.0 and above)	15	2.9
The most skipped meal		
Breakfast	142	27.8
Lunch	340	66.7
Dinner	28	5.5
Snacking		
Yes	330	64.7
No	180	35.3
Total	**510**	**100.0**

The participant students were asked to state what has changed in their diets since the COVID-19 pandemic and accordingly, 17.7% of the participants stated that they started to consume more home-cooked meals, 13.2% started eating healthy, 11.5% had a regular diet. On the other hand, 9.4% expressed that their diet did not change.

The results indicated that students' age significantly correlated with the uncontrolled eating and emotional eating dimensions of TFEQ. Uncontrolled eating score decreased by 0.124 (p=0.005) and emotional eating score decreased by 0.095 (p=0.032) with every 1-year increase in the participants' age.

The comparison of students' BMI, smoking, and alcohol use status with Three-Factor Eating Questionnaire (TFEQ) scores is presented in **Table 2**.

Table 2: Relationship between specific characteristics of participants and TFEQ scores

Characteristics	Three-Factor Eating Questionnaire (TFEQ)				
	Uncontrolled Eating	Emotional Eating	Cognitive Restraint of Eating	Sensitivity to Hunger	TFEQ Total
BMI					
Underweight (18.5 and below)[a]	11.04±3.89	5.33±2.71	11.56±3.18	8.28±3.32	36.21±10.25
Normal weight (18.6-24.9)[b]	11.73±3.69	6.37±2.98	13.90±3.56	9.16±3.53	41.17±10.25
Overweight (25.0-29.9)[c]	12.57±3.95	7.47±3.06	14.75±3.56	10.69±3.84	45.50±10.49
Obese (30.0 and above)[c]	14.73±3.39	9.13±3.77	15.13±1.92	12.46±3.54	51.46±10.01
p	**0.001***	**0.0001***	**0.0001***	**0.0001***	**0.0001***
Smoking					
Never smoked	11.50±3.72	6.36±2.94	13.95±3.60	9.11±3.54	40.93±10.40
Smoked but quitted	12.41±3.39	6.95±3.23	13.22±3.45	9.74±3.27	42.33±9.83
Still smoking	13.01±4.21	6.79±3.48	13.29±3.66	10.43±4.21	43.54±12.23
p	**0.002***	0.325	0.110	**0.017***	0.128
Alcohol drinking					
Never drank	11.59±3.65	6.30±2.95	13.81±3.53	9.19±3.51	40.91±10.27
Drank but quitted	12.81±4.44	7.42±3.52	13.67±3.98	9.93±4.09	43.85±12.29
Still drinking	13.28±4.06	7.26±3.40	13.40±3.78	10.70±4.19	44.58±11.86
p	**0.006***	**0.029***	0.627	**0.038***	**0.022***

*p<0.05
a, b, c: The difference between groups with different letters is significant (p<0.05).

It was found that the mean Generalized Anxiety Disorder Scale-7 (GAD-7) score of the participant students was 8.73±5.80. Furthermore, the results revealed that 25.9% of the participants experienced mild anxiety, 35.5% moderate anxiety, 21.8% high anxiety, and 17.8% severe anxiety. A negative correlation was obtained between students' GAD-7 scores and daily sleep durations. The comparison between certain participant characteristics and GAD-7 scores is shown in **Table 3**.

Table 3: Relationship between specific characteristics of participants and GAD-7 scores

Characteristics	Generalized Anxiety Disorder (GAD-7)				
	Mild Anxiety	Moderate Anxiety	High Anxiety	Severe Anxiety	GAD-7 Mean Total Score
	% (n)	% (n)	% (n)	% (n)	$\bar{X} \pm SS$
Gender					
Male	25.7 (28)	33.9 (37)	27.5 (30)	12.8 (14)	8.37±5.64
Female	25.9 (104)	34.7 (139)	20.2 (81)	19.2 (77)	8.82±5.84
p	0.253				0.622
BMI					
Underweight (18.5 and below)[a]	18.7 (14)	36.0 (27)	13.3 (10)	32.0 (24)	10.48±6.50
Normal weight (18.6-24.9)[b]	27.7 (90)	33.2 (108)	22.8 (74)	16.3 (53)	8.47±5.64
Overweight (25.0-29.9)[c]	26.3 (25)	34.7 (33)	26.3 (25)	12.6 (12)	8.27±5.65
Obese (30.0 and above)[c]	20.0 (3)	53.3 (8)	13.3 (2)	13.3 (2)	8.26±5.25
p	**0.031***				**0.048***
Smoking					
Never smoked	28.6 (103)	38.6 (139)	18.6 (67)	14.2 (51)	8.01±5.47
Smoked but quitted	23.8 (15)	25.4 (16)	25.4 (16)	25.4 (16)	9.69±6.15
Still smoking	16.1 (14)	24.1 (21)	32.2 (28)	27.6 (24)	11.01±6.20
p	**0.000***				**0.000***
Alcohol drinking					
Never drank	28.0 (115)	34.5 (142)	19.5 (80)	18.0 ()74	8.47±5.35
Drank but quitted	22.4 (11)	32.7 (16)	26.5 (13)	18.4 (9)	9.57±6.36
Still drinking	12.0 (6)	36.0 (18)	36.0 (18)	16.0 (8)	9.98±5.39
p	0.088				0.074

*p<0.05,
a, b: The difference between groups with different letters is significant (p<0.05).

The comparison of students' generalized anxiety (GAD-7) classifications and TFEQ total and subscale scores are given in **Table 4**.

Among the generalized anxiety groups; the TFEQ total score of the students with mild anxiety was 38.03 ± 10.57, students with moderate anxiety were 41.65 ± 10.74, students

with high anxiety were 45.22 ± 8.58, and students with severe anxiety were calculated as 41.97 ± 11.62. Statistically significant differences were obtained between the GAD-7 classifications and TFEQ scores of the participants.

Table 4: Comparison of the GAD-7 and TFEQ

GAD-7 (n)	Three-Factor Eating Questionnaire (TFEQ)				
	Uncontrolled Eating	Emotional Eating	Cognitive Restraint of Eating	Sensitivity to Hunger	TFEQ Total
Mild anxiety (132)[a]	10.65±3.72	5.35±2.73	13.87±3.89	8.14±3.62	38.03±10.57
Moderate anxiety (176)[b]	11.59±3.46	6.63±3.07	14.31±3.26	9.11±3.43	41.65±10.74
High anxiety (111)[c]	13.18±3.44	7.39±2.85	13.81±3.49	10.83±3.29	45.22±8.58
Severe anxiety (91)[b]	12.59±4.38	6.84±3.35	12.42±3.63	10.10±3.88	41.97±11.62
p	0.000*	0.000*	0.001*	0.000*	0.000*

*p<0.05

a, b, c: The difference between groups with different letters is significant (p<0.05).

DISCUSSION

Several recent reports indicated that eating behaviors are affected by many factors. The Covid-19 pandemic, which continues to affect for more than 1 year, also triggers anxiety and therefore negatively affects eating behavior. The current study evaluated the correlation between students' eating behaviors and general anxiety disorders during the pandemic.

The participant students were 21.4% males and 78.6% females. It is suggested that this difference in the ratio is because the study was conducted in a department containing health-related departments and female students preferred these programs more. Two-thirds of the participating students stated that they have never smoked and 17.1% expressed they still smoke. In a previous study conducted on students in health programs, the prevalence of smoking was found to be 26% (19). According to the National Adult Tobacco Survey (2014) conducted in Turkey, the prevalence of daily tobacco use in the 15-24 age group was 27.1%, and this rate was found to be higher in men (41.5%) than in women (13.1%) (20).

The mean BMI of the participant students was calculated as 22.26±3.50 kg/m². According to the BMI classification, we determined that 14.7% of the participants were underweight, 63.7% were normal weight, 18.6% were overweight, and 2.9% were obese. In a previous study involving 1676 college students, 12.1% of the students were found to be underweight, 70.4% were normal weight, 14.0% were overweight, and 3.6% were obese (19). Moreover, a literature survey revealed that the prevalence of obesity varied between 4.0%-28.3% in men and 6.2%-36.5% in women (21, 22).

In the current study, 7.1% of the participants stated that their alcohol consumption has increased. Both alcohol use and smoking potentially increase the susceptibility to SARS-CoV-2 infection and therefore, may worsen the clinical course of COVID-19. Besides, chronic alcohol exposure, with the effect of innate and acquired immune mechanisms, has a complex and negative effect on individuals and is known to increase susceptibility to viral infection (23). Staying at home for longer times than usual has a potential impact on smoking and alcohol consumption. As determined in the previous studies, prolonged isolation increases the level of stress; and increased stress is the most effective risk factor for smoking and alcohol abuse (24). Therefore, it can be argued that some people are more prone to excessive alcohol use during quarantine measures.

It determined that the participants' TFEQ total and sub-scale scores significantly differ according to their BMI classifications. Underweight and normal-weight students' TFEQ total and subscale scores were significantly lower than those of overweight and obese students. Verzijl et al. obtained a significant correlation between uncontrolled eating behaviors and BMI (25). Previous studies involving university students indicate that students' emotional eating and hunger sensitivity positively and significantly correlated with their BMI (26, 27). Löffler et al. conducted a large-scale study involving 3144 participants and found that BMI values significantly correlated with uncontrolled eating, emotional eating, and sensitivity to hunger (28). They determined that the strongest correlation was between 'uncontrolled eating' and BMI. Furthermore, French et al. examined the uncontrolled eating variable and highlighted

that a consistent relationship between uncontrolled eating and BMI was found in 10 of the 11 cross-sectional studies and 7 of the 9 prospective studies (29). Eating behaviors including the choices about when and where to eat, the decisions to start and stop eating, as well as types and amount of food chosen affect energy intake. Therefore, the BMI values of those who have problems in controlling their eating behavior are greatly affected by this situation.

According to the participants' smoking status and three-factor eating questionnaire scores, no significant differences were obtained in total, emotional eating, and cognitive restraint of eating scores according to smoking. On the other hand, uncontrolled eating and sensitivity to hunger subscale scores were found to be significantly higher in students who stated that they still smoke. The COVID-19 pandemic can be considered a stressful life event. Country-wide quarantines require individuals to adapt to staying at home for prolonged periods. And this causes people to face more stress. A study examining young adults determined that uncontrolled eating behavior was more frequently exhibited in response to stress (30). Therefore, it can be claimed that the prevalence of obesity will increase due to uncontrolled eating behaviors during quarantine practices.

It was found that total TFEQ and uncontrolled eating, emotional eating, and sensitivity to hunger sub-scale scores significantly differ according to the increase in alcohol consumption during quarantine. It is suggested that increased stress levels during the quarantine period change alcohol consumption and eating behaviors. It is a generally accepted fact that increased alcohol consumption will cause significant public health problems (31). Considering the impact of alcohol and tobacco consumption on health, the fight against these factors should continue even in pandemic conditions. The long-term destructive effects of alcohol and tobacco consumption will be much more severe.

Contagious and deadly epidemics negatively affect public mental health. The high spread and mortality rate of COVID-19 raises concerns about the mental health and psychological adaptation of the public (32 - 34). After Covid-19 was declared a pandemic by WHO, schools and universities were closed and long quarantine durations caused concern among students. Our findings showed that 25.9% of the students had mild anxiety, 35.5% had moderate anxiety, 21.8% had high anxiety, and 17.8% had severe anxiety. In a review study examining 62 studies with 162,639 participants from 17 countries, including China, Turkey, Iran, Spain, and Italy, the anxiety rate was reported as approximately 33% (28-38%) (35). Furthermore, a previous study reported that the prevalence of severe anxiety symptoms among Asian university students was 7.04% (36). Moreover, in another study involving 3,881 university students in China, the country where the COVID-19 pandemic first started, the incidences of mild, moderate, and severe anxiety were found to be 23.19%, 2.71%, and 0.70%, respectively (5). The possible reason for the different results in these studies is probably sample selection, the evaluation duration, the differences in the analyzes, and cut-off scores.

Although the anxiety rate among female students was found to be higher than male students in our study, this difference is not significant. The results of similar studies indicate female students were more emotional and more prone to tension than male students, so they exhibit more anxiety rates (5).

It was obtained a significant correlation between students' BMI values and GAD-7 scores. Students with a BMI of <18.5 and below had higher anxiety scores. Since appearance is more important in this period, concerns about gaining weight, and deterioration of body image increase students' anxiety. Similar results were also observed in underweight individuals who have high anxiety about being obese and were diet-oriented (37 - 39). The high spread rate throughout the world and high death numbers of the COVID-19 pandemic increased the anxiety level of people living in quarantine and affected their BMI values. It was found that a significant relationship exists between smoking and GAD-7 scores. According to our findings, mild and moderate anxiety rates were high in non-smokers, whereas high and severe anxiety rates were higher in constantly smoking students. Similarly, although smokers perceive smoking as a

stress reliever and experimental studies have reported that smoking temporarily reduces stress levels, research has shown that continued smoking may eventually lead to the formation or exacerbation of negative emotional states, support negative coping strategies, and increase overall stress levels (20, 30, 40).

Mental health is highly sensitive to traumatic events as well as the social and economic consequences of these events. The pandemic has deeply affected all individuals around the world and has therefore caused many mental problems. The mental problems experienced by individuals due to the pandemic were accompanied by loss of income and social isolation, naturally, this situation changed the eating behaviors of the society. People have stayed at home during quarantine and have become more dependent on digital life, and physical activities have decreased. The results of research showed that students with mild and moderate anxiety had higher cognitive restraint of eating scores; however, eating control decreased as their anxiety level increased. It was found that participants with mild anxiety had significantly lower TFEQ scores than those with moderate, high, and severe anxiety. On the other hand, the TFEQ scores of the participants with high anxiety were found to be statistically significantly higher than those with moderate and severe anxiety. The interruption of work routine due to the quarantine measures caused distress in people and accordingly, individuals consumed more food and got more energy at home. However, constantly following the updates and getting information about the COVID-19 pandemic from the media are also effective in increasing the level of stress. Increased stress leads individuals to overeat, especially to sugar-rich foods which are described as "relaxing". The main purpose here is serotonin, whose synthesis is triggered by carbohydrate-rich foods (41, 42).

As the pandemic continues, actions should be planned to protect the physical, mental, and social health of individuals. During staying at home, time spent using computers, telephones, and the internet has increased; therefore, the concepts of health and media literacy have become more important for young people to prevent technology addiction. Young people should be provided with accurate information based on scientific data about healthy lifestyles, eating behaviors, and other issues. Young people should also be properly informed about nutrition and lifestyle through TV programs, telephone apps, and social media. Planning exercises and gaining new occupations/hobbies is thought to be effective in making the time spent at home more productive and reducing anxiety.

Nutrition courses given at universities are important in terms of focusing on the relationship between stress and diet and stress management. In addition, it will be beneficial to increase the practices to protect the mental health of the society during epidemic periods and to draw attention to different directions with crisis management trainings.

The current study is limited to college students cannot be generalized to the whole society. Therefore, further research with different age groups should comprehensively reveal how this issue affects the whole population.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

ÇOCUKLARDA HELİKOBAKTER PYLORİ ENFEKSİYONU İLE PLAZMA 25 HİDROKSİ VİTAMİN D3 DÜZEYİ ARASINDAKİ İLİŞKİ

RELATIONSHIP BETWEEN PLASMA 25 HIDROXY VITAMIN D3 LEVEL AND HELICOBACTER PYLORI INFECTION IN CHILDREN

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ÖZET

AMAÇ: Helicobacter pylori (H.pylori) enfeksiyonunun şiddeti ve ilişkili hastalıkların varlığı konakçı, bakteriyel ve çevresel faktörlerden etkilenir. Bu çalışmada, H.pylori enfeksiyonu saptanan çocuklarda inflamatuar yanıtın düzenlenmesinde önemli rolü olan plazma 25 hidroksi vitamin D3 (vitD3) ile H.pylori enfeksiyonu arasındaki ilişkinin gösterilmesi amaçlanmıştır.

GEREÇ VE YÖNTEM: Mart 2010 - Mart 2011 tarihleri arasında Celal Bayar Üniversitesi Tıp Fakültesi gastroentroloji bölümünde dispeptik yakımalar ve medikal tedaviye dirençli demir eksikliği anemisi nedeni ile üst gastrointestinal endoskopi yapılan 3-18 yaş arası 201 hasta bu çalışmaya alındı. Biyopsi örneklerinin histopatolojik tanıları değerlendirildiğinde, H.pylori pozitif grupta 98, H.pylori negatif grupta 103 hasta vardı. Vitamin D3 düzeyi, H.pylori pozitif ve H.pylori negatif gruplarda karşılaştırıldı. Helicobacter pylori pozitif grupta ise gastrik mukozal aktivite ve inflamasyon şiddetinin derecesi ile vitD3 düzeyleri karşılaştırıldı.

BULGULAR: Helicobacter pylori pozitif hastaların 80'inde (81.6%), H.pylori negatif hastaların 76'sında (73%) vitD3 düzeyleri düşüktü. Bu fark istatistiksel olarak anlamlı değildi (p>0.05). Helicobacter pylori pozitif ve negatif grupların plazma vitD3 düzeylerinin ortalama değeri sırasıyla 15.64±8.9 ng/mL ve 16.36±1.35 ng/mL idi. Gruplar arasındaki fark istatistiksel olarak anlamlı değildi (p>0.05). Helicobacter pylori pozitif ve negatif gruptaki hastalar, plazma vitD3 düzeyine göre eksiklik, şiddetli eksiklik, yetersizlik ve yetmezlik olarak dört farklı grupta sınıflandırıldığında ise H.pylori pozitif grupta vitD3 eksikliği H.pylori negatif gruba göre daha sıktı. Bu sonuç istatistiksel olarak anlamlıydı (p<0.05). Her iki grupta kronik inflamasyonun şiddeti ve doku H.pylori aktivitesi ortalama vitD3 düzeyi ile ters orantılı olarak arttığı görüldü (p<0.05).

SONUÇ: Çalışmamızın sonuçları bölgemizde çocuklarda vitD3 düşüklüğünün yaygın olduğunu göstermektedir. Vitamin D3 eksikliği H.pylori enfeksiyonu için risk faktörüdür. Bu çalışma H.pylori enfeksiyonunda vitD3'ün antibakteriyel etkiyi artırdığını ve inflamasyonun şiddetini azalttığını göstermektedir.

ANAHTAR KELİMELER: Çocukluk Çağı, Helicobacter pylori, Vitamin D3, Risk Faktörleri, Komplikasyonlar.

ABSTRACT

OBJECTIVE: The severity of the Helicobacter pylori (H.pylori) infection and the presence H.pylori related diseases are affected by host, bacterial and environmental factors. In this study it is aimed to show relationship between H.pylori infection and plasma Vitamin D3 (vitD3) has significant role in regulation inflamatory response in children with H.pylori infection.

MATERIAL AND METHODS: Two hundred one patients aged between 3-18 years, referred to pediatric gastroentrology department of Celal Bayar University Medical Faculty between March 2010 to March 2011 and performed upper gastrointestinal endoscopy because of gastrointestinal symptoms and iron deficiency anemia refractory to medical therapy were enrolled in this study. Histopathologic diagnosis of biopsy speciments of the patients were evaluated. There were 98 patients in H.pylori positive group and 103 patients in H.pylori negative group. Plasma level of vitD3 of H.pylori positive and H.pylori negative cases were compared. Relationship between gastric mucosal activity the degree of inflammation severity and vitD3 level were evaluated in the H.pylori positive group.

RESULTS: Vitamin D3 levels were low in 80 (81.6%) H.pylori positive patients and in 76 (73%) H.pylori negative patients. This difference was not statistically significant (p>0.05). The mean value of plasma level of vitD3 H.pylori positive and negative groups were 15.64±8.9 ng/mL and 16.36±11.35 ng/mL respectively. The difference between the groups was not statistically significant (p>0.05). When patients in H.pylori positive and negative groups were classified according to plasma vitD3 level in four different groups as severe deficiency, deficiency, insuficiency and sufficiency. Vitamin D3 severe deficiency in H.pylori positive group was statistically more frequent than H.pylori negative group (p<0.05). Severity of chronic inflamation and tissue H.pylori activity increased inversely with the mean vitD3 level in both groups (p<0.05).

CONCLUSIONS: Results of this study suggests that vitD3 deficiency is common in children in our region. Vitamin D3 deficiency is risk factor for H.pylori infection. The findings of this study shows vitD3 increasing antibacterial effect and reducing the severity of inflammation in H.pylori infection.

KEYWORDS: Childhood, Helicobacter pylori, Vitamin D3, Risk Factors, Complications.

INTRODUCTION

Vitamin D3 has well known effects on calcium phosphor and bone metabolism however nowadays roles of vitD3 on other biological sistem is being studied profoundly. In recent years, vitD3 deficiency and insufficiency have been found to be associated with many chronic diseases including metabolic syndrome, cardiovascular diseases, cancer, infectious and autoimmune diseases (1 - 3).

Vitamin D3 acts as a transcription factor in its biological activities, acting on the transcription of many different genes. It performs its function by binding to the nuclear receptor (VDR: vitamin D receptor) (4). The effects of vitD3 on the innate and adaptive immune system gained importance with the detection of the presence of VDR in immune system cells (1). In studies examining the relationship between vitD3 level and infections, especially tuberculosis, upper and lower respiratory infection; a positive correlation has been reported between low vitD3 levels and increased susceptibility to infections and the severity of infection (5 - 8).

The role of vitD3 in infection control is related to its effects on the innate and adaptive immune system and is mainly related to mechanisms mediated by innate immunity (1, 4, 9). Cationic antimicrobial peptides (CAMP), one of the most important elements of the innate immune system, disrupt the membrane integrity of pathogenic microorganisms such as H.pylori (10, 11). In cell culture studies by Gombart et al. showed that the CAMP and defensin ß 2 genes have VDR in the promoter region (12). It has been found that β-Defensins with known antibacterial effects inhibit H.pylori (12- 14). Vitamine D3 has inhibitor affect on adaptive immune system. This helps supression of inflamation (4, 15).
World Health Organization defines range of sufficient, insufficient, deficient, severe deficient vitD3 plasma levels are 20-100 ng/mL (50-250mmol/L), 15-20 ng/mL (22.5-50mmol/L), 5-15ng/mL (12.5-37.5mmol/L), 5ng/mL(12.5mmol/L) respectively (16 - 17).

Helicobacter pylori is gram negative pathogen infected half of the world population. Infection with H.pylori during childhood causes different clinical spectrum of diseases like asemptomatic carriers, chronic gastritis, peptic ulcers (PU), mucosa associated lymphoid tissue lymphoma, and gastric cancer (18, 19). Incidence and severity of disease related to H.pylori changes in different geographical regions even in children living in the the same regions. Chronic inflamation causes asemptomatic gastritis, PU or gastric cancer. Course of inflamation is related to interaction between virulance factors of H.pylori, host and environmental factors (20, 21).

Although many studies on host factors effecting immune resposes in H.pylori infection, to date complete host factors are not clearly defined. In this study probable relation between H.pylori and vitD3 which has important role in immune response is evaluated.

MATERIAL AND METHODS

In this cross sectional study patients age of 3-18 years underwent upper gastrointestinal endoscopy because of gastrointestinal symptoms and iron deficiency anemia refractory to medical therapy between March 2010 to March 2011 at the pediatric gastroenterology clinics of Celal Bayar University Hospital, Manisa, Turkey were enrolled. Patients' clinical findings, histopathologic diagnosis of biopsy speciments of the patients and plasma vitD3 levels were evaluated.

Exculation Criteria

Those who have received anti-acid, non-steroidal anti-inflammatory drugs and antibiotic treatment in the last 3 months; patients who have had H.pyori eradication in the last one year; children with a diagnosis of systemic disease and those younger than 3 years old were not included in the study.

In the study during upper gastrointestinal endoscopy two antral and two corpus biopsy specimen were taken from four different locations for each patient. Fragments fixed in Hollande solution and stained with hematoxylin eosin and Toluidin blue for histopathological examination and H.pylori evaluation according to 1994 updated Sydney scoring system for each antral and corpus biopsy specimens. For evaluation of tissue atrophy in biopsy specimens 2000 Atrophy Club criteria used and each biopsy material defined as atrop-

hy positive and negative. Presence of intestinal metaplasia is evaluated for each patient.

Plasma vitD3 Level Analysis

Plasma vitD3 level measured using HPLC method with vitD3 kit RECIPE Chemicals+Instruments GMBH, Labortechnik Dessauerstrabe 3, mD-80992 München/Germany (internet:www.recipe.de). Samples were separated chromatographicly and analysis performed with UV detector. After samples were precipitated with precipitant P. internal standart were added. After each sample were mixed with vortex for 30 seconds and santrifujed at 10000Xg for 5 minutes, obtained supernatants were used for HPLC analysis. Measurements calculated according to "İnternal standart-Via peak" area method.

Consensus values is used for classification of plasma vitD3 level (severe deficiency ≤ 12. 5 (5) nmol/L (ng/m), deficiency ≤ 37. 5 (15) nmol/L (ng/m), insufficient 37. 5–50.0 (15–20) nmol/L (ng/m), sufficient 50–250 (20–100) nmol/L (ng/m), high >250 (100) nmol/L (ng/m), toksik >375 (150nmol/L(ng/mL)).

Ethical Committee

In this study written informed concent were obtained from all patients and parents. All procedures performed in this study were approved by Ethics Committee of Celal Bayar University (protocol number 0046/2010).

Statistical Analysis

Statistical analyses to compare these parameters between groups were performed using the Statistical Package for the Social Sciences (SPSS) (Version 16.0; SPSS, Inc., Chicago, IL, USA). Means were compared between two groups by Student's t tests. Pevelance rates were compared between groups by the chi square test. A value of $p < 0.05$ was considered statistically significant.

RESULTS

In the study a total of 201 patients consists of H.pylori positive 98 (48.7%) children 43 (43.1%) males and 55 (56.9%) females), H.pylori negative 103 (51.3%) children, 33 (32%) males and 70 (68%) females), were enrolled.

The mean age of H.pylori negative and positive groups were 11.6 ± 3.81, 12.4 ± 3.37. years respectively. No significant statistical difference in sex and mean age were found between H.pylori negative and positive groups ($p > 0.05$).

Mean plasma vitD3 level of H.pylori negative, H.pylori positive were 16.36±11.35 ng/mL, 15.64±8.91 ng/Ml respectively. There was no significant statistical difference between H.pylori positive and negative groups ($p > 0.05$).

Vitamin D3 deficiency was detected in 76 (73%) and 80 (81.6%) of H.pylori negative and positive children respectively. There is no statistical difference between percentage of vitD3 deficiency in H.pylori positive and negative groups. The H.pylori positive and negative groups consists of 6 (6.1%) 6 (5.8%) patients with severe deficient plasma level of vitD3 (<5ng/mL), 49 (50%), 41 (39.8%) patients with deficient plasma level of vitD3 (<15ng/mL), 25 (25.6%), 29 (28.2%) patients with insufficient plasma level of vitD3 (15-20ng/mL) and 18 (18.3%), 27 (26.2%) patients with sufficient plasma level of vitD3 respectively. Plasma level of vitD3 deficiency was more frequent in H.pylori positive group than H.pylori negative group. Statistical difference was significant between groups ($p < 0.05$) **(Table 1)**.

Table1: Frequencies and percentage of degree of severity of 25 OH Vit D deficiency in H.pylori positive and negative groups

25OH Vit D Level	H.pylori (-) N (%)	H.pylori(+) N (%)	Total N (%)
Severe Deficiency	6 (5.8)	6 (6.1)	12(6)
Deficiency	41 (39.8)	49 (50)	90(44.8)
Insufficiency	29 (28.2)	25 (25.6)	54(27)
Sufficiency	27 (26.2)	18 (18.3)	45(22)
Total	103 (100)	98 (100)	201(100)

Chi square test P<0.05, p=0.04,

When the severity of gastric mucosal H.pylori activity and plasma level vitD3 were compared in H.pylori positive cases, there was statistical significant relation between decrease in vitD3 level and severity of gastric mucosal H.pylori activity ($p < 0.05$) **(Table 2)**. When the plasma vitD3 level of the cases and the severity of chronic inflammation were compared, gastric chronic inflamation increases when mean plasma vitD3 level of H.pylori positive patients decreases. This was statistically significant ($p < 0.05$)**(Table 3).**

Table 2: Association of mean plasma 25OH vitamin D plasma level with H.pylori activity

H.pylori Activity	n	25OH Vit D Level(ng/ml) (Mean±SD)
Mild	27	21.48±9.36
Moderate	31	17.64±9.28
High	40	12,72±6.30
Total	98	15.64±8.91

Annova test, p<0.05,p= 0.031

Table 3: Association of mean plasma 25 OH vitamin D level with chronic inflamation in H.pylori cases

Chronic Inflamation	n	25OH Vit D level (Mean± SD)
None	32	18.58±6.71
Mild	23	15.68±8.4
Moderate	35	15.54±5.71
Severe	8	7.12±3.56
Total	98	15.64±8.91

nova test p<0.05, p=0.04

DISCUSSION

In this study mean plasma mean vitD3 level were found not sufficent in both H.pylori positive and negative groups. Vitamin D3 plasma level was not statistically different between H.pylori positive (15.64±8.91 ng/mL) and negative (16.36±11.35 ng/mL) groups. Maternal vitD3 related rickets and subclinic viD3 deficiency is common in pediatric and adolescent age groups in different regions of Turkey in different seasons (22 - 24). Vitamin D3 deficiency is worldwide common public health problem specially in northern hemisphere. Andersen et al. reported during winter plasma vitD3 level almost all the children is under 10ng/mL in which 30 percent of the children is lower than 10ng/mL in northern Europe (25). In a study reported from Uganda, 38.5% of children were found to have low vitD3, and 2.7% of them had vitD3 deficiency (26). An other study conducted in Ireland showed 70% of children of 2 years of age were vitD3 deficient (27). In subgroup analysis of mean plasma level of vitD3 deficiency subgroup, H.pylori positivity statistically higher than other subgroups. The lack of difference in mean vitD3 levels between H.pylori positive and H.pylori negative groups in our study can be explained by low vitD3 levels in our region.

Kawaura reported that H.pylori infection was less common in elderly women who took vitD3 supplements compared to those who did not (28). In the study of Antico et al. vit D3 levels, which were found to be 11.3 ± 8.4 ng/mL in H.pylori gastritis, were found to be statistically significantly lower than in healthy individuals (29). In children there are limited number of studies related to H.pylori and vitD3 level in literature. Gao et al found the prevalence of vitD3 deficiency in H.pylori seropositive and seronegative groups was 20.7% and 12.1%, respectively in children (30). This study is different from our study because of no hystopathologic H.pylori verification.

In this study, there was no significant difference between vitD3 levels and H.pylori positive or H.pylori negative groups, but when the H.pylori positive groups were divided into subgroups as severe deficient, deficienct, insufficient and sufficient vitD3 level, there was significant difference between the deficiency of vitD3 level and the presence of H.pylori infection. In the study of Shafri et al. H.pylori positivity was found to be 31% higher when patients with vitD3 levels <20 ng/mL were compared with patients with vitD3 levels ≥20 ng/mL. In the same study, vitD3 level was found to be moderately higher in the group with H.pylori positive in which eradication was successful, compared to the group in which eradication treatment failed (19.34 ± 9.55 vs 18.64 ± 9.61) (31). In our study, unlike the study of Shafri et al. the presence of H.pylori infection was confirmed by gastric biopsy samples.

Helicobacter pylori triggers inflammation in two ways which are by secreting specific toxins or other aggressive factors; the latter by stimulating the natural and acquired immune response of the host (20, 21). Despite the strong immune response in H.pylori infection, clearance of the infection is often not possible (19, 32, 33). Vitamin D3, has an important role in signaling pathways that play a role in the antimicrobial effect of innate immunity. It has been shown that vitD3 (found in macrophages, monocytes, epithelial cells) stimulates the expression of genes encoding the antimicrobial peptide (CAMP and DEFB2) (34, 35). Guo, L et al reported that vitD3 increases CAMP expression and decreases cytokine activation in gastric epithelial cells, and it has been suggested to play a role in the inhibition of H.pylori (36). In the study of Hosada et al. VDPs (vitamin D3 decomposition products) and H.pylori were shown to have a bactericidal effect by providing membrane solubility and cell ly-

sis (37). In the study of Zhou et al. it was shown that VitD3 inhibited H.pylori infection by increasing CAMP secretion in vivo in mice (38). In our study, the increase in gastric mucosal H.pylori activity correlated with the severity of low vitD3 supports the importance of the antimicrobial effect of vitD3. A strong local immune response develops initially in a host infected with H.pylori. Neutrophils, macrophages, monocytes, and dendritic cells are the first cells to aggregate in the gastric mucosa (20). Histopathologically, chronic gastric inflammation is characteristic in the majority of cases (39). The production of almost all cytokines is increased in the inflammatory response against H.pylori. In H.pylori infection, damage to the gastric mucosa by indirect means caused by the host's immune response, as well as by various cytotoxins and enzymes such as urease, is responsible for the destructive effect (40). Compared with adults, decreased Th1 and Th17 response, increased TGF-β1, IL-10 secretion, resulting in less gastric inflammatory response and neutrophil infiltration have been shown in children (19, 41). Active vitD3 increases the release of the anti-inflammatory cytokine IL-10 and shifts the balance towards Th2. Vitamin D3 achieves this direct effect by binding to the NFAT (nuclear factor activated T cell) and IFγ promoter regions that cause the Th1 response and inhibiting synthesis (9). In vitD3 deficiency, there is a defect in T cell maturation (42). IL-8, which plays an important role in the pathogenesis of H.pylori-induced diseases, is a potent chemoattractant for neutrophils and lymphocytes. It also has effects on cell proliferation, migration and tumor angiogenesis. A correlation has been established between IL-1, IL8, and the severity of inflammation (43). It has been reported that vitD3 reduces the expression of IL-1, IL-6, IL-8 and TNF-α in different cell types (9, 44). Proinflammatory cytokines secreted in increased inflammatory reactions in the gastric mucosa in H.pylori infection result in intense infiltration by increasing chemotaxis of mononuclear cells and neutrophils (45). In this study, increase in gastric mucosal bacterial activity and the severity of chronic inflammation compare with the vitD3 levels of H.pylori positive cases the difference between the groups was statistically significant. Low vitD3 level causes increase in the severity of inflammation and gastric mucosal bacterial activity. These molecular mechanism supports increase in gastric mucosal H.pylori activity and severity of chronic inflamation in this study. To our knowledge, this study is the first report of mean vitD3 level inversely correlated with severity of H.pylori activity and chronic inflamation in children with H.pylori infection to date. These results reveals the importance of adequate vitD3 supplementation in preventing inflammation in addition to antimicrobial effect in H.pylori infection.

Vitamin D3 deficiency is a risk factor for H.pylori infection. The findings of this study shows vitD3 increasing antibacterial effect and reducing the severity of inflammation in H.pylori infection. These results supports during childhood and adolescence period providing sufficient vitD3 supplementation is important in H.pylori infection control and prevention of H.pylori related early and late complication.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

MODERN EĞİTİMDEKİ YENİLİKÇİ YAKLAŞIMLAR ÇERÇEVESİNDE ANATOMİ DERSİNİN ÖĞRENCİ BAKIŞ AÇISIYLA DEĞERLENDİRİLMESİ

EVALUATION OF ANATOMY COURSE FROM THE STUDENT'S PERSPECTIVES WITHIN THE FRAMEWORK OF INNOVATIVE APPROACHES IN MODERN EDUCATION

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ÖZET

AMAÇ: Son 30 yılda tıp fakültelerinin eğitim öğretim programlarında görülen müfredat değişikliklerine rağmen anatomi eğitimi temel bir disiplin olarak önemini korumuştur. Bu çalışmanın amacı Kahramanmaraş Sütçü imam Üniversitesi Tıp Fakültesi'ndeki anatomi eğitiminin mevcut durumunun ve eğitim-öğretim sürecine ilişkin sorunların öğrencilerin geribildirimleri ışığında belirlenmesidir.

GEREÇ VE YÖNTEM: Çalışmamıza 2021 - 2022 Eğitim–Öğretim yılında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesinde eğitim gören 482 gönüllü katıldı. Çalışmada Dönem I' den 167 (% 94,35), Dönem II' den 151 (%88,30) ve Dönem III 'den ise 164 (%89,13) öğrenci bulunmaktadır. Tüm öğrencilere gönüllük esasına uygun olarak anatomi eğitimiyle ilgili Google Forms üzerinden 17 soruluk bir anket uygulandı (Teorik eğitimle ilgili 6, İnternetle ilgili 2, Sınavlarla ilgili 4 ve Pratik eğitimle ilgili 5 soru).

BULGULAR: Tıp Fakültesi öğrencilerinin %96,9'u anatomi dersinin iyi bir hekim olmak için mutlaka gerekli olduğunu belirtti. Sunumların ve maketlerin Anatomi eğitiminin teorik kısmının anlaşılmasını kolaylaştırdığını ifade edenlerin oranı sırasıyla %88,4 ve %97,7'dir. Öğrencilerin % 87,82'si öğretim elemanlarının ders panosunun son dersinde vaka raporlarının tartışılmasını önerdi. Almayı planladığımız 3D (üç boyutlu) interaktif anatomi programları hakkında öğrencilerin %78,4'ü olumlu görüş bildirdi. Öğrencilerin %92,1'i laboratuvar derslerinin yararlı olduğunu, %89'u laboratuvarın daha iyi organize edilmesi gerektiğini ve %78,4'ü kadavra diseksiyonun önemli olduğunu belirtti.

SONUÇ: Tıp fakültesi öğrencilerinin geri bildirim sonuçları anatomi eğitimiyle ilgili yeni eğitim metodolojisin geliştirilmesinde, mevcut eksikliklerin giderilmesinde yararlı olacağını düşünmekteyiz.

ANAHTAR KELİMELER: Tıp, Anatomi, Müfredat, Kadavra.

ABSTRACT

OBJECTIVE: Despite the changes in the curriculum of medical faculties in the last 30 years, anatomy education has maintained its importance as a basic discipline. The aim of this study is to evaluate the current situation of anatomy education in Kahramanmaraş Sütçü İmam University Faculty of Medicine and determine the problems related to the education-teaching process in the light of students' feedback.

MATERIAL AND METHODS: 482 volunteers studying at Kahramanmaraş Sütçü İmam University Faculty of Medicine participated in our study in the 2021-2022 academic year. In the study, there were 167 (94.35%) students from Term I, 151 (88.30%) from Term II and 164 (89.13%) students from Term III. 17-question survey was applied to all students on a voluntary basis over Google Forms about anatomy education (6 questions about theoretical education, 2 questions about Internet, 4 questions about exams, and 5 questions about practical education).

RESULTS: 96.9% of the students of the faculty of medicine reported that the anatomy course is essential to be a good physician. The rate of the presentations and models have facilitated the understanding of the theoretical part of anatomy education is 88.4% and 97.7%, respectively. 87.82% of the students suggested that the lecturers should perform a discussion of case reports on the last lesson on the lecture board. 78,4% of the students reported a positive opinion about the 3D (three dimensions) interactive anatomy programs that we are planning to receive. 92.1% of the students stated that laboratory courses were beneficial, 89% of them stated that the laboratory should be better organized, and 78.4% of them stated that cadaver dissection is important.

CONCLUSIONS: We consider that the feedback results of the medical faculty students' will develop the education methodology related to anatomy education and will be useful to eliminate the current deficiencies.

KEYWORDS: Medicine, Anatomy, Curriculum, Cadaver.

GİRİŞ

Tıp eğitiminin temel taşı olan genel anatomi, temel tıp bilimi içinde en eski geçmişe sahip olan bir bilim dalıdır (1). Günümüzde güvenli cerrahi tekniklerin eğitimi ve geliştirilmesinde cerrahi dallarla birlikte anatomi bilimi, temel disiplinler arasında önemini korumaktadır. Anatomi geniş anlamda vücudu oluşturan yapıları, organları, bunların şekillerini, yerleşimlerini, komşuluklarını ve görevsel ilişkileri inceleyen bilim dalıdır. Kadavralar, yüzyıllardan beri yerine alternatif bulunamamış bir eğitim aracıdır. Kadavra tarihçesinde ilk belgelerin Kadıköy'lü (Chalcedon) Herophilos'a (M.Ö. 335-280) ait olduğu görülmektedir. Kadavranın yasak olduğu dönemlerde ise Bergama'lı (Pergamon) Galen (M.S. 131-201) bazı çalışmalarında hayvan materyalleri kullanarak kadavra tarihinin gelişimine destek olmuştur (2). Günümüzde teknolojinin getirdiği imkanların giderek artması kuşkusuz anatomi eğitimine de olumlu katkılar sağlamıştır. Teknoloji ne kadar ilerlerse ilerlesin teknolojik materyallerin hiçbiri insan bedeni üzerinde yapılan çalışmaların yerini alamamıştır (3). İyi bir anatomi eğitimi için ortalama kadavra başına düşen öğrenci sayısı 6-12 arasında olması istenmektedir. Kadavra temini konusunda yaşanan olumsuzluklar nedeniyle uygulamak zorunda kalınan "kadavrasız anatomi eğitimi" ise öğrencilere yeterli olmayacaktır (4). Bunlara ek olarak anatomi eğitimi veren öğretim elemanlarının kesinlikle kadavra üzerinde disseksiyon uygulamaları yaparak anatomi bilgilerini pekiştirmeleri önerilmektedir. Mümkünse lisans öğrencilerinin de dahil olduğu disseksiyon uygulamalarının yapıldığı gelişmiş laboratuvarların kurulması Türkiye'de anatomi eğitimine sınıf atlatacaktır (3).

Türkiye'de tıp eğitimi 6 yıllık bir süreyi kapsar. Öğrenciler ilk 3 yıl temel bilimlerden, 2 yıl klinik bilimlerden dersler alırlar. Son 1 yılda ise intörnlük eğitimi alarak tıp doktoru ünvanı ile mezun olurlar. Temel bilimler içerisinde yer alan anatomi eğitimi fakültelerin ilk yıllarında Dönem I ve Dönem II öğrencilerine teorik ve pratik dersler şeklinde verilmektedir. Diğer ülkelerdeki pek çok tıp fakültelerinde olduğu gibi ülkemizdeki tıp fakültelerinin son dönemlerinde de temel bilimler ile klinik bilimler arasında entegrasyonu sağlamaya yönelik eğitim modelleri ile tıp eğitimi yapılmaktadır. Öğrenciye öğrenmeyi öğretmeyi hedefleyen bu eğitim modelleri arasında entegre-eğitim ve probleme dayalı öğrenim modelleri bulunmaktadır (5). Tıp biliminin ve uygulamalarının dinamik olarak sürekli değiştiği düşünüldüğünde, tıp eğitimin en iyi nasıl sunulacağına dair arayışların ivme kazanarak sürmesi çokta şaşırtıcı değildir. Öğrenme sürecinin her anında veri toplama aracı olarak, öğrencilerden elde edilen geribildirimler kullanılmaktadır (6). Öğrencilerin bilgi-beceri düzeylerini ve mesleki başarılarını artırmak için tıp eğitiminde geribildirim, öğretme sürecinin tamamlayıcı ve önemli bir bileşeni olarak günümüzde kullanılmaktadır (7).

Bu çalışmanın amacı Kahramanmaraş Sütçü imam Üniversitesi Tıp Fakültesi'ndeki anatomi eğitiminin mevcut durumunun ve eğitim-öğretim sürecine ilişkin sorunların öğrencilerin geribildirimleri ışığında belirlenmesidir.

GEREÇ VE YÖNTEM

Bu araştırmaya Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi'nde 2021 - 2022 eğitim öğretim yılında öğrenim gören Dönem I (n=177), Dönem II (n=171) ve Dönem III (n=184) öğrencilerinin tamamı (n=532) dahil edildi. Çalışmamızda örneklem seçme yoluna gidilmemiş, evrenin tamamına ulaşılması hedeflenmiştir. Dönemlere göre kayıtlı öğrenci sayıları ve e-posta adresleri tıp fakültesi öğrenci işlerinden alındı. Tıp Fakültesinde Anatomi dersi Dönem I müfredatını oluşturan beş kurulun son üç kurulunda yer alırken, Dönem II müfredatında ise yedi kurulun altısında anatomi eğitimi verilmektedir. Dönem I' de 38 saat teorik ve 50 saat pratik olmak üzere toplam 88 saat, Dönem II' de 122 saat teorik ve 96 saat pratik olmak üzere toplam 218 saatlik bir ders programı uygulanmaktadır. Dönem I ve II' de toplam 306 saatlik anatomi eğitimi verilmektedir. Dönem III müfredatında ise anatomi dersi yer almamaktadır. Tüm öğrencilere eğitim döneminin sonunda tamamen gönüllülük esasına dayalı olarak Google Forms üzerinden anatomi eğitimiyle ilgili 17 soruluk (Teorik eğitim 6, İnternet kullanımı 2, Testler 1, Sınavlar 4 ve Pratik eğitim 5 soru) bir anket gönderildi. Ayrıca, öğrencilerden ad-soyad ve başarı durum bilgileri istenmedi.

Soruların cevaplarında seçenek olarak "katılmıyorum", "fikrim yok" ve "katılıyorum" şeklinde üçlü Likert tipi ölçek uygulandı. Anketin hazırlanmasında Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Anatomi Ana bilim dalı öğretim üyelerinin görüşleri ve Manyacka Ma Nyemb ve ark.'nın çalışmaları etkili olmuştur (8).

Etik Kurul

Tanımlayıcı, kesitsel tipteki bu araştırma öncesinde Kahramanmaraş Sütçü İmam Üniversitesi Tıp Fakültesi Tıbbi Araştırmalar Etik Kurulu'ndan 14.06.2022-10 nolu kararı ile çalışmanın onayı alınmıştır.

İstatistiksel Analiz

Verilerin değerlendirilmesinde nicel değişkenlerin normal dağılıma uygunluğu Kolmogorov-Smirnov testi ile incelenmiştir. Nicel veriler normal dağılmıştır. Kategorik değişkenlerin gruplar arasındaki dağılımsal farklılıkları Chi Sqaure test ve Exact test ile incelenmiştir. İstatistik parametreleri sayı(%) ve ortalama±standart sapma ile ifade edilmiştir. İstatistiksel anlamlılık p<0,05 olarak kabul edilmiştir. Verilerin değerlendirilmesinde IBM SPSS versiyon 22 yazılımlarından yararlanılmıştır

BULGULAR

Anket çalışmamıza Dönem I' den 167 (%94,35), Dönem II' den 151 (%88,30) ve Dönem III' den 164 (%89,13) olmak üzere toplam 482 (%90,60) gönüllü öğrenci katılmıştır. Öğrencilerin yaşları 17-25 yıl arasında değişirken; yaş ortalamaları ise 20,28±1.72 yıl olarak hesaplandı. Öğrencilerin 258'i (%53,5) kadın ve 224'ü (%46,5) erkektir. Çalışmaya katılan öğrencilerin anatomi eğitimi hakkındaki düşüncelerini, eğiticilerin ders anlatımında kullandıkları materyallere (pdf, sunumlar, çizimler vb.) erişimlerini, uygulanan anatomi sınavları hakkındaki düşüncelerini ve anatomi eğitiminin pratik kısmını oluşturan laboratuvar (kadavra/maket) ile ilgili düşüncelerini 3 ölçekli Likert yöntemiyle sorgulayan sorularla değerlendirildi ve verdikleri yanıtlar **Tablo 1** ve **Tablo 2**'de gösterildi.

Tablo 1: Öğrencilerin anatomi eğitimi (teorik/pratik) hakkındaki düşüncelerinin değerlendirilmesi

Anket soruları	Katılmıyorum n (%)	Fikrim Yok n (%)	Katılıyorum n (%)
Anatomi dersi iyi bir hekim olmam için gereklidir	10(2,1)	5(1,0)	467(96,9)
PowerPoint sunuları dersi anlamayı kolaylaştırır	39(8,1)	17(3,5)	426(88,4)
Her ders kurulunun son dersi vaka tartışmalarına ayrılmalıdır.	11(2,3)	48(10,0)	423(87,8)
Anatomik maketler teorik bilgilerin kolay anlaşılmasını sağlar	7(1,5)	4(0,8)	471(97,7)
Kurullardaki Anatomi ders saatleri yeterlidir	140(29,0)	82(17,0)	260(53,9)
Anatomi dersleri sabah olmalıdır	115(23,9)	116(24,1)	251(52,1)
Ders materyalleri (pdf dosyaları, sunumlar, çizimler vb) web sayfasında yer almalıdır	13(2,7)	18(3,7)	451(93,6)
İnteraktif 3 D Anatomi programları derslerde kullanılmalıdır.	58(12,0)	66(13,7)	358(74,3)
Her kurulda konuyla alakalı quiz şeklinde değerlendirme testleri yapılmalıdır	154(32,0)	124(25,7)	204(42,3)
Kurul /Final sınavlarında klinik soruların sayısı arttırılmalıdır	168(34,9)	138(28,6)	176(36,5)
Kurul /Final sınavlarında anatomi soru sayısı yeterlidir	27(5,6)	63(13,1)	392(81,3)
Kurul /Final sınavlarında çizim (resim) mutlaka yer almalıdır	126(26,1)	97(20,1)	259(53,7)
Laboratuvar dersleri yararlıdır	31(6,4)	7(1,5)	444(92,1)
Laboratuvar ders saatleri arttırılmalıdır	58(12,0)	42(8,7)	382(79,3)
Daha iyi organize edilmelidir	21(4,4)	32(6,6)	429(89,0)
Laboratuvar dersleri teorik derslerden daha önemlidir	59(12,2)	77(16,0)	346(71,8)
Kadavra diseksiyonu anatomi eğitiminin olmazsa olmazıdır	29(6,0)	75(15,6)	378(78,4)

n: sayı f(%): yüzde

Tablo 2: Dönemlere göre öğrencilerin anatomi eğitimi (teorik/pratik) hakkındaki düşüncelerinin karşılaştırılması

Anket soruları		Dönem I n (%)	Dönem II n (%)	Dönem III n (%)	p
Anatomi dersi iyi bir hekim olmam için gereklidir	Katılmıyorum	2 (1,2)	1 (0,7)	7 (4,3)	
	Fikrim Yok	3 (1,8)	0 (0,0)	2 (1,2)	0,072
	Katılıyorum	162 (97,0)	150 (99,3)	155 (94,5)	
PowerPoint sunuları dersi anlamayı kolaylaştırır	Katılmıyorum	11 (6,6)	12 (7,9)	16 (9,8)	
	Fikrim Yok	7 (4,2)	6 (4,0)	4 (2,4)	0,754
	Katılıyorum	149 (89,2)	133 (88,1)	144 (87,8)	
Her ders kurulunun son dersi vaka tartışmalarına ayrılmalıdır	Katılmıyorum	4 (2,4)	3 (2,0)	4 (2,4)	
	Fikrim Yok	17 (10,2)	18 (11,9)	13 (7,9)	0,832
	Katılıyorum	146 (87,4)	130 (86,1)	147 (89,6)	
Anatomik maketler teorik bilgilerin kolay anlaşılmasını sağlar	Katılmıyorum	1 (0,6)	3 (2,0)	3 (1,8)	
	Fikrim Yok	0 (0,0)	1 (0,7)	3 (1,8)	0,310
	Katılıyorum	166 (99,4)	147 (97,4)	158 (96,3)	
Kurullardaki Anatomi ders saatleri yeterlidir	Katılmıyorum	88 (52,7)	30 (19,9)	22 (13,4)	
	Fikrim Yok	22 (13,2)	20 (13,2)	40 (24,4)	<0,001*
	Katılıyorum	57 (34,1)	101 (66,9)	102 (62,2)	
Anatomi dersleri sabah olmalıdır	Katılmıyorum	25 (15,0)	52 (34,4)	38 (23,2)	
	Fikrim Yok	20 (12,0)	53 (35,1)	43 (26,2)	<0,001*
	Katılıyorum	122 (73,1)	46 (30,5)	83 (50,6)	
Ders materyalleri (pdf dosyaları, sunumlar, çizimler vb) web sayfasında yer almalıdır.	Katılmıyorum	3 (1,8)	6 (4,0)	9 (5,5)	
	Katılıyorum	162 (97,0)	145 (96,0)	144 (87,8)	0,001*
İnteraktif 3 D Anatomi programları derslerde kullanılmalıdır.	Katılmıyorum	21 (12,6)	11 (7,3)	26 (15,9)	
	Fikrim Yok	38 (22,8)	12 (7,9)	16 (9,8)	<0,001*
	Katılıyorum	108 (64,7)	128 (84,8)	122 (74,4)	
Her kurulda konuyla alakalı quiz şeklinde değerlendirme testleri yapılmalıdır	Katılmıyorum	59 (35,3)	58 (38,4)	37 (22,6)	
	Fikrim Yok	46 (27,5)	45 (29,8)	33 (20,1)	<0,001*
	Katılıyorum	62 (37,1)	48 (31,8)	94 (57,3)	
Kurul /Final sınavlarında klinik soruların sayısı arttırılmalıdır	Katılmıyorum	61 (36,5)	41 (27,2)	66 (40,2)	
	Fikrim Yok	62 (37,1)	45 (29,8)	31 (18,9)	<0,001*
	Katılıyorum	44 (26,3)	65 (43,0)	67 (40,9)	
Kurul /Final sınavlarında anatomi soru sayısı yeterlidir	Katılmıyorum	4 (2,4)	9 (6,0)	14 (8,5)	
	Fikrim Yok	23 (13,8)	8 (5,3)	32 (19,5)	<0,001*
	Katılıyorum	140 (83,8)	134 (88,7)	118 (72,0)	
Kurul /Final sınavlarında çizim (resim) mutlaka yer almalıdır	Katılmıyorum	23 (13,8)	57 (37,7)	46 (28,0)	
	Fikrim Yok	34 (20,4)	42 (27,8)	21 (12,8)	<0,001*
	Katılıyorum	110 (65,9)	52 (34,4)	97 (59,1)	
Laboratuvar dersleri yararlıdır	Katılmıyorum	7 (4,2)	12 (7,9)	12 (7,3)	
	Fikrim Yok	2 (1,2)	0 (0,0)	5 (3,0)	<0,001*
	Katılıyorum	158 (94,6)	139 (92,1)	147 (89,6)	
Laboratuvar ders saatleri arttırılmalıdır	Katılmıyorum	9 (5,4)	24 (15,9)	25 (15,2)	
	Fikrim Yok	6 (3,6)	15 (9,9)	21 (12,8)	<0,001*
	Katılıyorum	152 (91,0)	112 (74,2)	118 (72,0)	
Daha iyi organize edilmelidir	Katılmıyorum	3 (1,8)	7 (4,6)	11 (6,7)	
	Fikrim Yok	6 (3,6)	13 (8,6)	13 (7,9)	0,057
	Katılıyorum	158 (94,6)	131 (86,8)	140 (85,4)	
Laboratuvar dersleri teorik derslerden daha önemlidir	Katılmıyorum	9 (5,4)	30 (19,9)	20 (12,2)	
	Fikrim Yok	15 (9,0)	34 (22,5)	28 (17,1)	<0,001*
	Katılıyorum	143 (85,6)	87 (57,6)	116 (70,7)	
Kadavra diseksiyonu anatomi eğitiminin olmazsa olmazıdır	Katılmıyorum	0 (0,0)	11 (7,3)	18 (11,0)	
	Fikrim Yok	26 (15,6)	25 (16,6)	24 (14,6)	0,001*
	Katılıyorum	141 (84,4)	115 (76,2)	122 (74,4)	

n: sayı;f(%): yüzde; Chi Square test; Exact test;a:0.05;* gruplar arasındaki dağılımsal farklılık istatistiksel olarak anlamlı.

Tüm öğrencilerin %96,9'u ''Anatomi dersi iyi bir hekim olmam için gereklidir", %88,4'ü "PowerPoint sunuları dersi anlamayı kolaylaştırır" ve %97,7'si ise "Anatomik maketler teorik bilgilerin kolay anlaşılmasını sağlar" ifadelerine katılıyorum yanıtı vermişlerdir. Dönem I öğrencilerinin %34,1'i, dönem II öğrencilerinin %66,9'u, dönem III öğrencilerinin %62,2'si "Kurullardaki Anatomi ders saatleri yeterlidir" ifadesine katılıyorum cevabı verdiler. Kurullardaki Anatomi ders saatlerinin yeterliliği konusunda dönem I, dönem II ve dönem III öğrencilerinin görüş fark-

lılıkları anlamlı bulunmuştur (p<0,001). Dönem I öğrencilerinin %73,1'i, dönem II öğrencilerinin %30,5'i, dönem III öğrencilerinin %50,6'sı "Anatomi dersleri sabah olmalıdır" ifadesine katılıyorum yanıtını vermişlerdir. Anatomi derslerinin sabah işlenmesi konusunda dönem I, dönem II ve dönem III öğrencilerinin görüş farklılıkları anlamlı bulunmuştur (p<0,001). "Her ders kurulunun son dersi vaka tartışmalarına ayrılmalıdır" ifadesine tüm öğrencilerin %87,8'i katılıyorum cevabı vermişlerdir. Tüm öğrencilerin %93,6'sı "Ders materyalleri (pdf dosyaları, sunumlar, çizimler vb.) fakülte web sayfasında yer almalıdır", %74,3'ü ise "İnteraktif 3D Anatomi programları derslerde kullanılmadır." ifadesine katılıyorum cevabını verdiler Tablo 1 ve 2. Dönem I öğrencilerinin %37,1'i, dönem II öğrencilerinin %31,8'i, dönem III öğrencilerinin %57,3'ü "Her kurulda konuyla alakalı quiz şeklinde değerlendirme testleri yapılmalıdır" ifadesine katılıyorum yanıtını verdiler. Her kurulda konuyla alakalı quiz şeklinde değerlendirme testleri yapılması konusunda dönem I, dönem II ve dönem III öğrencilerinin görüş farklılıkları anlamlı bulunmuştur (p<0,001). Dönem I öğrencilerinin %34,1'i, dönem II öğrencilerinin %66,9'u, dönem III öğrencilerinin %62,2'si "Kurullardaki Anatomi ders saatleri yeterlidir" ifadesine katılıyorum yanıtını verdiler. İstatistiksel olarak dönem I, dönem II ve dönem III öğrencilerinin görüş farklılıkları anlamlı bulunmuştur (p<0,001). Sınavlarda klinik soru sayısının arttırılması konusunda dönem I, dönem II ve dönem III öğrencilerinin görüş farklılıkları anlamlı bulunmuştur (p<0,001). Dönem I öğrencilerinin %26,3'ü, dönem II öğrencilerinin %43'ü, dönem III öğrencilerinin %40,9'u "Kurul veya Final sınavlarında klinik soru sayısı arttırılmalıdır" ifadesine katılıyorum cevabı verdiler. Tüm öğrencilerin %81,3'ü "Sınavlarda anatomi soru sayısı yeterlidir" ifadesine katılıyorum yanıtını verdiler. Dönem I öğrencilerinin %65,9'u, dönem II öğrencilerinin %34,4'ü, dönem III öğrencilerinin %59,1'i "Sınavlarda çizim (resim) mutlaka yer almalıdır" ifadesine katılıyorum cevabını verdiler. Ancak, dönem I, dönem II ve dönem III öğrencilerinin görüş farklılıkları anlamlı bulunmuştur (p<0,001) (Tablo 1 ve 2). Tüm öğrencilerin %92,1'i "Laboratuvar ders-

leri yararlıdır" ifadesine katılıyorum cevabı verirken, %71,82'si ise Laboratuvar derslerini teorik derslerden daha önemli buldular. Öğrencilerin %89'u "Anatomi laboratuvarı daha iyi organize edilmeli", %79,3'ü ise "Laboratuvar ders saatleri arttırılmadır" ifadesine katılıyorum cevabı verdiler. Bir diğer önemli bulgu öğrencilerin %78,4'ü "Kadavra diseksiyonu anatomi eğitiminin olmazsa olmazıdır" ifadesine katılıyorum yanıtı verdiler (Tablo 1).

TARTIŞMA

Anatomi bilimi tarih boyunca hep tıp eğitiminin temel taşı olmuştur. Zaman içerisinde gelişen pedagojik yöntemlerin süzgecinden önemini koruyarak geçse de, tıp fakültelerin müfredat programlarında anatomi ders saatlerinin azaltılmaya başlandığı görülmektedir. Halbuki, anatomi bilgisi hastanın muayenesinde, tanının konulmasında, bulguların hasta ve diğer hekimlerle paylaşılmasında önemli rol oynamaktadır. Temel bilimler içerisinde yer alan birçok bilim dallarının müfredatlarının, hekimlerin profesyonel mesleki yaşamlarındaki ihtiyaçlara bağlı olarak değiştiği ve bir "Çekirdek Eğitim Programına" dahil edildiği görülmektedir. Sağlık çalışanlarının ortak bilgi platformu olan anatomi biliminin, müfredat değişikliklerinden daha az etkileneceği düşünülmektedir. Anatomi bilgisi cerrahların yetişmesi ve ameliyat tekniklerinin ortaya konulmasında ayrı bir öneme sahiptir (9). Çalışmamızda öğrencilerin %96,9'u "Anatomi dersi iyi bir hekim olmam için gereklidir" şeklinde görüş belirtmiştir. Bu da hekimlerin elde ettikleri temel tıbbi becerilerini etkili bir şekilde uygulayabilmelerinin, iyi bir anatomi bilgi seviyesi ile sağlanacağı gerçeği ile örtüşmektedir. 2014 yılında yapılan bir çalışmada hemşirelik öğrencileri anatomi eğitiminin mesleki yaşantıları için çok önemli olduğunu bildirmiştir (10) "Kurullardaki anatomi ders saatleri yeterlidir" ifadesine toplam öğrencilerin %53,9'u katılıyorum yanıtını verdi. Ancak, Dönem I öğrencilerinin %52,7'si bu ifadeyi katılmıyorum şeklinde yanıtlarken, Dönem II öğrencilerin %66,9'u ve Dönem III öğrencilerin %62,2'si katılıyorum şeklinde yanıtladı. Dönem I müfredatında anatomi dersi son 3 kurulda yer almakta olup, 38 saat teorik ve 50 saat pratik eğitimden oluşmaktadır.

Dönem II'de ise anatomi dersi her ders kurulunda yer almaktadır. Dönem I'deki anatomi ders saatlerinin az oluşu, öğrencilerin farklı cevap vermelerine neden olduğunu düşünmekteyiz. Tıp fakültesi öğrencilerinin yeterli anatomik bilgiye sahip olduklarını düşünmelerinde; anatomi öğreniminin bilgileri öğrenme, unutma, yeniden yapılandırma ve uygulama aşamalarından oluşan zihinsel süreçleri içermesi etkili olmuştur (11, 12). Uzmanlara göre en verimli saatlerin sabah ya da vücudun iyice dinlenmiş olduğu saatlerdir. Bu zaman aralığında zihnin uyanık ve dikkatin en yüksek seviyede olduğu ifade edilmektedir (13). Çalışmamızda öğrencilerin %52,1'i haftalık ders programında anatomi derslerinin sabah saatlerinde işlenmesi gerektiğini bildirmiş olup, özellikle sabah saatlerinde anatomi derslerine Dönem I öğrencilerinin diğer dönem öğrencilerine kıyasla daha yüksek bir katılım gösterdiği görülmüştür. Bu farkın Dönem I öğrencilerinin girmiş oldukları Yükseköğretime Geçiş Sınavı (YGS) ve Alan Yeterlilik Testleri (AYT) sınavlarından kalan ders çalışma alışkanlıklarının hala devam etmesinden ve uykularını daha kaliteli aldıklarından kaynaklandığını düşünmekteyiz.

Gelişen teknoloji ile geleneksel sınıf ortamları yavaş yavaş yerini yeni öğrenme ortamlarına bırakmaktadır. Daha önceki yıllarda ülkemizde anatomi eğitiminin teorik kısmında eğitmenler derse ait önemli görselleri yazı tahtası üzerine çizerek anlatırlardı. Sınıf ortamında kullanılan PowerPoint sunumları bilgilerin daha kolay iletilmesini sağlamıştır. Ayrıca, eğitmenler önemli buldukları konuları çeşitli görseller ve animasyonlarla zenginleştirerek daha kolay anlatma olanağı bulmuşlardır. 2015 yılında 140 Tıp Fakültesi öğrencisi ile yapılan bir çalışmada öğrencilerin %90,7'sinin PowerPoint sunumlarının anatomi eğitimin kolaylaştırdığını ifade etmişlerdir (14). Başka bir çalışmada ise bu oran %66,10 olarak bildirilmiştir (15). Bizim çalışmamız da ise bu oran %88,40'dır. Sonucun yüksek çıkmasının nedeni günümüzde öğrencilerin ders sunularına ve interaktif 3D anatomi programlarına, bilgisayar, internet ve cep telefonları vasıtasıyla kolay erişilebilir olmasından kaynaklandığını düşünmekteyiz.

Bulgularımızın yukarıda belirtilen çalışmalar ile uyum içerisinde olduğu görülmektedir. Bir diğer teknolojik ürün ise 3D yazıcılar ile üretilen anatomi eğitim maketleridir. Bunlar laboratuvar eğitiminde yaygın olarak kullanılmaktadır. Şeker ve ark.'ları (2013) çalışmalarında kullanılan eğitim modellerin ne kadar mükemmel olursa olsun yakın zamanda insan kadavrası ile eğitimin yerini alamayacağını bildirilmişlerdir (4). Dönem II ve Dönem III öğrencileri ile yapılan bir başka araştırmada ise öğrenciler laboratuvar eğitiminde maket ve kadavranın birlikte kullanılması gerektiğini, ayrıca eğitim maketlerinin anatomik yapıların öğrenilmesini kolaylaştırdığını ifade etmişlerdir (16). Bizim çalışmamızda ise öğrencilerin %97,7'si anatomik eğitim maketlerinin konuların daha kolay anlaşılmasını sağladığını bildirmişlerdir.

Kadavra temin etmenin zorluğu ve artan maliyetler sebebiyle bazı fakültelerde kadavra diseksiyon dersleri yeterince yapılamadığından eğitimciler bilgisayar temelli (animasyon, 3D görüntüler) teknolojileri kullanmaya büyük ilgi göstermeye başlamıştır (17). Son yıllarda görüntüleme teknolojisinin gelişmesine paralel olarak anatomik yapılarında daha ayrıntılı bir şekilde görüntülenmesine imkan sağlanmıştır (18). Elde edilen bu görüntüler, teknoloji yardımıyla anatomik yapıların daha ayrıntılı bir şekilde gösterildiği 3D etkileşimli simülasyonlar haline dönüşmüştür (19). Yapılan araştırmalar nöroanatomi gibi anlaması zor ve karmaşık derslerin, 3D platformlarının yardımıyla birçok yapının sanal olarak anlatıldığı konuları içeren simülasyonlar ile anatomi dersini öğrenmeyi kolaylaştırdığı bildirilmiştir (20, 21). Ayrıca, öğrenciler interaktif 3D platformlarından oluşan programları herhangi bir eğitmene gerek duymadan kolayca kullanabilirler (22). Başka bir çalışmada, laboratuvar eğitimlerinde bir çeşit interaktif 3D platformu olan "Virtual Human Dissector" programı kullanan öğrenciler ile kadavra ve eğitim maketi kullanan öğrencilerin sınavlarda benzer notları aldıkları bildirilmiştir (23). 2015 yılında Murgitroyd ve ark. tarafından yapılan bir çalışmada ''İnteraktif 3D uygulamaları için sınırsız olanaklara sahip yardımcı bir platformdur.''

vurgusu yapılmıştır (24). 2019 yılında 236 Tıp Fakültesi öğrencisi üzerinde yapılan başka bir çalışmada öğrencilerin %90,68'i e-öğrenmenin konuların öğrenilmesine yardımcı olduğunu bildirirken, %84,32'si ise geleneksel öğrenme biçiminin e-öğrenme ile takviye edilmesi gerektiğini önermişlerdir. Ancak, araştırmacılar bu iki grup arasında istatistiksel bir anlamlılığın olmadığını bildirmiştir (25). Mevcut araştırmanın gerçekleştiği fakültenin herhangi bir interaktif 3D platformuna aboneliği bulunmamaktadır. Bu platformun temininin mevcut üniversitede sağlık alanında eğitim veren diğer birimlerinde asistan ve öğrenci eğitimlerine katkı sağlayacağını düşünmekteyiz. Tüm bunlar dikkate alındığında "Derslerde İnteraktif 3D platformlarından da faydalanılmalıdır" ifadesine %74,32 kişi katılıyorum şeklinde yanıt vermişlerdir. Bu cevaplar da bizlerin öngörüsünü desteklemektedir.

Yapmayı planladığımız bir uygulama da ders materyallerinin (pdf, sunumlar, çizimler vb.) fakülte web sayfasında yer almasıdır. Bununla ilgili olarak katılımcıların %93,60'ı olumlu yanıt vermişlerdir. 2002 yılında yapılan bir çalışmada, araştırmacılar genel ve gelişimsel anatomi dersi almış öğrencilerden dersle ilgili iki ifadeyi puanlandırmalarını (1'in "Kesinlikle Katılmıyorum" ve 5'in "Kesinlikle Katılıyorum; 1'den 5'e kadar olan bir aralıkta) istemişlerdir. "Tüm derslerin animasyonlu PowerPoint ile sunulması bir gelişmedir" ifadesi için öğrencilerin verdiği yanıtların ortalama puanı 4,7'dir. "Web sayfasında PowerPoint sunumlarının bulunması bir gelişmedir" ifadesine ise 5,0 puan vermişlerdir (26). Yapmayı planladığımız bir başka uygulama ise her ders kurulunun son ders saatini vaka tartışmalarına ayırmayı düşünmekteyiz. Vaka tartışmalarının, öğrencilerin akıl yürütme, bağımsız düşünme ve problem çözme becerilerinin gelişmesine katkı sağlayacağı bildirilmiştir (27). Başka bir çalışmada ise öğrencilerin % 67'si anatomi derslerinin klinik bilgilerle beraber anlatılmasını isterken yine öğrencilerin % 90,1'i klinik bilgilerle birlikte verilen anatomi eğitiminin kendilerine olumlu katkılar sağlayacağını ifade etmiştir (28). Bizim çalışmamızda ise öğrencilerin % 87,8'i her ders kurulunun son dersinde vaka tartışmalarının yapılmasını istemişlerdir.

Kadavra, vital fonksiyonlarını tamamen yitirmiş bir insanın bedeninin eğitim ve araştırmalarda incelenmek amacıyla muhafaza edilmesidir. Kadavra diseksiyonları anatomi eğitiminde altın standart olarak kabul edilmektedir (29). Bugün tıp fakültesinin Anatomi eğitimde yoğun bir şekilde kadavra kullanılmaktadır. Lakin ülkemizde bağış sayısı yetersizliğinden dolayı toplam kadavra sayısında eksiklik bulunmakta ve bu durum da Anatomi eğitiminin en ciddi sorunlarından birisi olarak karşımıza çıkmaktadır (3). Çalışmamızda ankette katılan öğrencilerin %92,1'i laboratuvar uygulamalarını önemli bulurken, teorik dersleri önemli bulanların sayısı ise %71,8'i dir. Dönem I öğrencilerinin % 94,6'sı bu ifadeye verdikleri "Katılıyorum" yanıtı istatistiksel olarak anlamlı çıkmıştır. Fakültemizde öğrenci eğitimlerinde kullandığımız anatomi laboratuvarının artan öğrenci sayısına cevap verecek büyüklükte olmaması, kadavra azlığı ve destekleyici anatomik modellerinin azlığı eğitiminin verimliliğini kısıtlamaktadır. Tüm bu olumsuzluklar öğrenci anketlerine % 89'u laboratuvarın daha iyi organize edilmesi, % 79,3'ü pratik ders saatlerinin yeterli olmadığı, % 78,4'ü kadavra diseksiyonlarının çok önemli olduğu şeklinde yansıdığı görülmektedir. Hekimlerin mesleki evrensel temel gereklilikleri sağlaması gerektiğini düşünmekteyiz. Bu amaçla Tıp fakültesi dönem I, II ve III öğrencilerinin anatomi eğitimi hakkında görüşlerinin değerlendirilmesi amacıyla yapılan bu çalışmanın sonuçları ve öneriler aşağıda verilmiştir.

Öğrenciler internet ortamında ders materyallerine kolay ulaşabileceği, interaktif 3D anatomi eğitim programlarından faydalanmak, vaka tartışmaları yapmak, anatomi laboratuvar şartlarının (öğrenci kapasitesi, yeterli kadavra ve maket sayısı) düzeltilmesini istemektedirler. Elde edilen geri bildirim sonuçlarının sonraki yıllarda eğitim sürecine yansıtılmasını planlamaktayız. Ayrıca, çalışmamızın anatomi eğitiminin geliştirilmesinde ve diğer bilim dallarına yol gösterici nitelikte olmasında etkili olacağını düşünmekteyiz.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

ATORVASTİN VE ROSUVASTATİNİN NEDEN OLDUĞU MİYOPATİYE KARŞI KAFEİK ASİD FENETİL ESTERİN KORUYUCU ETKİSİ

PROTECTIVE EFFECT OF CAFFEIC ACID PHENETHYL ESTER AGAINST MYOPATHY INDUCED BY ATORVASTIN AND ROSUVASTATIN

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ÖZET

AMAÇ: Statinlerin bazı hastalarda myopatiye yol açması nedeni ile hastanın tedaviye uyumu azalmakta, ilacın kullanılmasına son verilmekte veya kullanılan ilaç değiştirilmektedir. Bu çalışmada statinlerin myopatiye neden olabileceği iki durum olarak oksidatif stress ve inflamasyon üzerinde çalışılmış ve Kafeik asit fenil ester (CAPE)'in koruyucu rolü deneysel olarak test edilmiştir.

GEREÇ VE YÖNTEM: Çalışmada rabdomiyosarkom (RD) hücre hatları kullanılmıştır. Hücreler kontrol, atorvastatin, rosuvastatin, CAPE, atorvastatin+CAPE ve rosuvastatin+CAPE olmak üzere 6 gruba ayrılmıştır. Spektrofotometrik olarak Total Antioksidan Kapasite (TAC), Total Oksidan Kapasite (TOC) ve Oksidatif Stres İndeksi (OSI) analizleri yapılmış; İnterlökin 6 (IL-6) düzeyleri hem protein düzeyinde hem de real time PCR ile mRNA ekpresyonu düzeyinde gösterilmiştir.

BULGULAR: Kontrol grubunda 1739 olan OSI atorvastatin uygulaması ile 3814'e çıkmış, atorvastatinin CAPE ile kombinasyonu sonucunda ise 2109'a inmiştir. Rosuvastatin ve Rosuvastatinin CAPE ile kombinasyonu sonucunda kontrol grubuna göre OSI bakımından bir değişiklik olmamıştır. Atorvastin grubunda IL-6 mRNA ekspresyon düzeyleri kontrol grubuna benzer bulunurken, Rosuvastatin grubunda kontrol grubuna nazaran 2,369 kat artış gözlenmiştir. Rosuvastatinin CAPE ile kombinasyonu neticesinde IL-6 mRNA ekspresyon düzeylerinin kontrol grubu seviyesine çekildiği tespit edilmiştir.

SONUÇ: Bu çalışmada Atorvastatinin RD hücre hatlarında oksidatif stresi tetiklediği, rosuvastatinin ise IL -6 mRNA ekspresyon düzeyini artırarak proinflamasyona giden sürecin önünü açtığı gözlemlenmiştir. Atorvastatinin neden olduğu oksitadif stresin ve rosuvastatinin neden olduğu inflamasyonun baskılanmasında CAPE kombinasyonunun işlevsel olduğu tespit edilmiştir. Bu bakımdan tedavide atorvastatin ve rosuvastatinin CAPE ile kombinasyonunun statinlerin neden olduğu kas hasarı üzerine hasta yararına olumlu sonuçlarının olabileceği gösterilmiştir.

ANAHTAR KELİMELER: Atorvastatin, Rosuvastatin Kalsiyum, Miyopati, Kafeik Asid Fenetil Ester.

ABSTRACT

OBJECTIVE: Due to the fact that statins cause myopathy in some patients, the patient's compliance with the treatment decreases, and the treatment is interrupted or drug is changed. In this study, oxidative stress and inflammation, two conditions in which statins can cause myopathy, were studied and the protective role of Caffeic acid phenethyl ester (CAPE) was tested experimentally.

MATERIAL AND METHODS: Rhabdomyosarcoma (RD) cell lines were used in the study. Cells were divided into 6 groups as control, atorvastatin, rosuvastatin, CAPE, atorvastatin+CAPE and rosuvastatin+CAPE. Total Antioxidant Capacity (TAC), Total Oxidative Capacity (TOC), and Oxidative Stress Index (OSI) analyzes were made spectrophotometrically; Interleukin 6 (IL-6) levels were demonstrated both at the protein level by ELISA and at the level of mRNA expression by real time PCR.

RESULTS: OSI, which was 1739 in the control group, increased to 3814 with atorvastatin application and decreased to 2109 with the combination of atorvastatin and CAPE. There was no change in OSI levels in Rosuvastatin and Rosuvastatin and CAPE combination compared to the control group. While IL-6 mRNA expression levels were found to be similar to the control group in the atorvastin group, an increase of 2.369 times was observed in the Rosuvastatin group compared to the control group. As a result of the combination of rosuvastatin with CAPE, it was determined that IL-6 mRNA expression levels were reduced to the level of the control group.

CONCLUSIONS: In this study, it was observed that atorvastatin triggered oxidative stress in RD cell lines, while rosuvastatin increased the expression level of IL-6 mRNA and paved the way for the process leading to proinflammation. The combination of CAPE was found to be functional in suppressing oxidative stress caused by atorvastatin and inflammation caused by rosuvastatin. In this regard, it has been shown that the combination of atorvastatin and rosuvastatin with CAPE may have positive results for the benefit of the patient on muscle damage caused by statins.

KEYWORDS: Atorvastatin, Rosuvastatin Calcium, Myopathy, Caffeic Acid Phenethyl Ester.

GİRİŞ

Sterol biyosentez yolağındaki kilit adımlardan biri olan Hidroksimetilglutaril-CoA (HMG-CoA) redüktaz enziminin inhibitörleri olan statinler, mantar kökenli moleküllerdir. Statinler, güçlü kolesterol düşürücü ilaçlardır ve kardiyovasküler hastalıkların önlenmesine olağanüstü katkılar sağlamıştır. Statin kullanımı nedeniyle kas ağrısı, miyotoksisite ve rhabdomyoliz geliştiği önceki çalışmalarda sıklıkla rapor edilmiştir (1 - 4).

Statinler günümüzde dislipidemiye bağlı kardiyovasküler hastalıkların önlenmesi ve tedavisi için en etkili oral ajanlar olarak bilinmektedir. Atorvastatin ve rosuvastatin aktif β-hidroksi asit formunda reçete edilmektedir. Statinlerin farmakolojik tepkisi, HMG-CoA redüktazı inhibe edecekleri hepatosite ulaşma yeteneklerine bağlıdır (5). HMG-CoA redüktazın inhibisyonu sadece kolesterol sentezini değil, aynı zamanda ubikinon, steroidler, safra asitleri, D vitamini ve ayrıca geranilgeranil pirofosfat ve farnesil pirofosfat sentezini de azaltmaktadır (6).

Propolisin önemli bir fenolik aktif bileşeni olan kafeik asid fenetil ester (CAPE), antimikrobiyal, antitümöral, antioksidan, antiinflamatuar ve benzeri gibi geniş bir farmakolojik aktiviteye sahiptir (7). ROS'u temizleme ve immünomodülatör yetenekleri nedeniyle, CAPE'nin kardiyomiyosit apoptozunun zayıflaması ve miyokardiyal enfarktüs boyutunun azaltılması dâhil olmak üzere hem in vitro hem de in vivo çalışmalarda kalp kası koruyucu etkinlikte olduğu bildirilmiştir (8, 9). Bu araştırmada atorvastatin ve rosuvastin uygulanan Rhabdomyosarkom (RD) hücre hattında bu statinlerle CAPE kombinasyonunun inflamasyon ve oksidatif stress üzerine etkisinin incelenmesi hedeflenmiştir.

GEREÇ VE YÖNTEM

Bu çalışmada Türkiye Şap Enstitüsü hücre kültürü kataloğundan elde edilen insan rabdomiyosarkom hücre hatları olan RD hücre hatları kullanıldı. Hücreler %10 (v/v) oranında ısı ile inaktif edilmiş fetal bovibe serumu (FBS) ve 5 mM glutamin, 100 U/ml penisilin, 1 mM sodyum piruvat içeren DMEM besiyerinde 37°C, %5 CO_2 ve %95 hava içeren bir atmosferde inkübe edildi.

MTT Hücre Viabilite Testi

Hücre canlılığı ölçümü için metabolik olarak aktif hücreler tarafından redüksiyona uğratılarak formazon kristallerini oluşturan MTT ayıracının(3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2H-tetrazolium bromide)kullanıldığı MTT testi yapıldı (10).96 kuyucuklu well platelere her bir kuyucuğa $1x10^4$ hücre olacak şekilde ekim yapıldı. Hücreler flask tabanına yapışıp %70'ini kapladığında IC50 doz belirleme çalışması için ajanların uygulamasına geçildi. Atorvastatin (was purchased from Adooq Bioscience, Cat No: A11800), Rosuvastatin (was purchased from Adooq Bioscience, Cat No: A10810) ve CAPE(was purchased from Selleckchem, Cat. No: S7414)'nin 24 saat süreyle 8 tekrar olacak şekilde 1 μM, 5 μM, 10 μM, 20 μM, 40 μM, 80 μM, 100 μM, 500 μM ve 1000 μM konsantrasyonlarında 8 farklı dozu uygulandı. Tüm ajanlar DMSO'da çözüldü ve kontrol grubu hücrelerine ise %0.05 lik DMSO uygulandı. Uygulama sonunda ajan bulunan mediumlar taze ve FBS'siz mediumla ile değiştirildi. 100μl medium hacmine 10 μl MTT solüsyonu (5mg/ml) eklenerek 4 saat 37°C, %5 CO_2 ve %95 hava ortamında inkübe edildi. İnkübasyon sonunda kuyucuklar boşaltıldı, oluşan formazon kristalleri 100 μl DMSO ile çözünerek 570 nm dalga boyunda Optik Dansite (O.D.) değerleri ELISA readerda (Epoch, Biotek, USA) okundu. Konsantrasyon ve O.D. değerleri GraphPad Prism version 8.0.1 (GraphPad Software, Inc., CA, USA) programına girilip konsantrasyonların logaritmalarının normalize edilmiş O.D. değerlerine göre grafiğe geçirilip IC50 dozları hesaplandı.

Deney Grupları

Çalışmada kontrol, atorvastatin, rosuvastatin, CAPE, atorvastatin+CAPE ve rosuvastatin+CAPE olmak üzere 6 deney grubu kullanıldı. Her bir gruba bahsedilen ajanlar tek, tek ve CAPE ile kombine edilmiş halde 24 saat süreyle IC50 dozlarında maruz bırakıldı.

Hücre Lizatlarının Hazırlanması ve Total Protein Ölçümü

$2,2x10^6$ hücre olacak şekilde 100mm'lik petri kaplarına (VWR, PA, USA) hücrelerin ekimi yapıldı. Petri kabı tabanını %70 kaplayan hücre hatlarına belirlenen IC50 dozlarında 24

saat boyunca Atorvastatin, Rosuvastatin ve CAPE uygulaması yapıldı. İnkübasyon sonunda medium atıldı ve hücrelerden buz üzerinde lizis buffer (%1 TritonX 100, 50mM HEPES Buffer, 100mM $Na_2HPO_4.2H_2O$, %8 protease inhibitor cocktail) uygulaması ile lizatlar elde edildi. İlgili lizatlardan BCA metodu (TaKaRa, Shiga, Japan) ile total protein ölçümü yapıldı.

IL-6 Düzeylerinin Belirlenmesi

Lizatlardan IL-6 seviyeleri ölçümü ELISA kiti (eBioscience, Vienna, Austria) vasıtasıyla gerçekleştirildi. Her grup için ölçülen IL-6 değeri o grubun total protein seviyelerine bölünerek gruplar arasındaki IL-6 seviyeleri kıyaslandı.

TAC, TOC ve OSI Düzeylerinin Belirlenmesi

TOC ve TAC ölçümleri Erel'in geliştirdiği metodlara göre (10, 11) yapıldı. Her iki ölçüm sonucunda tespit edilen değerler total protein değerlerine bölündü. TAC ve TOC ölçümleri yapıldıktan sonra, oksidan ve antioksidan dengeye ilişkin daha net yorum yapılabilmesine olanak veren oksidatif stres indeksi (OSI) aşağıdaki formüle göre hesaplandı (11, 12).

$$OSI=[(TOC, \mu mol/L)/(TAC, (mmolTroloxEquiv/L)x100]$$

Real Time QPCR

mRNA transkripsiyon düzeyi analizlerinde kullanılacak RNA'lar spin kolon yöntemi ile çalışan hazır ticari kit kullanılarak yapıldı (EURx GeneMatrix, Gdansk, Poland, Catalog No: E3598). İzole edilen RNA'ların miktar tayini ve saflık derecesi Epoch Take3 plate sistemi kullanılarak analiz edildi. PCR reaksiyonunda kalıp olarak kullanılmak üzere her bir örneğe ait RNA'dan 1μg alınarak önce reverz transkriptaz (RT) ile komplementari DNA (cDNA) sentezi yapıldı. Daha sonra her bir örneğe ait cDNA'den 1μl alınarak üzerine SYBR green master miks ve bir çift primer (oligonükleotid) konuldu. House keeping gen olarak beta aktin (Forward: 5'- GCTCTTTTCCAGCCTTCCTT-3' / Reverse: 5'-CTTCTGCATCCTGTCAGCAA-3') kullanıldı. Beta aktin PCR protokolünde PCR miksi hot start için 95 °C 2 dk 1 döngü tutulduktan sonra 35 döngü 95 °C 30 sn/62 °C, 30 sn/72 °C 45 sn termal profili uygulandı. IL-6 geni için Forward: 5'-TGGTCTTTTGGAGTTTGAGGTA-3' / Reverse: 5'-AGGTTTCTGACCAGAAGAAGGA-3' primer olarak kullanıldı. IL-6 PCR protokolüde PCR miksi hot start için 95 °C 10 dk 1 döngü tutulduktan sonra 40 döngü 95 °C 15 sn/60°C 60 sn/72 °C 30 sn termal profili uygulandı. Elde edilen amplifikasyon eğrilerine ait döngü eşiği (Ct) değerlerinden hareketle, hedef genlerin mRNA ekspresyon düzeylerinin nisbi değişimleri $2^{-\Delta\Delta Ct}$ metodu (13) ile REST2009 programı kullanılarak hesaplandı ve istatistiği yapıldı.

Etik Kurul

Bu çalışmada tamamen ticari olarak elde edilen hücre hatları üzerinde laboratuvar deneyleri yapılmıştır, bu nedenle etik onayı gerektirmemektedir.

İstatistiksel Analiz

Çalışma kapsamında elde edilen veriler GraphPad Prism version 8.0.1 (GraphPad Software, Inc., CA, USA) programı kullanılarak analiz edildi. Verilerin Kolmogorov-Smirnov testi ile normal dağılım gösterip göstermedikleri analiz edildi. Veriler normal dağılım gösterdiği için üç ya da daha fazla grubun kıyası maksadıyla parametrik testlerden One Way ANOVA testi kullanıldı. Değişkenler arasındaki ilişkilerin incelenmesi için Dunnett's korelasyon analizleri yapıldı. $P<0,05$ istatistiksel anlamlılık düzeyi olarak kabul edildi.

BULGULAR

Atorvastatin IC_{50} dozu 30,83 μM, Rosuvastatin IC_{50} dozu 149,6 μM ve CAPE IC_{50} dozu 114 μM olarak tespit edildi (Şekil 1).
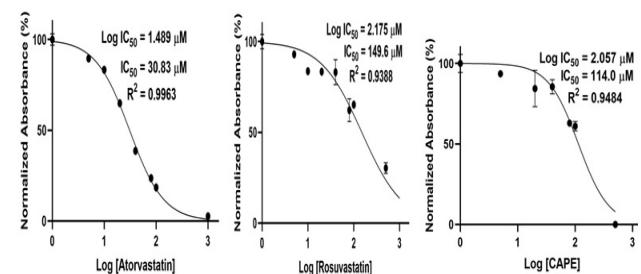
Şekil 1: Atorvastatin, Rosuvastatin ve CAPE'in IC_{50} dozları.

Atorvastatin uygulanan grupta total oksidan kapasite 0,02796 µmol H_2O_2 Equiv./mg protein olarak bulunurken total antioksidan kapasite 0,000748 mmol Trolox Equiv./mg protein olarak tespit edilip, oksitatif stress indeksi 3814 olarak hesaplandı **(Tablo 1, Tablo 2 ve Şekil 2)**.

**Tablo1:** Gruplar arasındaki OSI ve IL-6 düzeylerinin istatistiksel karşılaştırılması.

Parametreler	Grupların birbirlerine kıyası	Ortalama Fark	%95,00 güven aralığı	Düzeltilmiş p değeri
	Kontrol vs. Rosuvastatin	-57,65	-789,4 to 674,1	0,9997
	Kontrol vs. Atorvastatin	-2075	-2647 to -1502	<0,0001
	Kontrol vs. CAPE	-369,6	-892,9 to 153,7	0,2549
	Kontrol vs. Ros+CAPE	237,6	-39,69 to 514,9	0,1082
	Kontrol vs. Ato+CAPE	-811,5	-1561 to -62,04	0,0302
	Rosuvastatin vs. Atorvastatin	-2017	-2692 to -1341	<0,0001
	Rosuvastatin vs. CAPE	-312	-1143 to 519,5	0,7899
OSI (pg/µg protein)	Rosuvastatin vs. Ros+CAPE	295,3	-447,2 to 1038	0,7503
	Rosuvastatin vs. Ato+Cape	-753,9	-1652 to 144,0	0,1186
	Atorvastatin vs. CAPE	1705	945,7 to 2464	<0,0001
	Atorvastatin vs. Ros+CAPE	2312	1618 to 3007	<0,0001
	Atorvastatin vs. Ato+Cape	1263	544,0 to 1982	0,0007
	CAPE vs. Ros+CAPE	607,2	1,893 to 1213	0,0492
	CAPE vs. Ato+Cape	-441,9	-1109 to 225,6	0,3146
	Ros+CAPE vs. Ato+Cape	-1049	-1855 to -243,3	0,0096
	Kontrol vs. Rosuvastatin	0,01126	0,002710 to 0,01980	0,0234
	Kontrol vs. Atorvastatin	0,01767	0,002436 to 0,03290	0,0333
	Kontrol vs. CAPE	0,02054	0,01382 to 0,02726	0,0020
	Kontrol vs. Ros + CAPE	0,008989	-0,001718 to 0,01970	0,0794
	Kontrol vs. Ato+CAPE	0,01851	0,01280 to 0,02423	0,0018
	Rosuvastatin vs. Atorvastatin	0,006413	-0,001404 to 0,01423	0,0842
	Rosuvastatin vs. CAPE	0,009283	0,006161 to 0,01241	0,0022
IL-6 (pg/µg protein)	Rosuvastatin vs. Ros + CAPE	-0,002267	-0,006409 to 0,001874	0,2200
	Rosuvastatin vs. Ato+CAPE	0,007255	0,003455 to 0,01106	0,0080
	Atorvastatin vs. CAPE	0,002870	-0,007765 to 0,01351	0,6755
	Atorvastatin vs. Ros + CAPE	-0,008680	-0,01660 to -0,0007590	0,0390
	Atorvastatin vs. Ato+CAPE	0,0008423	-0,01067 to 0,01235	0,9966
	CAPE vs. Ros + CAPE	-0,01155	-0,01825 to -0,004855	0,0108
	CAPE vs. Ato+CAPE	-0,002028	-0,004534 to 0,0004777	0,0872
	Ros + CAPE vs. Ato+CAPE	0,009523	0,003637 to 0,01541	0,0130

P<0,05 istatistiki olarak anlamlı kabul edilmiştir.

Tablo 2: TOC, TAC ve OSI düzeyleri

		Kontrol	Rosuvastatin	Atorvastatin	CAPE	Ros+CAPE	Ato+Cape
TOC	Ortalama	0,01923ª	0,01704ª	0,02796ᵇ	0,02103ª	0,02172ᶜ	0,02818ᵈ
	Standart Sapma	0,002518	0,003939	0,003867	0,003160	0,002016	0,003643
	Standart ortalama hatası	0,0006294	0,001137	0,001034	0,0007900	0,0005821	0,0009106
TAC	Ortalama	0,001124ª	0,000993ª	0,000748ᵇ	0,001068ª	0,00151ᶜ	0,001211ª
	Standart Sapma	0,000142	0,000205	0,0001288	0,0002937	0,0003248	0,0003618
	Standart ortalama hatası	0,0000355	0,00005918	0,00003442	0,00007343	0,00009375	0,00009046
OSI	Ortalama	1739ª	1797ª	3814ᵇ	2109ª	1502ª	2551ᵈ
	Standart Sapma	335,2	629,5	686,8	622,9	376,1	872,6
	Standart ortalama hatası	83,80	181,7	183,6	155,7	108,6	218,2

TOC (µmol H_2O_2 Equiv./mg protein), TAC (mmol Trolox Equivalent/mg protein), OSI düzeyleri. Farklı üssü ifadeli gruplar arasında istatistiksel farklılık bulunmaktadır. p<0,05 değeri istatistiksel olarak anlamlı kabul edilmiştir.
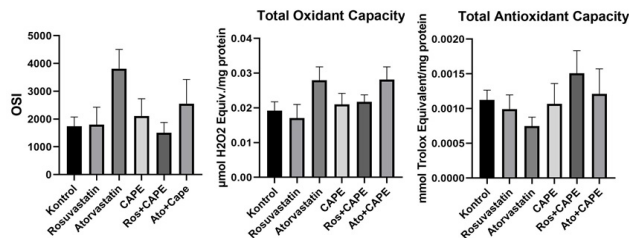
**Şekil 2:** Gruplar arasındaki TOC, TAC ve OSI düzeyleri.

Atorvastatinle beraber CAPE uygulanan grupta total oksidan kapasite 0,02818 µmol H_2O_2 Equiv./mg protein olarak tespit edilmişken antioksidan kapasite 0,001211 mmol Trolox Equ-

iv./mg protein olarak bulunmuş olup oksidatif stress indeksi 2551 olarak hesaplandı (Tablo 1, Tablo 2 ve Şekil 2). Rosuvastatin uygulanan grupta total oksidan kapasite 0,01704 µmol H_2O_2 Equiv./mg protein olarak bulunurken total antioksidan kapasite 0,000993 mmol Trolox Equiv./mg protein olarak tespit edilip, oksitatif stress indeksi 1797 olarak hesaplandı (Tablo 2). Rosuvastatinle beraber CAPE uygulanan grupta total oksidan kapasite 0,02172 µmol H_2O_2 Equiv./mg protein olarak tespit edilmişken antioksidan kapasite 0,00151 mmol Trolox Equiv./mg protein olarak bulunmuş olup oksidatif stress indeksi 1502 olarak hesaplandı (Tablo 2). IL-6 mRNA ekspresyon düzeyleri Rosuvastatin grubunda kontrol grubuna nazaran 2,369 kat (p=0,012), Atorvastatin grubunda 1,415 kat (p=0,531) ve Ros+CAPE grubunda 1,223 kat (p=0,565) uyarıldı. CAPE ve Ato+CAPE gruplarında ise IL-6 mRNA ekspresyon düzeyleri kontrol grubuna nazaran sırasıyla 0,005 kat (p=0,001) ve 0,669 kat (p=0,734) baskılandı **(Tablo 3, Şekil 3)**.

Tablo 3: IL-6 mRNA ekspresyon düzeylerinin kontrol grubuna kıyasla nispi artışlarının karşılaştırılması.

Gruplar	Ekspresyon	Standart Hata	P Değeri
Rosuvastatin	2,369	1,624 - 3,939	0,012
Atorvastatin	1,415	0,586 - 2,661	0,531
CAPE	0,005	0,002 - 0,013	0,001
Ros+CAPE	1,223	0,614 - 2,258	0,565
Ato+CAPE	0,669	0,026 - 6,718	0,734

P<0,05 istatistiki olarak anlamlı kabul edilmiştir.
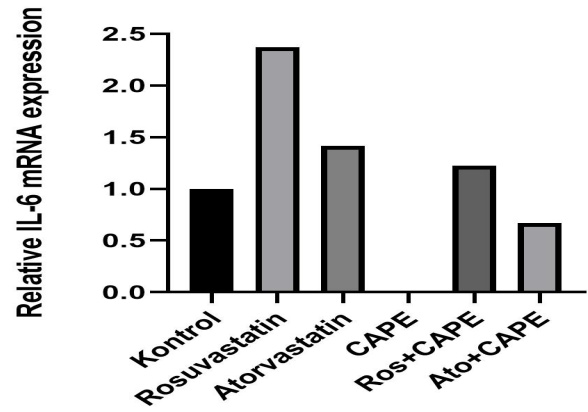
Şekil 3: Hücre lizatlarından elde edilen IL-6 protein miktarları.

TARTIŞMA

CAPE uygulamasıyla hem hücre lizatlarından elde edilen IL-6 seviyelerini (p=0,002) hem de IL-6 mRNA ekspresyon düzeyleri kontrol grubuna nazaran düştü (p=0,001). Bu bakımdan literatür verilerinde IL-6 blokörü olarak akta-rılan CAPE için bu bilgi doğrulanmış oldu (14,

15). Rosuvastatin uygulaması IL-6 mRNA ekspresyon düzeylerini artırmasına rağmen aynı etki protein düzeyinde görülmedi. Bu durumun 24 saatlik uygulama süresi ile alakalı olabileceği düşünüldü. Rosuvastatin ile beraber CAPE kombinasyonu hem IL-6 mRNA ekspresyon düzeyini hem de IL-6 protein düzeylerini kontrol grubuna kıyasla benzer değerlere indirdi (p=0,565). Bu bakımdan Rosuvastatinin proinflasmasyona neden olmasının CAPE tarafından başarı ile baskılandığı gösterildi.

Dünya genelinde en sık reçetelenen kolesterol düşürücü ilaçlar olan statinler (16) nedeni tam bilinmemekle beraber kas hasarına neden olmaktadır (17). Bu çalışmada atorvastatin grubunun TOC düzeyi kontrol grubuna nazaran daha yüksek (p<0,0001), TAC ise daha düşük tespit edildi (p<0,0001). Bu bakımdan atorvastatinin RD hücrelerinde antioksidan kapasiteyi baskılamak ve oksidan kapasiteyi tetiklemek suretiyle OSI değerini yukarı çektiği ve kontrol grubuna nazaran oksidatif strese neden olduğu gözlemlendi (p<0,0001)(Tablo 1, Tablo 2). Atorvastatinin neden olduğu oksidatif stress, CAPE kombinasyonu ile baskılandı ve bu baskılanma istatistiksel olarak anlamlı bulundu (p=0,0007). Buna rağmen yalnız CAPE uygulanan hücrelerin TAC (p=0,9292), TOC (p=0,0911) ve OSI (p=0,2549) değerleri kontrol grubuyla benzerdi (Tablo 2, Şekil 2).

Bu bulgulara benzer şekilde Bouitbir ve ark. statin kullanan ve myopati semptomlarına rastlanan hastaların deltoid kas biyopsilerinde oksidadif stresin kontrol grubuna nazaran belirgin bir şekilde daha yüksek olduğunu tespit etmiştir (18). Literatür verileri ele alındığında özellikle atorvastatin grubunda elde edilen oksidatif stres bulgularımızla çelişen yayınlara rastlanmış fakat bu yayınlarda deney materyali olarak kas hücresi ya da kas biyopsi numunesi değil hasta serumu kullanılmıştır (19, 20).

Her ne kadar yukarıda sunulduğu şekliyle atorvastatinin kaslarda oksidatif hasara neden olması ile alakalı yayınlar olsa da bunun tersini söyleyen yayınlara da rastlanmıştır. Bu yayınların çoğu hipekolesterolemili hastaların statin kullanımına yönelik çalışmalardır. Bilinmektedir ki, hiperkolesterolemi, esas olarak nitrik oksiti yok edebilen ve damar duvarındaki yararlı ve koruyucu etkilerini bozabilen serbest oksijen radikallerinin üretiminden kaynaklanan endotelyal disfonksiyon ile ilişkilendirilmektedir. Dolayısıyla başlı başına hiperkolesterolemi oksidatif stres açısından risk faktörüdür (21, 22).

Hali hazırda hiperkolesteroleminin yol açtığı bir oksidatif stresin olduğu in-vivo çalışmalarda Atorvastatinin hiperkolesterolemiyi baskılamak suretiyle oksidatif stresten korunma açısından olumlu katkılarının olduğu bilinmektedir (23). Bu bağlamda bu çalışma kapsamında ele alınan her iki statin için de uygulanan doz, uygulama süresi ve hiperkolesterolemi varlığının OSI değeri açısından önemli olduğu düşünülmüştür.

Rosuvastatin uygulaması sonucunda gerek total oksidan kapasite (p=0,1749) gerek total antioksidan kapasite (p=0,5305) gerekse de oksidatif stress indeksi (p=0,9997) bakımından kontrol grubuna nazaran istatistiki anlamlı olacak bir değişim olmadı (Şekil 2, Tablo 2). Hücre lizatlarında IL-6 seviyelerinin tespitinde; en yüksek oranda CAPE grubunda (p=0,002) olmak üzere Atorvastatin (p=0,033) ve Rosuvastatin (p=0,0234) gruplarında IL-6 seviyelerinin kontrol grubuna nazaran düştüğü gözlemlendi (Tablo 1, Şekil 3).

IL-6 mRNA ekspresyon düzeylerindeki Kontrol grubuna nazaran Rosuvastatinin neden olduğu artış istatistiksel olarak anlamlı bulunurken (p=0,012) Atorvastatin grubundaki eksresyon düzeyi istatistiki olarak kontrol grubuna benzer bulundu (p=0,531). Rosuvastatinin neden olduğu IL-6 mRNA ekspresyon düzeyi artışı CAPE kombinasyonu ile kontrol grubu seviyesine indirildiği tespit edildi. Bu bakımdan Rosuvastatinin neden olduğu IL-6 mRNA ekspresyon düzeyi artışına CAPE tedavi edici etkide bulundu. Yalnız CAPE uygulanan grupta tüm gruplara nazaran IL-6 mRNA ekspresyon düzeyinde dramatik bir şekilde düşüş gözlendi bu düşüş kontrol grubuna nazaran istatistiki olarak anlamlı bulundu (p=0,001).

Bu sonuçlar bağlamında CAPE'in IL-6 seviyelerini düşürmesi literatür verileri ile uyumlu bulunmuştur (24, 25). CAPE'nin kardiyomiyosit apoptozunun zayıflaması ve miyokardiyal enfarktüs boyutunun azaltılması dâhil olmak üzere hem in vitro hem de in vivo çalışmalarda kalp kası koruyucu etkinlikte olduğu bildirilmiş olup (8, 9) daha önceki literatür verilerinde CAPE'in statinlerle kombinasyonuna rastlanamadı. Bu çalışmada in vitro olarak atorvastatinin RD hücrelerinde neden olduğu oksidatif strese karşı CAPE'in koruyucu etki gösterdiği tespit edildi. Ayrıca Rosuvastatinin RD hücrelerinde neden olduğu inflamatuvar sürecin CAPE tarafından baskılandığı tespit gösterildi. Bununla birlikte CAPE'in atorvastatin ve rosuvastatinin neden olduğu kas hasarına karşı olumlu etkilerinin hangi mekanizmalarla gerçekleştiğinin açığa kavuşturulması için hayvan deneyleri ve insan çalışmalarına ihtiyaç olacağı düşünülmektedir.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

GENÇ HİPERTANSİYON HASTALARINDA NON-DİPPER HİPERTANSİYON VE KAN BASINCI DEĞİŞKENLİĞİ

NON-DIPPER HYPERTENSION AND BLOOD PRESSURE VARIABILITY IN YOUNG HYPERTENSION PATIENTS

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ÖZET

AMAÇ: Hipertansiyon, genç popülasyonu da etkileyen ve kardiyovasküler mortaliteyi artıran global bir sağlık sorunudur. Genç hipertansif hastalar, yüksek kan basıncına maruz kaldıkları süre uzun olduğundan uç organ hasarına ve hipertansiyonun neden olduğu komplikasyonlara daha yatkındırlar. Biz çalışmamızda 24 saatlik ambulatuar kan basıncı ölçümü ile genç hipertansif hastaların, 40 yaş üstü hipertansif hastalara göre ortalama sistolik ve diyastolik tansiyon değerlerini ve özellikle uç organ hasarı ile ilişkili olan non-dipper hipertansiyon durumlarını ve kan basıncı değişkenliğini araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Çalışmaya, 83'ü genç hipertansif hasta olmak üzere toplam 337 hasta alındı. Hastaların 24 saatlik tansiyon holter kayıtları retrospektif olarak incelendi. Hastaların ortalama sistolik ve diyastolik tansiyon değerleri, dipper ve non-dipper hipertansiyon durumları ve kan basıncı değişkenliği hesaplandı. Genç hipertansif hastaların sonuçları, 40 yaş üstü hipertansif hastalarla karşılaştırıldı.

BULGULAR: Genç hipertansif hastaların, 24 saatlik diyastolik tansiyon ortalamaları 40 yaş üstü hipertansif hastalara göre daha yüksek saptandı. Non-dipper hipertansiyon olma durumuna göre her iki grup karşılaştırıldığında, 40 yaş üstü hipertansiyon grubunda non-dipper hipertansiyon olma durumu daha yüksek bulundu. 24 saatlik diyastolik tansiyon değişkenliği, genç hipertansif hastalarda daha yüksek saptanırken, gündüz sistolik kan basıncı değişkenliği, 40 yaş üstü hipertansif hastalarda daha yüksek bulundu.

SONUÇ: Genç hipertansiyon hastalarında, 24 saatlik Ambulatuar kan basıncı ölçümü (ABPM) ile non-dipper tansiyon olma durumu ve kan basıncı değişkenliğinin değerlendirilmesi uç organ hasarı gelişimi yönünden riskli hasta grubunu belirlemede yardımcı olabilir.

ANAHTAR KELİMELER: Genç Hipertansiyon, Non-dipper hipertansiyon, Kan basıncı değişkenliği

ABSTRACT

OBJECTIVE: Hypertension is a global health problem that also affects the young population and increases cardiovascular mortality. Young hypertensive patients are more prone to end-organ damage and complications from hypertension due to the long exposure time to high blood pressure. In our study, we aimed to investigate the mean systolic and diastolic blood pressure values of young hypertensive patients compared to hypertensive patients over 40 years of age with 24-hour ambulatory blood pressure measurement, and especially non-dipper hypertension states and blood pressure variability associated with end organ damage.

MATERIAL AND METHODS: The study included 337 patients, 83 of whom were young hypertensive patients. 24-hour ambulatory blood pressure monitoring records of the patients were reviewed retrospectively. The mean systolic and diastolic blood pressure values, dipper and non-dipper hypertension status, and blood pressure variability of the patients were calculated. The results of young hypertensive patients were compared with hypertensive patients aged above 40.

RESULTS: The mean 24-hour diastolic blood pressure was found to be higher in young hypertensive patients than hypertensive patients aged above 40. When both groups were compared according to non-dipper hypertension, non-dipper hypertension was found to be higher in the hypertensive patients group aged above 40. While 24-hour diastolic blood pressure variability was found to be higher in young hypertensive patients, daytime systolic blood pressure variability was found to be higher in the hypertensive patients aged above 40.

CONCLUSIONS: Evaluation of non-dipper blood pressure and blood pressure variability with 24-hour Ambulatory blood pressure monitoring (ABPM) in young hypertension patients may help to identify the patient group at risk for end-organ damage development.

KEYWORDS: Young Hypertension, Non-dipper hypertension, Blood pressure variability

GİRİŞ

Hipertansiyon, Avrupa Kalp Cemiyetinin tanımına göre sistolik kan basıncının 140 mmHg ve/veya diyastolik kan basıncının 90 mmHg'nın üzerinde olmasıdır (1). Türkiye'de hipertansiyon görülme prevalansı %24.8'dir (2). Genç hipertansiyon, 40 yaş altında görülmekle beraber hipertansif hastaların yaklaşık %7-10'unu oluşturmaktadır (3). Hipertansiyon hastalarında, hem sistolik hem de diyastolik kan basıncı yüksekliği görülebilmekle baraber, izole sistolik kan basıncı veya izole diyastolik basıncı yükseklikleri de görülebilmektedir. İzole diyastolik kan basınç yüksekliği, sıklıkla endokrin sistem kaynaklı olurken izole sistolik kan basıncı yüksekliği sıklıkla nefrolojik kaynaklıdır veya vücut kütle indeksindeki artış ile ilişkilidir (4). İzole diyastolik hipertansiyon sekonder hipertansiyon ile ilişkili iken diğer hipertansiyon tipleri genellikle primer hipertansiyon ile ilişkilidir (5). Hipertansiyon, sistolik ya da diyastolik tansiyonun yüksek olmasından bağımsız olarak koroner arter hastalığı, miyokard enfarktüsü, kalp yetersizliği, hemorajik ve iskemik serebrovasküler olaylar, böbrek yetmezliği, aort diseksiyonu gibi birçok hastalığın etiyolojisinde rol oynamaktadır (6). Diyastolik hipertansiyonun sıklıkla sekonder hipertansiyon ile bağlantılı olması nedeniyle altta yatan hastalığın tedavisi, uç organ hasar riskinde koruyucu olmaktadır. Tansiyon ölçümleri fiziksel aktivite, postür, beslenme, emosyonel durum, ağrı, vücut sıcaklığı, uyku ve uyanıklık gibi durumlara bağlı olarak farklılık gösterebilir (7, 8). Normalde uyku esnasında tansiyon ortalaması, uyanıklık esnasındaki tansiyon ortalamasına göre düşüş göstermektedir. Uyku esnasında beklenen tansiyon düşüşünün olmaması metabolizmada bozulmaya işaret eder ve bu durumun sebebi tam olarak aydınlatılamamış olmakla beraber uyku esnasındaki sempatik sistem aktivite artışının bu duruma neden olabileceği düşünülmektedir (9). Uyku sırasında meydana gelen tansiyon değişimleri dipper ve non-dipper fenomenleri ile isimlendirilir. Uyku esnasında ölçülen tansiyonların ortalamasında, uyanıkken ölçülen tansiyonların ortalamasına göre %10 veya üzerinde düşme olmasına dipper tansiyon fenomeni, %10'dan az düşme olmasına da non-dipper tansiyon fenomeni denir. Non-dip-

per hipertansiyonun artmış uç organ hasarı ile ilişkili olduğu çeşitli çalışmalarda gösterilmiştir (7, 8, 10-12). Genç hastalarda görülen hipertansiyonun tanı ve tedavisi, gençlerin toplumun iş gücünün önemli bir kısmını oluşturması ve hipertansiyona maruz kalınan sürenin uzun olması nedeniyle hem iş gücü kaybı, hem de hipertansiyonun neden olduğu komplikasyonlar açısından önemlidir. Çalışmamızda 24 saatlik ambulatuar kan basıncı ölçümü (ABPM) ile genç hipertansif hastaların, 40 yaş üstü hipertansif hastalara göre ortalama sistolik ve diyastolik tansiyon değerlerini, dipper ve non-dipper hipertansiyon durumlarını ve gün içi kan basıncı değişkenliğini araştırmayı amaçladık.

GEREÇ VE YÖNTEM

Araştırmamızda, 01.01.2015 ile 01.09.2022 yılları arasında merkezimizde takip edilen hipertansiyon tanılı 337 hastanın 24 saatlik ABPM sonuçları retrospektif olarak değerlendirilmiştir. Tansiyon ölçümü için noninvazif osilometrik WatchBP ve Cardioline walk200b ABPM cihazları kullanıldı. Cihaz gündüz 30 dakika aralıklarla ve gece 60 dakika aralıklarla ölçümler yapmış olup, sistolik tansiyon ortalaması 130 mmHg ve/veya diyastolik tansiyon ortalaması 80 mmHg üzerinde olan hastalar araştırmaya dahil edildi. Gece tansiyon ortalaması, gündüz tansiyon ortalamasına göre %10 ve daha fazla düşen hastalar dipper, %10'dan az düşen hastalar ise non-dipper tansiyonu mevcut olarak kabul edildi. 18 yaş ile 40 yaş arasında olan hastalar genç hipertansiyon hastası olarak kabul edilmiş olup hastalarımızın 83'ü genç grupta, 254'ü 40 yaş üstü grupta yer aldı. Kan basıncı değişkenliği, 24 saatlik ABPM kayıtlarından elde edilen verilerin standard sapması olarak her iki grup için ayrı ayrı hesaplandı.

Etik Kurul

Çalışma için Afyonkarahisar Sağlık Bilimleri Üniversitesi Tıbbi Etik Kurulundan 04/03/2022 tarih ve 2022/3 sayılı etik kurul onayı alınmıştır.

İstatistiksel Analiz

İstatistiksel analizler için Statistical Package for the Social Sciences (SPSS) versiyon 15.0 kullanıldı. Sürekli değişkenlerin karşılaştırılmasında Student-t testi, kategorik değişkenlerin karşılaştırılmasında Ki-kare testi kullanıldı. Sürekli değişkenler ortalama±standart sapma ile katego-

rik değişkenler yüzde olarak ifade edildi. P<0.05 değeri anlamlılık düzeyi olarak belirlendi.

BULGULAR

Çalışmaya toplam 337 hipertansiyon hastası alınmakla beraber bu hastalardan 83 tanesi, 40 yaş altı 18 yaş üstü, 254 tanesi ise 40 yaş üstü idi. İki grup arasında 24 saatlik sistolik kan basıncı ortalamaları arasında istatistiksel olarak anlamlı fark bulunmazken, diyastolik kan basıncı ortalamaları, genç hipertansiyon grubunda 40 yaş üstü hipertansiyon grubuna göre anlamlı olarak yüksek bulunmuştur (sırasıyla p=0.96 ve p<0.001). Sistolik kan basıncının gündüz ortalama değerleri bakımından iki grup karşılaştırıldığında, iki grup arasında anlamlı fark bulunmamakla beraber diyastolik kan basıncının gündüz ortalama değerleri genç hipertansiyon grubunda 40 yaş üstü hipertansiyon grubuna göre istatistiksel olarak yüksek bulunmuştur (sırasıyla p=0.35 ve p<0.001). Sistolik ve diyastolik kan basıncının gece ortalama değerleri bakımından iki grup karşılaştırıldığında, hem sistolik hem de diyastolik gece ortalama değerleri, genç hipertansiyon grubunda 40 yaş üstü hipertansiyon grubuna göre istatistiksel olarak yüksek bulunmuştur (sırasıyla p=0.32 ve p=0.007). Non-dipper hipertansiyon olma durumuna göre her iki grup karşılaştırıldığında genç hipertansiyon grubunda non-dipper hipertansiyon olma durumu % 59 olarak bulunurken, 40 yaş üstü hipertansiyon grubunda bu oran % 74 olarak bulunmuş olup 40 yaş üstü hipertansiyon grubunda non-dipper olma durumu istatistiksel olarak yüksek bulunmuştur (p=0.009). Arteriyel tansiyon verileri **Tablo 1**'de gösterilmiştir.

Tablo1: Genç hipertansiyon hastaları ile 40 yaş üstü hipertansiyon hastalarının kan basıncı ortalamalarının ve non-dipper olma durumlarının karşılaştırılması.

Parametre	Genç Hipertansiyon	40 yaş üstü Hipertansiyon	P value
Hasta sayısı (n)	83	254	
24 saatlik sistolik kan basıncı ortalaması (mmHg)	151.3±10.5	151.4±10.6	0.96
24 saatlik diyastolik kan basıncı ortalaması (mmHg)	89.6±12.4	84.6±9.4	<0.001
Sistolik kan basıncının gündüz ortalama değerleri (mmHg)	154.7±11.1	153.5±11.1	0.35
Diyastolik kan basıncının gündüz ortalama değerleri (mmHg)	93.5±9.9	86.1±9.8	<0.001
Sistolik kan basıncının gece ortalama değerleri (mmHg)	142.6±13.3	146.2±13.5	0.032
Diyastolik kan basıncının gece ortalama değerleri (mmHg)	84.2±9.6	80.8±10.4	0.007
Nondipper hipertansiyon olma durumu (n)	49(%59)	188(%74)	0.009

Kan basıncı değişkenliği açısından iki grup karşılaştırıldığında 24 saatlik sistolik kan basıncı değişkenliği açısından iki grup açısından anlamlı fark bulunmazken 24 saatlik diyastolik kan basıncı değişkenliği açısından, genç hipertansiyon grubunda 40 yaş üstü hipertansiyon grubuna göre anlamlı olarak yüksek bulunmuştur (sırasıyla p=0.94 ve p=0.03). Gündüz diyastolik kan basıncı değişkenliği açısından iki grup arasında anlamlı fark bulunmazken gündüz sistolik kan basıncı değişkenliği, 40 yaş üstü hipertansiyon grubunda genç hipertansiyon grubuna göre istatistiksel olarak yüksek bulunmuştur (sırasıyla p=0.8 ve 0.006). Hem sistolik hem diyastolik gece kan basıncı değişkenliği açısından iki grup arasında anlamlı fark bulunmamıştır (sırasıyla p=0.47 ve p=0.25). Kan basıncı değişkenliği **Tablo 2**'de gösterilmiştir.

Tablo 2: Genç hipertansiyon hastaları ile 40 yaş üstü hipertansiyon hastalarının kan basıncı değişkenliğinin karşılaştırılması.

Parametre	Genç Hipertansiyon	40 yaş üstü Hipertansiyon	P value
24 saatlik sistolik kan basıncı değişkenliği (mmHg)	16.4±3.8	16.8±3.8	0.94
24 saatlik diyastolik kan basıncı değişkenliği (mmHg)	12.6±3.5	11.8±3.4	0.03
Gündüz sistolik kan basıncı değişkenliği (mmHg)	14.8±3.9	16.1±4.1	0.006
Gündüz diyastolik kan basıncı değişkenliği (mmHg)	11.3±4.0	11.1±3.7	0.8
Gece sistolik kan basıncı değişkenliği (mmHg)	14.7±5.2	14.8±4.9	0.47
Gece diyastolik kan basıncı değişkenliği (mmHg)	11.3±4.1	10.9±4.1	0.25

TARTIŞMA

Hipertansiyon çoğunlukla asemptomatik seyreden ve komorbid hastalıklara neden olan ciddi bir hastalıktır (6, 13). Literatürde, genç hipertansiyon hastalarının sistolik ve diyastolik tansiyonlarını, gündüz ile gece tansiyon takiplerini ve gün içi kan basınç değişimlerini inceleyen ve bu değerleri 40 yaş üstü hipertansiyon hastalarıyla karşılaştıran çalışmalar sınırlıdır. Hipertansiyon hastalarının tanısında ve gün içinde tansiyon ölçümlerinin değerlendirilmesinde altın standart yöntem 24 saatlik ABPM dir. Sistolik tansiyonu normal fakat diyastolik tansiyonu yüksek olan izole diyastolik hipertansiyonun hastalarında endokrinolojik sebepler daha sık görülmektedir (5). Kaplan ve ark.'larının 349 çocuk hasta ile yaptıkları çalışmada izole diyastolik hipertansiyon hastalığını endokrinolojik kaynak ile ilişkili

bulmuşlardır. Ayrıca sekonder hipertansiyonu olan çocuk hastaların diyastolik kan basınçlarını primer hipertansiyon hastalarına göre daha yüksek bulmuşlardır (4). Biz bu çalışmada, genç hasta grubunun 24 saatlik diyastolik tansiyon ortalamasını, 40 yaş üstü hasta grubuna göre yüksek bulmakla beraber, genç hastalarda 40 yaş üstü hastalara göre diyastolik tansiyonlarının yüksek olmasının genç hastalardaki hipertansiyonun fizyopatolojisinde sekonder hipertansiyon nedenlerinin etkili olabileceğini ve genç hipertansiyon hastalarında, bu nedenlerin araştırılması gerektiğini düşündük. Gece tansiyon değerleri gündüz değerlerine göre %10 ve üzerinde düşme olması dipper, %10'un altında düşme olması nondipper tansiyon fenomeni olarak tanımlanmakla beraber dipper tansiyon iyi prognoz ile ilişkiliyken, nondipper hipertansiyon artmış uç organ hasarı riski nedeniyle daha kötü prognoz ile ilişkili bulunmuştur (7, 10, 11). Konu ile ilgili yapılan çalışmalarının çoğunda nondipper tansiyon olma oranı 40 yaş üstü hastalarda yüksek bulunmuş olup Ordu ve arkadaşlarının 88 hastada yaptığı çalışmada nondipper tansiyon hastalarının çoğu 40 yaş üstü hastalardan oluşmaktadır (14). Musialik ve ark.'larının genç ve 40 yaş üstü hipertansiyon hastalarında ABPM ile sirkadiyen tansiyon değişimini inceledikleri çalışmada genç hasta grubunda nondipper tansiyon olma oranı 40 yaş üstü hasta grubuna göre yüksek çıkmıştır (15).

Biz çalışmamızda 40 yaş üstü hastaların nondipper tansiyon oranını genç hastalara göre yüksek bulduk. Fakat genç hastalarının yarısından fazlası nondipper (% 59) tansiyona sahipti. Nondipper tansiyonun daha fazla uç organ hasarıyla ilişkisi olması, genç hastalarının daha uzun süre bu hasara maruz kalabileceğini göstermekte olup bu yüzden, genç hastalarda nondipper tansiyon tanısının ABPM ile daha sık bir şekilde taranması gerektiğini düşünmekteyiz. Kan basıncı değişkenliği son yıllarda hipertansiyon alanında araştırmacıların ilgisini çekmektedir.

Kan basıncı, kalp atımından atımına hızlı dalgalanmalar gösterir. Kan basıncı değişkenliğinin artmasının, artmış sempatik sinir sistemi aktivitesi ile anormal nörohümoral regülasyon ve bozulmuş arteriyel barorefleks ile ilişkili olduğu düşü-

nülmektedir (16). Temel olarak 24 saatlik ABPM kayıtlarından elde edilen verilerin standard sapması olarak hesaplanan kan basıncı değişkenliği ile ilgili olarak, literatürde çalışmalar sınırlıdır.

Yapılan bu çalışmalarda uç organ hasarının bir göstergesi olan artmış kan basıncı değişkenliğin sol ventrikül kütlesi ve kütle indeksi ile ilişkili olduğu saptanmıştır (17). Ayrıca koroner arter hastalığının patofizyolojisinde rol oynayan, arter sertliğinin kan basıncı değişkenliği ile ilişkili olduğunu gösteren çalışmalar mevcut olup kan basıncı değişkenliğinin, uç organ hasarını artırması nedeniyle koroner arter hastalığı ve kalp yetersizliği riskini artırdığı düşünülmektedir (18).

Çalışmamızda, genç hipertansif hastalarda özellikle diyastolik tansiyon ölçümlerinin değişkenliğini 40 yaş üstü hipertansiyon hastalarına göre anlamlı düzeyde yüksek saptadık. Genç hipertansif hastalarda, artmış vücut kütle indeksi, sedanter yaşam, tuz tüketiminde fazlalık, yağlı ve kolesterolden zengin diyet, stres, sigara içimi ve alkol tüketimi gibi hipertansiyonun değiştirilebilir risk faktörlerinin nondipper hipertansiyona ve artmış kan basıncı değişkenliğine neden olarak uç organ hasarı riskinde artışa neden olabilir. Bu faktörlerinin önüne geçilmesi, genç hastalarda hipertansiyon ve hipertansiyona bağlı uç organ hasarlarından korunmada önemlidir. Bu veriler ışığında, genç hipertansif hastaları uç organ hasarı açısından değerlendirirken, kan basıncı değişkenliğinin de göz önünde bulundurulması faydalı olacaktır.

Sonuç olarak, genç hipertansiyon hastaları değerlendirilirken, 24 saatlik ABPM ile ortalama kan basıncı, non-dipper tansiyon olma durumu ve kan basıncı değişkenliğinin değerlendirilmesi uç organ hasarı gelişimi yönünden riskli hasta grubunu belirlemede yardımcı olabilir.

Çalışmamızın kısıtlılıkları, retrospektif bir çalışma olması ve hastaların demografik özelliklerinin olmamasıdır.

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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

İDAME HEMODİYALİZ HASTALARINDA ORTALAMA TROMBOSİT HACMİ'NİN MORTALİTE ÜZERİNE ETKİSİ

EFFECT OF MEAN PLATELET VOLUME ON MORTALITY IN MAINTENANCE HEMODIALYSIS PATIENTS

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ÖZET

AMAÇ: Hemodiyaliz son dönem böbrek hastalığı olan hastalarda en sık tercih edilen renal replasman tedavisi tipidir. İdame hemodiyaliz tedavisi alan hastalarda mortaliteyi etkileyen parametrelerin bilinmesi bu hasta grubunda sağkalımı artırabilir. Ortalama trombosit hacmi (MPV) tam kan sayımı parametrelerinden biridir. MPV yüksekliğinin birçok hastalıkta mortaliteyi artırabileceği gösterilmiştir. Bu çalışmamızda idame hemodiyaliz hastalarında MPV'nin mortalite üzerine etkisini araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Ocak 2010 ve Ocak 2020 tarihleri arasında hastanemizde idame diyaliz tedavisine başlanan tüm hastaların dosyaları retrospektif olarak tarandı. Hastaların demografik verileri ve laboratuar parametrelerine hasta dosyalarından ulaşıldı. MPV değeri için idame diyaliz tedavisi başlanan ilk 3 ay rutin bakılan tam kan sayımındaki MPV değerlerinin ortalaması alındı. Takip süresince ölen ve yaşayan hastalar MPV değerleri açısından karşılaştırıldı.

BULGULAR: Çalışma 129 hasta ile yapıldı. Hastaların %24.8'i (n= 32) takipler süresince ölmüştü. Ölen hastaların MPV'si yaşayan hastalara göre anlamlı şekilde daha yüksekti (11.14±1'e karşı 10.12±0.8, p<0.001). Mortaliteyi öngörmek açısından en iyi MPV değeri 10.73 olarak bulundu (%75 sensitivite ve %81.4 spesifisite ile).

SONUÇ: Yüksek MPV idame hemodiyaliz hastalarında mortalite için bağımsız bir risk faktörüdür. MPV'si yüksek olan hemodiyaliz hastalarında değiştirilebilir risk faktörlerinin daha sıkı yönetilmesi sağkalımlarını artırabilir.

ANAHTAR KELİMELER: Hemodiyaliz, Mortalite, Ortalama trombosit hacmi.

ABSTRACT

OBJECTIVE: Hemodialysis is the most preferred type of renal replacement therapy in patients with end-stage renal disease. Knowing the parameters affecting mortality in patients receiving maintenance hemodialysis treatment may increase the survival rate in this patient group. Mean platelet volume (MPV) is one of the parameters of the complete blood count. It has been shown that high MPV can increase the mortality rate in many diseases. In this study, we aimed to investigate the effect of MPV on the mortality rate in maintenance hemodialysis patients.

MATERIAL AND METHODS: The files of all patients who were started on maintenance dialysis treatment in our hospital between January 2010 and January 2020 were reviewed retrospectively. Demographic data and laboratory parameters of the patients were obtained from the patient files. For the MPV value, the mean of the MPV values in the routine complete blood count for the first 3 months after maintenance dialysis treatment was started. Patients who died and survived during the follow-up were compared in terms of MPV values.

RESULTS: The study was conducted with 129 patients. 24.8% (n= 32) of the patients died during follow-up. MPV of deceased patients was significantly higher than survived patients (11.14±1 vs. 10.12±0.8, p<0.001). The best MPV value for predicting mortality was found to be 10.73 (with 75% sensitivity and 81.4% specificity).

CONCLUSIONS: High MPV is an independent risk factor for mortality in maintenance hemodialysis patients. Tighter management of modifiable risk factors in hemodialysis patients with high MPV may improve their survival.

KEYWORDS: Hemodialysis, Mortality, Mean platelet volume.

INTRODUCTION

Chronic kidney disease (CKD) is defined as the persistence of kidney dysfunction for more than three months. End-stage renal disease is present when the estimated glomerular filtration rate is less than 15 ml/min/1.73 m^2, and such a patient has renal replacement therapy options such as kidney transplantation, peritoneal dialysis, and hemodialysis (1). According to the Turkish Society of Nephrology Registry data, as of 2020, hemodialysis has been the most frequently used treatment modality among patients receiving renal replacement therapy, with 72.6% (2). There are many factors affecting mortality in patients under the maintenance dialysis treatment. While some factors related to dialysis may be risk factors for mortality, some demographic and laboratory characteristics related to the patient may also be risk factors for mortality (3, 4). In the study of Erdoğmuş et al., diabetes mellitus, cerebrovascular disease and high CRP were found to be independent risk factors for mortality (5).

Mean platelet volume (MPV) is defined as the mean volume of platelets as femtoliters (fL) in the circulating blood. In recent years, it has been shown that MPV not only shows the mean platelet volume, but also can be a risk factor for many clinical conditions (6 - 9). Henning et al. showed that hemodialysis patients having higher MPV had more frequent coronary heart disease than patients having lower MPV (10). Considering that cardiovascular causes are the leading cause of mortality in hemodialysis patients, we designed our study considering that MPV may also play a role in this mortality.

In this study we aimed to investigate the effect of MPV on mortality in patients on maintenance hemodialysis.

MATERIAL AND METHODS

Patients and MPV

The files of all patients (n= 154) who started to receive maintenance hemodialysis therapy in our hospital between January 2010 and January 2020 were reviewed retrospectively. Patients older than 18 years of age, receiving hemodialysis treatment for more than 3 months, without autoimmune disease, without hema-

tological or oncological disease were included in the study. Patients younger than 18 years of age, those with autoimmune disease, those receiving hemodialysis treatment for less than 3 months, and those with oncological or hematological malignancies were excluded from the study. Twenty five patients (thirteen because of the diagnosis of hematologic or oncologic malignancy, four due to hemodialysis treatment for less than 3 months, two because of autoimmune disease and six because of insufficient file data) were excluded from the study.

Ethical Committee

Ethics Committee approval was received at the Ethics Committee of Afyonkarahisar Health Sciences University; meeting dated 01.07.2022 (code of ethics committee: 2011-KAEK-2, meeting number: 2022/8, decision number: 359).

Statistical Analysis

Categorical variables were presented as frequencies and percentages. Categorical variables were compared with chi-square test between groups. Continuous variables were checked for the normal distribution with Shapiro Wilk test. Normally distributed continuous variables were presented as mean±standart deviation. Non-normally distributed continuous variables were presented as median and interquartile range (IQR25-75). Independent samples t test was used to compare the means of normally distributed continuous variables between groups. Mann Whitney U test was used to compare the median of non-normally distributed continuous variables between groups. Univariate and multivariate logistic regression analysis carried out to determine risk factors associated with mortality. The ROC curve was used to determine the threshold values that could be used to predict mortality. Youden index was used to select the best predictive value of MPV. Then patients were divided into two groups according to MPV threshold value. Kaplan Meier method was used for survival analysis. MPV groups were compared for survival with logrank test. Statistical analyzes were done using SPSS 26.0 (IBM Corp. 2019 IBM SPSS Statistics for Windows, version 26.0. Armonk, NY: IBM Corp) package program. All the p values presented were bidirectional and the values with $p<0.05$ were expressed as statistically significant.

RESULTS

The study was conducted with 129 patients on maintenance hemodialysis. While 75.2% (n= 97) of the patients were alive during the follow-up, 24.8% (n= 32) died. Of these 32 patients 43.8% (n= 14) died due to cardiovascular causes, 18.8% (n= 6) died due to cerebrovascular causes, 15.6% (n= 5) died due to sepsis, 12.5% (n= 4) died due to gastrointestinal bleeding and 9.4% (n= 3) died due to unknown causes. **Table 1** shows the comparison of the groups in terms of demographical parameters and comorbidities.

Table 1: Comparisons of groups in terms of demographical and comorbidities

Parameters	All patients (n=129)	Alive (n= 97)	Death (n= 32)	p
Age (years)	59.39±5.7	58.69±4.7	61.5±7.6	**0.015**
Female gender (%-n)	38.8-50	37.1-36	43.8-14	0.535
CKD etiology (%-n)				
DN	30.2-39	29.9-29	31.3-10	
HN	21.7-28	22.7-22	18.8-6	
CGN	17.1-22	16.5-16	18.8-6	0.814
PKD	4.7-6	5.2-5	3.1-1	
Obstructive	10.1-13	10.3-10	9.4-3	
Unknown	16.3-21	19.6-19	6.3-2	
Vascular access (%-n)				
Catheter	32.6-42	18.6-18	75-24	**<0.001**
AVF	67.4-87	81.4-79	25-8	
Diabetes mellitus (%-n)	30.2-39	29.9-29	31.3-10	0.876
Hypertension (%-n)	35.7-46	22.7-22	75-24	**<0.001**
Hyperlipidemia (%-n)	27.1-35	18.6-18	18.8-6	0.489
Smoking (%-n)	27.9-36	19.6-19	53.1-17	**0.001**
CAD (%-n)	21.7-28	16.5-16	18.8-6	0.674
CVD (%-n)	13.2-17	11.3-11	18.8-6	0.365
CHF (%-n)	13.2-17	8.2-8	9.4-3	0.759

CKD= chronic kidney disease, DN= diabetic nephropathy, HN= hypertensive nephropathy, CGN= chronic glomerulonephritis, PKD= polycystic kidney disease, AVF= arteriovenous fistula, CAD= coronary artery disease, CVD= cerebrovascular disease, CHF= congestive heart failure

Table 2 shows the comparison of the groups in terms of laboratory and clinical parameters. Multivariate regression analysis showed that vascular access as catheter, hypertension, smoking and higher MPV are independent risk factors for mortality in patients on maintenance hemodialysis (p= 0.001, p= 0.002, p= 0.014 and p=0.006, respectively). **Table 3** shows univariate and multivariate regression analysis for mortality. An MPV value of 10.73 fL was found to have the best predictive value with 75% sensitivity and 81.4% specificity in predicting mortality (AUC= 0.791, 95% CI= 0.693-0.889, p<0.001) **(Figure 1)**. Patients with an MPV≥10.73 fL had an overall survival of 42.9% [median survival was 56 months (95 %CI= 36.2-75.8 months)], while this rate was 90.8% [median survival was 73 months (95% CI= 48.9-97.1 months)] for patients with an MPV<10.73 fL. Patients with an MPV<10.73 fL had a statistically significantly higher survival (p= 0.008) **(Figure 2)**.

**Table 2:** Comparison of the groups in terms of laboratory and clinical parameters

Parameters	All patients (n=129)	Alive (n= 97)	Death (n= 32)	p
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Table 3: Univariate and multivariate regression analysis for mortality

Parameters	Univariate		Multivariare	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.086(1.014-1.165)	**0.018**	1.086(0.983-1.201)	0.104
Dialysis with catheter	13.167(5.093-34.041)	**<0.001**	15.256(4.125-24.511)	**0.001**
Hypertension	10.227(4.033-25.937)	**<0.001**	7.491(2.086-26.893)	**0.002**
Smoking	4.653(1.976-10.956)	**<0.001**	4.245(1.338-13.469)	**0.014**
MPV	3.731(2.118-6.578)	**<0.001**	4.173(2.673-7.749)	**0.006**

MPV= mean platelet volume
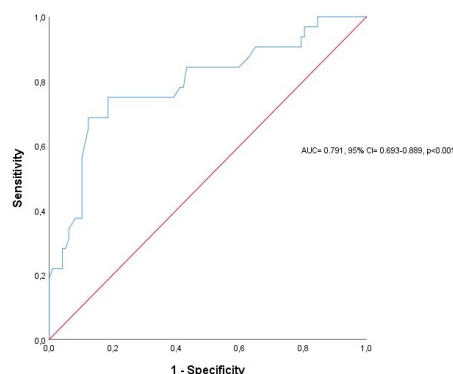
Figure 1: ROC curve as a mortality predictor for MPV
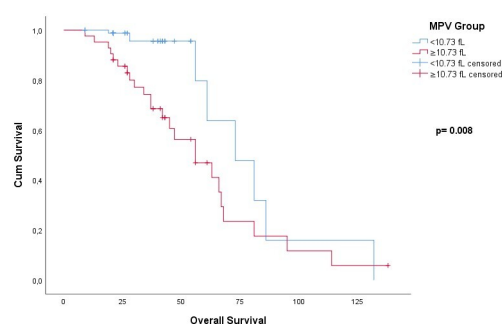
Figure 2: Comparison of survival between MPV groups

DISCUSSION

The present study revealed that higher MPV is closely associated with higher mortality rates

in patients on maintenance hemodialysis. In our literature search we did not find any study investigating MPV and mortality in patients on hemodialysis. Previous studies have found that higher MPV is associated with higher mortality in various clinical conditions. In a systematic review and meta-analysis Chu et al found that elevated MPV is associated with acute myocardial infarction, mortality after myocardial infarction and restenosis after coronary angioplasty (11). In a review published by Pafili et al., they emphasized that measuring MPV may prove useful in cardiovascular disease assessment in patients with established coronary artery disease (12). MPV has been associated with mortality not only in cardiovascular but also in many different diseases. Zampieri et al. investigated MPV changes and mortality in critically ill patients in a prospective study and they found that an increase in MPV was associated with higher mortality (13). Chen et al. found that higher MPV is an independent risk factor for mortality in patients with severe pneumonia (14). There have also been some publications on MPV in hemodialysis patients. Henning et al. investigated whether MPV was associated with coronary heart disease in hemodialysis patients. In this study they included 518 patients on maintenance hemodialysis and found that MPV may be associated with coronary heart disease in hemodialysis patients (10). In a 5-year cohort study of 149,118 incident hemodialysis patients, hemodialysis patients with a higher MPV were found to be at higher mortality risk (15). In our study, we found that patients with a higher MPV at the start of maintenance hemodialysis had higher mortality rates. We also found that MPV is an independent risk factor for all-cause mortality in patients on maintenance hemodialysis.

The best type of vascular access for maintenance hemodialysis is an arteriovenous fistula. Astor et al. showed that patients with catheter had higher complication and mortality rates than patients with arteriovenous fistula (16). In a study conducted using the DOPPS (Dialysis Outcomes and Practive Patterns Study) data system, 28,196 hemodialysis patients were examined between 1996 and 2004 (13). After correcting for demographics, comorbid conditions, and laboratory values, mortality was found to be 32% higher in patients with catheters compared to arteriovenous fistula (17). Our study revealed that having hemodialysis via a catheter is an independent risk factor for mortality in patients on maintenance hemodialysis. This finding is similar to the data in the literature.

Hypertension is a well-known cardiovascular risk factor for the general population (18). However, this close relationship has not been seen in patients on maintenance hemodialysis. Foley et al. showed that each 10 mmHg lower predialysis mean arterial blood pressure was associated with a 36% higher risk of death (19). Our study groups were similar in terms of both systolic and diastolic blood pressure values. We think that the patient's diagnosis of hypertension may be a risk factor for mortality as a result of complications that may have developed due to hypertension. We found that the history of hypertension is an independent risk factor for mortality in patients on maintenance hemodialysis.

Smoking is associated with an increased risk of mortality for patients of all age groups (20-22). Li et al. investigated the effects of smoking on mortality in 22,230 hemodialysis patients in the study they conducted (23). In this study, increased mortality risk was found in all smokers, although it was highest in hemodialysis patients who were heavy smokers compared to non-smoker hemodialysis patients. In another study, Causland et al. investigated the association of smoking status and all-cause, cardiovascular, and infection-related morbidity and mortality in patients on maintenance hemodialysis. They included 1842 patients and found that smoking was associated with higher all-cause mortality, higher cardiovascular mortality and higher infection-related mortality (24). In our study, we found that smoking negatively affects survival and is an independent risk factor for all-cause mortality in patients on maintenance hemodialysis.

In their cross-sectional study of 82 hemodialysis patients, Yayar et al. found that MPV was associated with carotid intima-media thickness (25). Based on this result, they emphasized that MPV may play a role in atherosclerotic processes. Our study also shows that high MPV is associated with an increased risk of mortality in hemo-

dialysis patients. We think that atherosclerotic processes associated with MPV play a role in this increase in mortality.

Our study has some limitations. First, it is a single-center study and second, it has a small number of patients. Our study is important because it is the first study investigating the effect of MPV on mortality in patients on maintenance hemodialysis.

In conclusion, in our study, MPV, smoking, the presence of hypertension, and catheter were found to be independent risk factors for all-cause mortality in maintenance hemodialysis patients. In order to reduce the risk of mortality in patients with high MPV, it would be logical to quit smoking and prefer more arteriovenous fistulas as vascular access. Prospective, larger studies may reveal more clearly the effects of MPV on mortality in hemodialysis patients.

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OLGU YAZISI / CASE REPORTS

CORYNEBACTERİUM TUBERCULOSTEARİCUM'A BAĞLI GELİŞEN SPONDİLODİSKİTİS OLGUSU

A CASE OF SPONDYLODISCITIS DUE TO CORYNEBACTERIUM TUBERCULOSTEARICUM

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ÖZET

Corynebacterium türleri sıklıkla klinik örneklerden izole edilmekle birlikte, normal cilt florasında yer almaları nedeniyle enfeksiyon ve kolonizasyon ayrımı yapmak zor olabilmektedir. Literatür değerlendirildiğinde *C tuberculostearicum* enfeksiyonları nadirdir. Altmış bir yaşındaki erkek hasta kliniğimize ateş, bel ve bacaklarda ağrı ve yürümede güçlük şikayeti ile başvurdu. Hastanın kliniği ve radyolojik bulguları spondilodiskitisle uyumluydu. Hastanın operasyonda alınan kültüründe *C. tuberculostearicum* üredi. Günümüzde Corynebacterium türleri hastanede gelişen enfeksiyonlarda ve/veya immün sistemi baskılanmış olanlarda ortaya çıkan enfeksiyonlarda etken olabilmektedir veya etken olarak karşımıza çıkabilmektedir. Olgumuzda olduğu gibi uzamış hastane yatışı olan ve altta yatan ciddi komorbiditeleri olan hastalarda çoklu ilaç direnci olan suşlar akla gelmeli ve *C. tuberculostearicum*'un enfeksiyon etkeni olabileceği göz önünde bulundurulmalıdır.

ANAHTAR KELİMELER: *Corynebacterium tuberculostearicum*, Enfeksiyon, Spondilodiskitis.

ABSTRACT

Although Corynebacterium species are often isolated from clinical specimens, it can be difficult to distinguish between infection and colonization due to their presence in normal skin flora. When the literature is evaluated, *C tuberculostearicum* infections are rare. A 61-year-old male patient was admitted to our clinic with fever, pain in the waist and legs, and difficulty in walking. The patient's clinical and radiological findings were consistent with spondylodiscitis. *C. tuberculostearicum* grew in the culture of the patient taken during operation. Today, Corynebacterium species can be a causative agent or may appear as a causative agent in infections that develop in hospitals and / or infections that occur in those with a suppressed immune system. Strains with multiple drug resistance should be considered in patients with prolonged hospitalization and severe underlying comorbidities as in our case, and it should be considered that *C. tuberculostearicum* may be an infectious agent.

**KEYWORDS:** *Corynebacterium tuberculostearicum*, Infection, Spondylodiscitis.

GİRİŞ

Corynebacterium izolatları aerop, Gram-olumlu basillerdir. *Corynebacterium diphtheriae* ve *Corynebacterium jeikeium*, iyi bilinen patojenlerdir, ancak *Corynebacterium striatum*, *Corynebacterium xerosis*, *Corynebacterium minutissimum, Corynebacterium urealyticum* ve *Corynebacterium amikolatum* gibi diğer türler de yara enfeksiyonları ve üriner enfeksiyonlara neden olmaktadırlar. Corynebacterium türleri insan cildini ve mukozasını kolonize eder. Sıklıkla klinik örneklerden izole edilmekle birlikte, normal cilt florasında yer almaları nedeniyle enfeksiyon ve kolonizasyon ayrımı yapmak zor olabilmektedir (1, 2).

Non-diphteriae corynebacterium türleri son yıllarda artan şekilde hem immünkompetan hem de immünkompremize hastalarda enfeksiyonlara neden olmaktadır (3). Corynebacterium tuberculostearicum lipofilik bir corynebacterium olup 2004 yılında bugün için geçerli olan şekliyle sınıflandırılmıştır. Literatür değerlendirildiğinde *C tuberculostearicum* enfeksiyonları nadirdir (1, 4 - 7). Biz de bu nedenle C. tuberculostearicum'a bağlı gelişen spondilodiskitis olgusunu sunmayı amaçladık.

OLGU

Altmış bir yaşındaki erkek hasta kliniğimize ateş, bel ve bacaklarda ağrı ve yürümede güçlük şikayeti ile başvurdu. Hastanın özgeçmişinde diabetes mellitus, kronik obstrüktif akciğer hastalığı, hipertansiyon ve kronik böbrek hastalığı tanıları mevcuttu. Hastanın öyküsünde yaklaşık üç hafta süreyle kronik böbrek yetmezliği tanısıyla yoğun bakımda yattığı ve yattığı süre içinde piperasilin tazobaktam tedavisi aldığı öğrenildi. Hastanın son bir haftadır ateş şikayetine yürüyememe ve baş dönmesi şikayeti eklenmişti. Fizik muayenede ateşi 39 °C idi, nörolojik muayenede ense sertliği ve meninks irritasyon bulguları yoktu. Bel hareketleri kısıtlı, sağ alt ekstremitede parestezi ve derin tendon reflekslerinde hipoaktivite tespit edildi. Laboratuvarda tam kan sayımında lökosit sayısı 13490 hücre/mm³, periferik yaymada sola kayma mev-

cut, sedimentasyon 69 mm/s, CRP: 186 mg/dL, Brusella ve tüberküloz için testler olumsuzdu, kan, idrar ve boğaz kültüründe üreme olmadı. Hastaya ampirik olarak meropenem başlandı. Çalışılan kontrastlı torakolomber manyetik rezonans görüntülemede (MRG) L4-L5 vertebra korpuslarında ve disk mesafesinde T2 ağırlıklı görüntülemede hiperintens ödemle uyumlu değişiklikler mevcuttu. L4-L5 intervertebral disk mesafesine bakan yüzlerde düzensizlik izlendi. Kontrastlı serilerde bu düzeyde vertebra korpuslarında ve diskte kontrastlanma ve T12-L5 düzeyinde durada kalınlaşma, kontrastlanma yanısıra L1 vertebra anteriorunda çepersel boyanan epidural abse formasyonu mevcuttu **(Şekil 1)**.
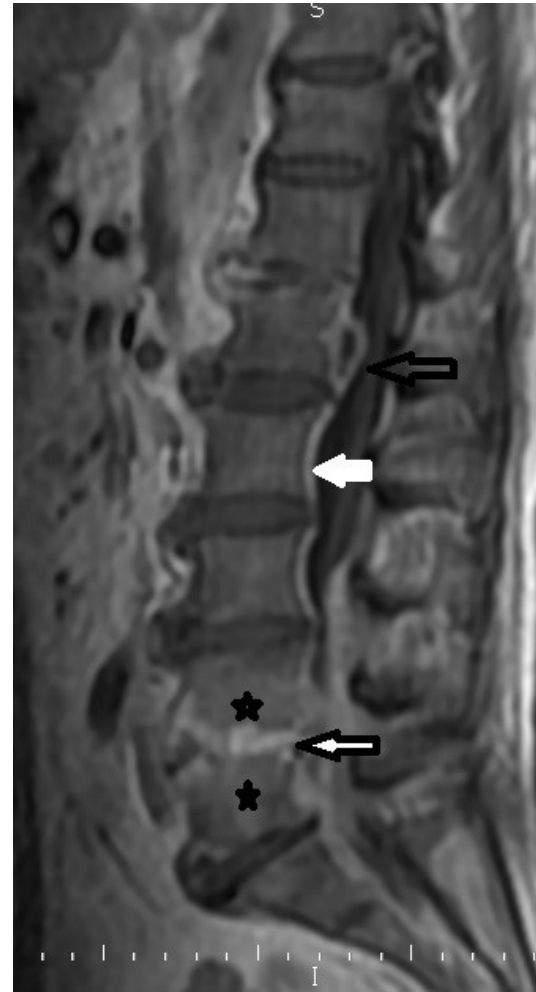
Şekil 1: Kontrastlı T1 ağırlıklı sagittal imajda L4-L5 vertebra korpuslarında (Şekil 1, yıldızlar)ve diskte kontrastlanma izlenmektedir (Şekil 1, içi beyaz, dışı siyah ok). Ayrıca L1-L5 düzeyinde durada kalınlaşma ve kontrastlanma (Şekil 1, kısa beyaz ok), L1 vertebra anteriorunda çepersel boyananan epidural abse formasyonu mevcuttur (Şekil 1, uzun siyah ok)). Bulgular spondilodiskitisle uyumlu olarak değerlendirildi.

Hastanın kliniği ve radyolojik bulguları spondilodiskitisle uyumlu olarak değerlendirildi ve hastanın tedavisine teikoplanin 2x400 mg eklendi, ancak ilk doz sonrası anafilaksi gelişen hastada teikoplanin kesilerek linezolide 2x600 mg tb başlandı. Hasta beyin cerrahisi tarafından opere edildi, peroperatif olarak posterior T12- L5 laminektomi yapılan hastanın bu mesafeleri transpediküler multiaksiyel vidalar ile stabilize edildi. Aynı seansta L4-5 bilateral mikrodiskektomi yapılarak mesafeden kültür ve biyopsi için örnek alındı ve bilateral 2 adet PLIFF kafes ile disk mesafesine füzyon yapıldı. T12- L5 arası posterior dura üzerinde yapışık sert- sarımtırak doku eksize edilerek dura dekomprese edildi. Biopsi materyalin histopatolojik incelemesinde diskitis saptandı.

Hastamızda tanı klinik ve radyolojik olarak konmuş olup, operasyon sırasındaki görünüm ve biopsi materyalinin histopatalojik incelemesi ile de desteklenmiştir. Hastanın operasyonda alınan kültüründe *C. tuberculostearicum* üredi. Gram boyamada coryneform basilller görüldü. Bakteri otomatize sistem (VITEK-2) ile tanımlandı.

Antibiyogramında linezolid ve vankomisin için zon çapları sırasıyla 28 ve 27 mm idi. Siprofloksasin, moksifloksasin, klindamisin, gentamisin, tetrasiklin, penisilin G ve rifampisin için zon çapları 6 mm idi. Hastanın antibiyogramında *C. tuberculostearicum*'un yalnızca vankomisin ve linezolide duyarlı olması nedeniyle mevcut linezolid tedavisine devam edilerek iki aya tamamlandı.

Hasta beyin cerrahisi ve enfeksiyon hastalıkları tarafından ortak olarak takip edilmiş, takiplerinde yürüyememe şikayetinde düzelme ve sağ alt extremitedeki parestezi ve derin tendon reflekslerindeki hipoaktivitenin kaybolduğu gözlenmiştir, hastanın laboratuvar değerlerinde sedimentasyon ve CRP değerlerinde gerileme, radyolojik olarak tedavi sonu 6.ayda çekilen kontrol MRG'da L1-5 vertebralarda diskitisle uyumlu tablonun ve L1 vertebra anteriorundaki absenin kaybolduğu tespit edilmiştir **(Şekil 2)**.
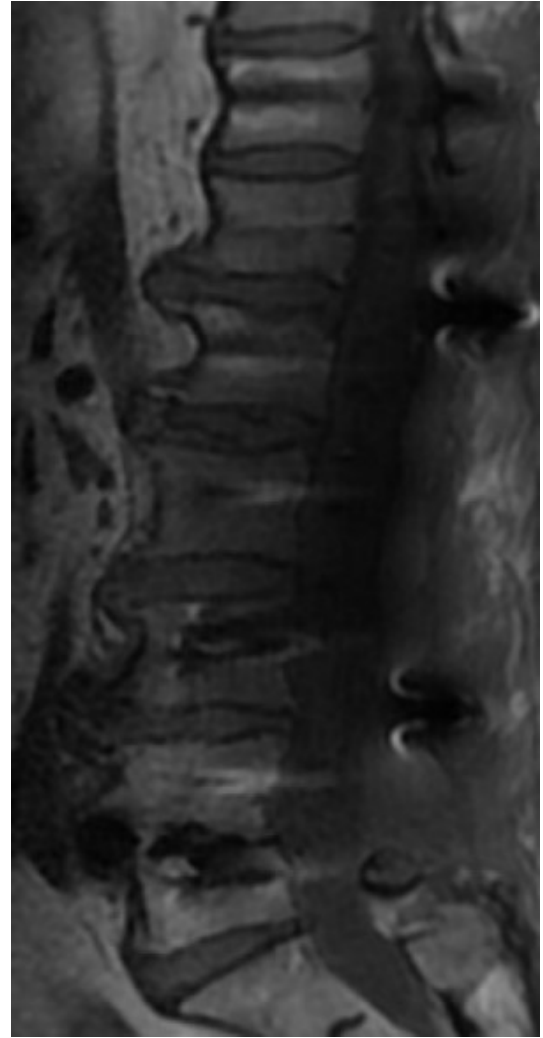
Şekil 2: Kontrol kontrastlı T1 ağırlıklı sagittal imajda T11-L5 düzeylerinde transpedinküler yerleştirilmiş fiksasyon materyali izlendi. Önceki tetkikinde tanımlanan patolojik kontrastlanmalar ve abse formasyonu izlenmemekteydi.

TARTIŞMA

C. tuberculostearicum lipofilik bir tür olup güncel literatür değerlendirildiğinde hakkındaki bilgi kısıtlıdır (8). Bugüne kadar bildirilen bakterinin etken olarak rol oynadığı mastit, cerrahi alan enfeksiyonu, osteomiyelit, pankreatik pannikulit, infektif endokardit bulunmaktadır (4 - 10). Uzamış hastane yatışı, geniş spektrumlu antibiyotikler ile tedavi ve hasarlanmış cilt mukozasının çok ilaç dirençli lipofilik bir tür olan *C. jeikeium* için risk faktörü olduğu bilinmektedir (11). Benzer olarak Hinic ve ark *C. tuberculostearicum*'un etken olduğu 18 hastaya ait serileri

incelendiğinde 15 hastanın uzun hastane yatışı olduğu, geniş spektrumlu antibiyotikler ile uzamış tedavi süreleri olduğu görülmüştür. Bu çalışma ile *C. tuberculostearicum*'un nosokomiyal enfeksiyonlarda oynadığı rol vurgulanmaktadır . Bu nedenle *C. tuberculostearicum*'un aynı *C. jeikeium* ve *C. urealyticum* gibi potansiyel çok ilaç dirençli suşlar gibi hastanede yatan hastalarda sık olarak cildi kolonize edebileceği bildirilmektedir (4). Olgumuzda da benzer olarak başvuru öncesi uzun bir hastane yatış öyküsü ve geniş spektrumlu antibiyotik kullanımı mevcuttur.

Diğer lipofilik Corynebacterium'lar gibi *C. tuberculostearicum* da birçok antimikrobiyal ajana dirençlidir. Hinic ve ark serilerinde suşların çoğunluğu 3 veya daha fazla kategorideki en az bir antimikrobiyale dirençli bulunmuş, tüm suşlar Vankomisine duyarlı bulunmuştur (4). Bakterinin azalmış membran geçirgenliği ve afinitede azalma nedeniyle B-laktam antibiyotiklere dirençli olduğu bildirilmiştir (12). Benzer olarak diğer bildirilen olgu sunumlarında da hastaların tedavisinde duyarlı olması nedeniyle vankomisin ve linezolid tedavilerinin tercih edildiği görülmüştür (4 - 10). Literatürde bildirilen 80 yaşında plevral ampiyem ile izlenen bayan bir hastada dekortikasyon amaçlı yapılan torakotomi sonrası yara yerinde açılma ile kendini gösteren cerrahi alan enfeksiyonunda *C. tuberculostearicum* ürediği, ilk olarak etkenin kolonizasyon olduğu düşünülerek piperasilin-tazobaktam tedavisine devam edildiği, ancak sonrasında yarada iyileşme olmaması üzerine Coryneform bakterileri de kapsaması için vankomisin eklendikten sonra hastanın iyileştiği bildirilmiştir (7). Diğer bir olguda 39 yaşında bir bayan hastada mastit nedeniyle yapılan drenaj sonrası alınan kültürde *C. tuberculostearicum* ürediği, hastaya antibiyogramdaki duyarlılığa göre vankomisin başlandığı tedavinin 7 güne tamamlandığı belirtilmiştir (1). Pankreatik pannikulit tanısı alan bir hastada ise yara yerinde *C. tuberculostearicum* ürediği, başlanılan linezolide tedavisi sonrası lezyonun kaybolduğu bildirilmiştir (9).

Literatürde *C. tuberculostearicum* enfeksiyonlarına ait bir çalışmada 8'i biyopsi materyali, 3'ü aspirat, 3'ü derin doku örneği, 2'si yüzeyel doku örneği, 2'si idrar olmak üzere toplam 18 örnekte *C. tuberculostearicu*m ürediği ve tüm suşların vankomisin, linezolide ve daptomisin duyarlı olduğu bildirilmiştir (4). Ortopedik en-

feksiyonlarda corynebacterium türlerinin araştırıldığı bir çalışmada 97 hastaya ait toplam 128 örnekte coryneform bakteri (26 *C. tuberculostearicum*) ürediği ve bu bakterilerin tümünün linezolide ve vankomisine duyarlı olduğu bildirilmiştir (5). Vankomisinin özellikle diğer Coryneform bakterilerde de etkili olması nedeniyle antibiyogram sonucu beklenen Coryneform bakterilerin neden olduğu ciddi enfeksiyonlarda ampirik olarak kullanımının düşünülebileceği belirtilmektedir (1, 11). Olgumuzda da cerrahi tedaviye ek olarak linezolide kullanılmış ve hastada tam bir kür elde edilmiştir.

Günümüzde *Corynebacterium* türleri hastane enfeksiyonlarının ve immün sistemi baskılanmış olanlarda ortaya çıkan enfeksiyonlarda etken olabileceği bilinmektedir. Klinik örneklerden izole edilen Corynebacterium türleri sıklıkla kontaminant olarak kabul edilmektedir. Ancak herhangi bir gram pozitif basil izolasyonunda mutlaka klinik ile korelasyonu değerlendirilmelidir (1). Olgumuzda olduğu gibi uzamış hastane yatışı olan ve altta yatan ciddi komorbiditeleri olan hastalarda çoklu direnci olan suşlar akla gelmeli ve *C. tuberculostearicum*'un enfeksiyon etkeni olabileceği göz önünde bulundurulmalıdır. Hastadan bilgilendirilmiş onam alındı.

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DERLEME/ REVIEW

PREEKLAMPSİ PATOFİZYOLOJİSİNDE ROL OYNAYAN MOLEKÜLER YOLAKLAR

MOLECULAR PATHWAYS THAT PLAY A ROLE IN THE PREECLAMPSIA PATHOPHYSIOLOGY

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ÖZET

Preeklampsi (PE) gebeliklerin yaklaşık % 4-5'inde görülen, hipertansiyon ve üriner proteinüri ile seyreden obstetrik bir hastalıktır. Maternal ve fetal komplikasyonlara neden olabilmektedir. PE alanında çok sayıda yapılan araştırmalara rağmen altta yatan patogenez hala belirsizdir. Ancak ilgili bu araştırmalar ile birlikte PE'yi tetikleyen çok sayıda moleküler mekanizma olduğu sonucuna varılmıştır. Bu moleküler mekanizmalardan yola çıkarak PE iki evrede incelenebilir. İlk evre anormal plasentasyon nedeniyle oluşan plasental iskemidir. İkinci evrede ise iskemik plasentadan dolaşıma salınan nekrotik ve apoptotik faktörler, sistemik inflamasyon ve endotelyal disfonksiyona neden olur. Plasental hücrelerden salınan bu faktörlerden biri de antianjiyogenik faktörlerdir. Ayrıca PE'de antioksidan ve prooksidan mekanizmalarda rekürren iskemi reperfüzyon hasarından dolayı olduğu düşünülen dengesizlik mevcuttur. PE'deki sistemik inflamatuar yanıt maternal immün hücrelerin trofoblastlarla teması sonucu ortaya çıkan immün yanıtla ilişkilendirilmektedir. Bu derlemenin amacı PE'ye giden yolda rol oynayan mevcut moleküler mekanizmaları göstermektir. İlgili moleküler mekanizmaların daha iyi anlaşılması doğrutusunda gelişen PE patogenezine dair yeni görüşler, ileriki çalışmalara ışık tutacaktır.

ANAHTAR KELİMELER: Preeklampsi, Anjiyogenik proteinler, İnflamasyon, Plasentasyon.

ABSTRACT

Preeclampsia (PE) is an obstetric disease seen in approximately 4-5% of pregnancies progressing with hypertension and urinary proteinuria. It may cause maternal and fetal complications. Despite numerous researches in the field of PE, the underlying pathogenesis remains unclear. However, with these related studies, it has been concluded that there are many molecular mechanisms that trigger PE. Based on these molecular mechanisms, PE can be examined in two stages. The first stage is placental ischemia caused by abnormal placentation. In the second stage, necrotic and apoptotic factors released from the ischemic placenta into the circulation cause systemic inflammation and endothelial dysfunction. One of these factors released from placental cells is the antiangiogenic factor. Also, there is an imbalance in the antioxidant and prooxidant mechanisms that are thought to be due to recurrent ischemia reperfusion injury in PE. The systemic inflammatory response in PE is associated with the immunological response resulting from the contact of the maternal immune cells with trophoblasts. The aim of this review is to present the current molecular mechanisms implicating the pathway leading to PE. The development of new insights into the pathogenesis of PE in conclusion of a better understanding of the relevant molecular mechanisms will guide further studies.

KEYWORDS: Preeclampsia, Angiogenic Proteins, Inflammation, Placentation.

INTRODUCTION

Preeclampsia (PE) is a complication seen in approximately 4-5% of pregnancies (1). Despite promising therapies, it remains a leading cause of fetal and maternal morbidity and mortality (2, 3). PE criteria are ≥140 mmHg systolic blood pressure or ≥90 mmHg diastolic blood pressure after 20 weeks of pregnancy in a previously normotensive patient and ≥300mg proteinuria in 24-hour urine, 0.3 g/g protein: creatinine ratio or urine dipstick +1. In the updated classification, proteinuria criterion is not essential for diagnosis in the presence of other end organ damage, such as thrombocytopenia, impaired liver function, new renal failure, pulmonary edema or recent cerebral/visual disturbances. PE with severe features is any of the following: blood pressure ≥160/110 mmHg twice; platelet count <100,000 per microliter; impaired liver function as evidenced by two-fold elevated liver enzymes based on normal concentration or severe persistent right upper quadrant / epigastric pain; > 1.1 mg/dl (97.2 µmol/l) serum creatinine level with renal failure or doubling the serum creatinine level; pulmonary edema or new-onset cerebral, visual disorders (4).

Although significant progress has been made in the field of PE, the underlying pathogenesis remains unclear (4). The pathogenesis of PE can be examined in two stages. The first stage is placental ischemia caused by abnormal placentation. In the second stage, necrotic and apoptotic factors released from the ischemic placenta to circulation cause systemic inflammation and endothelial dysfunction. Abnormal placentation occurs in the early stage of PE without showing any clinical features. Placental ischemia/hypoxia, oxidative stress and immune mechanisms are involved. This is followed by maternal clinical syndrome with cardiovascular and renal findings. PE is defined as a multiorgan syndrome (5).

Abnormal Placentation

Transformation of the spiral arteries is assumed to be necessary to ensure the blood flow requirement in the placenta and to override the maternal vasomotor control (4). PE pathology begins with abnormal formation of maternal uterine spiral arteries (6).

Spiral arteries that do not complete remodeling cause insufficient blood flow to the placenta at high pressure. The resulting placental ischemia/hypoxia causes the distortion of the placental villous structures, oxidative stress and following uteroplacental insufficiency (5).

Placental Ischemia and Hypoxia

Molecular mechanisms that mediate spiral artery remodeling are controversial. During normal pregnancy, cytotrophoblasts convert the adhesion molecules from the epithelial cell type to the vascular endothelial cell type. This transformation is necessary for the invasion of uterine spiral arterioles by cytotrophoblasts (7). Cytotrophoblasts that do not invade maternal spiral arterioles do not express endothelial adhesion markers such as vascular endothelial-cadherin (VE-cadherin) and alpha-V beta-3 (αVβ3) integrin, which are normally expressed by invading cytotrophoblasts (8). In human villus explants at 5-8 weeks of gestation, low oxygen tension triggers cytotrophoblast proliferation via hypoxia-inducible factor 1-alpha (HIF1α) (4). HIF1α and hypoxia-inducible factor 2-alpha (HIF2α) are products of oxygen sensing pathway. They regulate the expression of hypoxia-derived genes such as erythropoietin, vascular endothelial growth factor (VEGF) and nitric oxide (NO) synthase. The expression of HIF1α in human placentas increases in the first trimester. Permanently elevated levels of HIF1α may indicate placental stress and the development of PE (9). Studies have shown that preeclamptic placentas over-express HIF1α, HIF2α and do not reduce their expression on oxygenation. The reason for the consistently increased expression of HIF in preeclamptic placentas remains unclear, but it is associated with the pathway of 2-methoxy estradiol (2-ME) produced by catechol-O-methyltransferase (COMT) (4). 2-ME is an estradiol metabolite that increases during pregnancy and inhibits HIF1α (10).

Oxidative Stress

There is an imbalance between antioxidant and prooxidant mechanisms in PE. This imbalance is thought to be due to defective spiral artery remodeling which causes recurrent ischemia-reperfusion injuries (11).

The heme oxygenase (HO) pathway is an important mediator of oxidative stress. HO has three isoforms. HO1 and HO2 oxidize heme to produce biliverdin and carbon monoxide (CO). In the study, HO1 has been shown to be perivascular localized in human placental vessels and its induction has been shown to attenuate tumor necrosis factor (TNF) mediated cell damage. At the same time, the HO1 protein level decreased significantly in the preeclamptic placenta compared to the normotensive control placentas. In addition, adenoviral overexpression of HO1 in endothelial cells has been shown to inhibit placental release of antiangiogenic factors (4). In another study, induction of HO1 by cobalt protoporphyrin in PE animal model reduced sFlt-1 / VEGF (vascular endothelial growth factor) ratio and hypertension which is induced by placental ischemia (12).

Glrx (Glutaredoxin 1) is a cytosolic enzyme that reduces S-glutathionylation. It is an antioxidant enzyme whose localization is shown in the endometrium (13). Glrx activates the S-glutathionylation of nuclear factor kappa B (NFκB) components. With an increase of Glrx, the nuclear binding proteins of NFκB p65 / p50 increase. NFκB induces an increase in sFlt-1 with the Wnt5a pathway and inhibits angiogenesis in ischemia studies (14). Glrx, NFκB increase in PE has also been shown in various studies (15, 16).

Immune Mechanisms

The systemic inflammatory response in PE is associated with immunological response to the direct contact of the maternal immune cells with trophoblasts in the feto-maternal interface. This contact allows the tolerance of the maternal immune cells, resulting in trophoblast invasion or elimination of the feto-maternal interface. Also, this contact leads to the release of several factors, directly or indirectly. These are soluble factors (eg. cytokines), immunosuppressants (eg. progesterone and prostaglandins), specific suppressor molecules [eg. Human leukocyte antigen (HLA-G) and HLA-E], tolerogenic molecules [eg. TGF-β1 and interleukin (IL) -10] and immunomodulator products [eg. indoleamine 2,3-dioxygenase (IDO), Fas ligand (FasL) and TNF-associated apoptosis inducer ligand (TRAIL)] (17).

In the first trimester, 70% of the decidual lymphocytes are CD56bright CD16- NK (natural killer) cells. Other immune system cells in decidua are; 20% monocyte / macrophage, 10% T cells and 2% dendritic cells (18). These dNK cells are functionally different from the CD56dim, CD16+ NK cells in peripheral circulation. CD56bright CD16- dNK cells synthesize various chemokines, cytokines and growth factors and reduce cytotoxicity (17).

The recognition of HLA ligands expressed on trophoblasts by the maternal immune system induces immune response that controls trophoblast invasion and placentation via various factors (17). Extravillous cytotrophoblasts express an HLA class Ia molecule (HLA-C) and HLA class Ib molecules (HLA-E, HLA-F and HLA-G) (19). Fetal trophoblasts do not express HLA-A, HLA-B and MHC-II, which protect them from T cells (18). dNK and T cell subgroups express killer cell immunoglobulin-like receptors (KIRs) which interact with HLA ligands. Polymorphic KIRs are named according to their activator and inhibitory properties. While there are many activator receptors in maternal KIR haplotype B, there are only inhibitory receptors in KIR haplotype A (20). The interaction of KIR haplotype B and HLA-C stimulates the production of immunoregulatory cytokines and angiogenic factors from dNK cells (17). In particular, some of these factors serve as the major chemoattractants for trophoblasts [eg. CXCL10 / IP-10 (IFNγ induced protein), CXCL8 / IL-8, CXCL12 / SDF-1 (stromal cell derived factor) and CCL2 / MCP-1 (monocyte chemoattractant protein 1)] (18). These dNK cell-mediated factors provide sufficient trophoblast invasion and remodeling (17). HLA-G interacts with KIR2DL4, ILT2, ILT4 receptors in dNK cells and interacts with CD8 in T cells. This recognition causes apoptosis of CD8 + T cells via Fas / FasL pathway and protects trophoblasts from T cell-mediated cytotoxicity (21).

Interaction that can lead to a strong inhibition of KIRs, inhibits NK cell activation. This event is thought to play a role in PE. Inadequate activation of dNK cells leads to lysis of trophoblasts without HLA-G. The loss of trophoblasts that should invade the spiral arteries prevents placental development and spiral artery remode-

ling. For adequate activation of dNK cells, the haplotype B KIR receptor-ligand interaction is more important than the inhibitor haplotype A. Binding of KIR-AA haplotype without activator receptor to fetal HLA-C2 increases the sensitivity of PE. In PE, the interaction of KIR-AA and HLA-C causes defective angiogenic factors and increased antiangiogenic factor [sFlt-1, sEng (soluble endoglin)] release from dNK cells. At the same time, immunomodulators (IDO, TRAIL), CD30 (TNF receptor family, Th2 polarization marker) and HLA-G expression are also reduced (17).

Decidual macrophages existed throughout pregnancy and tissue repair, are associated with angiogenesis factors [eg. metalloproteinases (MMPs), vascular endothelial growth factor (VEGF)]. M2-type macrophages induce the expression of immunosuppressive cytokines (IL-10, IL-35), regulatory T cells (Treg) and phagocytose apoptotic trophoblast cells to prevent the release of proinflammatory cytokines. It also inhibits the cytotoxic function of dNK cells. Thus, it provides an immuntolerogenic environment. The polarization of M2 macrophages depends on Th2 immunosuppressive cytokines, which are present in low concentrations in PE (17). Studies have shown that decidua-specific VEGF stimulates the transition of macrophages into immunomodulatory M2-type macrophages. In PE, increased levels of sFlt1 prevent VEGF signal and M2 type macrophage population (22).

Normal placentation is also characterized by a profile of T cells and their cytokines. Decidual T cells are predominantly CD8 + phenotypes. While they regulate trophoblast invasion, CD4 + Treg cells increase the tolerance to the fetus. Decidual cells (DCs) are also thought to play a role in the differentiation of CD4 + T cells to the Th2 phenotype and in the regulation of dNK cell proliferation. Type 2 T helper (Th2) cytokines are predominant in the second trimester (eg. anti-inflammatory IL-4, IL-10, IL-13). Progesterone, estradiol, prostaglandin D2 and leukemic inhibiting factor promote the development of Th2 profile. In contrast, PE is characterized by an imbalance of Th1 cells and their associated cytokines, such as IFNγ. Upregulation of T helper 1 (Th1) cytokines containing IL-2, IL-6, IL-8, IL-12, TNF-α, IFN-γ and IL-17, and downregulation in IL-4, IL-10 production are observed in PE (17). This imbalance probably affects poor placentation and resulting maternal inflammation and endothelial dysfunction (4). The effective mediators of Th1 / Th2 transformation are not well understood (17).

IL-33 is a cytokine from the IL-1 family and induces Th2 response by binding to its receptor ST2 in normal pregnancy. sST2, in soluble form, triggers a predominant Th1 response with IL-33 inhibition. IL-33 and sST2 are thought to play a role in the pathogenesis of PE. In studies, IL-33 inhibition adversely affects trophoblast migration and invasion (23, 24).

Th1 cytokines (TNF-α, IL-2, IL-12, IL-18, and IFNγ) induce trophoblast apoptosis. Also, IFNγ and IL-12 inhibit angiogenesis. TNF-α from Th1 cytokines inhibits NO release and induces endothelial dysfunction (17). The chronic increase of proinflammatory cytokine TNF-α stimulates sFlt-1 secretion (25).

Th17 cells are the subgroup of CD4 + lymphocytes that produce proinflammatory IL-17. Some of the IL-17-producing cells have also been shown to produce Th1 cytokines (eg. IFNγ) (17). These are called Th17 / Th1. A small number of cells produce IL-4 together with IL-17, which is referred to as Th17 / Th2 (26). Pathogenic decidual Th17 / Th1 cells exist in unexplained recurrent abortions while Th17 / Th2 cells are present in healthy pregnancy. Treg and Th17 pass through similar stages of development. The increase at the ratio of Th17 to Treg cells in peripheral blood in PE is responsible for the increased maternal inflammatory response to the fetus (27). The proinflammatory cytokines and the predominant Th1 environment in the PE may be associated with Th17 differentiation. IL-1β and IL-6 inflammatory environment may contribute to the transformation of Treg cells into Th17. Also, dNK cells play a role in Th17 transformation and inflammatory response suppression by IL-10 and TGFβ1 (17). Another aspect of impaired immune tolerance in PE is reduction of CD4 + / CD25 + / FoxP3 + regulatory T cells (Treg) in peripheral blood and decidua (28). The proinflammatory environment in PE is thought to affect the Treg population (29). There are also studies on the effect of IL-33 on Treg function (30).

Complement activation from immunological mechanisms stimulates monocytes, leading to

the release of antiangiogenic factors. Recurrent pregnancy losses, preterm birth and PE are associated with complement activation, especially C5a, which increases the anti-angiogenic factor of sFlt-1 (17). It is also found that the possibility of developing PE was higher in women with higher levels of complement Bb (alternative pathway marker) (31). In another study, C4a deficiency and C4bp (classical pathway inhibitor) deposits are shown in preeclamptic placenta (17).

Maternal Syndrome

The symptoms of PE are not limited to the placenta. It can cause widespread effects that can be seen as maternal syndrome (4). In the second stage of PE, placental ischemia and increased placental oxidative stress result in severe systemic inflammation and endothelial dysfunction manifested by new-onset hypertension and proteinuria. Oxidative stress results in placental necrosis and apoptosis. The trophoblast microparticles shedding into maternal circulation indicate ischemia and apoptosis in placental cells. These microparticles create an inflammatory load and indirectly affect endothelial function (17).

Biochemical Factors

There are several possibilities for stimulating inflammation in PE. Some of these possibilities are factors released by endothelial injury. These are proinflammatory cytokines, oxidative stress markers, thrombomodulin, fibronectin, endothelin-1 and Von Willebrand factor. Some other factors release from placental cells such as antiangiogenic factors (17). Protein-toxic aggregates such as transthyretin also increase in PE. Transthyretin is released from the trophoblasts through vesicles and is transported to outside of the cell. Transthyretin in these vesicles can lead to cellular stress response by providing targeted delivery of toxic proteins to other maternal organs. Therefore, it is thought to play a role in the response of inflammation in PE (32).

Studies support the pathological role of imbalance in circulating angiogenic factors in the etiology of the maternal syndrome (4). VEGF is an endothelial mitogen factor and proangiogenic stimulating vasculogenesis. It also affects vascular permeability and vasodilatation. VEGF is mostly produced from the placenta, also from the monocyte and endothelium. Specific receptors are the vascular endothelial growth factor receptor (VEGFR1 / Flt-1) in the placenta and the VEGFR2 / kinase insert domain receptor (KDR) in the vascular endothelial cell (33). VEGF activates eNOS (endothelial NO synthase) by increasing intracellular calcium through PI3K (phosphatidylinositol 3 kinase) / Akt signaling pathway. Another pathway also activates MAPKs (mitogen-activated protein kinases) and PLA2 (phospholipase A2) via PKC (protein kinase C). As a result, PGI2 (prostacyclin) increases. Thus, vasodilatation and permeability are increased by PGI2 and NO (34). TGF-β1 also plays a role in angiogenesis by regulating VEGF expression (35). PlGF is a member of the VEGF family produced by trophoblasts. It is also released by the endothelium (36). PlGF is involved in vasculogenesis and vasodilatation via binding Flt-1 (33). In normal pregnancy, PlGF circulation begins at the 8th week and reaches its maximum concentration towards the end of the 2nd trimester and decreases until delivery (36). PlGF concentration decreases in PE (33).

Antiangiogenic sFlt-1 / sVEGFR-1 is produced by placenta and passed into maternal circulation. sFlt-1 increases in the third trimester of normal pregnancy. sFlt-1, overexpressed from endothelial cells and trophoblasts of ischemic placenta in PE, induces maternal endothelial dysfunction leading to preeclamptic symptoms (33). sFlt-1 is a soluble variant of membrane bound receptor VEGFR1 that binds to proangiogenic proteins VEGF and PlGF; therefore, sFlt-1 acts as a ligand trap, reducing free VEGF and PlGF. Nonfunctional VEGF which could not bind to its receptor leads to increased VEGF in preeclamptic placenta. High levels of sFlt-1 binding VEGF and PlGF cause endothelial cell dysfunction in various organs (4). It has also been shown that sFlt-1 indirectly inhibits VEGF mediated NO synthesis, thus leading to increased reactive oxygen products and vasoconstriction (2). Increased sFlt-1 causes placental insufficiency via inhibiting cytotrophoblast differentiation and invasi-

on (17). Syncytial fragments shedding into the maternal circulation have been described as an important source of placental sFlt-1 in PE (4).

sEng is an antiangiogenic protein that inhibits the TGFβ signaling pathway (2). ENG (endoglin) is a membrane glycoprotein involved in the TGF beta receptor complex (TGF-β1 and TGFβ3). It is produced by endothelium and monocytes. Trophoblasts in the placenta are also an important source of ENG. The primary roles of ENG are angiogenesis, endothelial cell differentiation and vascular tone regulation via eNOS (37). The proteolysis of the extracellular part of the ENG creates the sEng that limits eNOS due to the TGF-β function (2). TGF-β is an anti-inflammatory and vasodilatory factor and its elimination with sEng leads to vasoconstriction and endothelial dysfunction (33). sEng is highly expressed in PE and eclampsia (4). sEng regulators are not known exactly. However, similar to sFlt-1, angiotensin II receptor (AT-1) autoantibodies stimulate the release, while HO-1 inhibits the release (2). sEng, as in sFlt-1, is expressed in hypoxia and oxidative stress conditions but is also stimulated by inflammatory TNF-α and IFNγ released from endothelial and placental cells (38). Carbon monoxide (CO), the HO-1 metabolite, inhibits sFlt-1 and sEng expression. Due to HO-1 role in the pathogenesis of PE, women with PE have less CO exhalation than normal pregnants (39).

Hypertension

Hypertension occurring in PE does not appear to be mediated by the renin-angiotensin-aldosterone system (RAAS), because renin, aldosterone and angiotensin II levels decrease in PE compared to physiological increase in normal pregnancy. This hypertension may develop with antiangiogenic factors and angiotensin II type 1 receptor agonistic autoantibodies (AT1-AA) (4). Increased production of various mediators such as sFlt-1, sEng, STBMs(syncytiotrophoblast microparticles), inflammatory factors, AT1-AA and reactive oxygen species (ROS) released by the hypoxic placenta causes vascular endothelial dysfunction. In addition, in PE, NO, PGI2 levels which are endothelium-derived vasodilators in the plasma decrease and vasoconstrictors such as endothelin-1 (ET-1), thromboxane A2 (TXA2), Ang II and AT1R increase (33). Upregulation of the bradykinin (B2)

receptor and the heterodimerization of B2 with AT1s are thought to contribute to hypertension and increased angiotensin II response in PE. However, there is no human experimental study of the pathway yet (40). The hydrogen sulfide (H2S) system is another important pathway in vasodilatation and angiogenesis. H2S decreases in PE. Because placental expression of cystathionine lyase, the enzyme responsible for the production of H2S, has been reduced (4).

The mechanisms that are effective in the development of PE are not fully known. However, ischemic environment, oxidative stress, released immunological and biochemical factors, inflammation and endothelial dysfunction are factors triggering PE. This review summarizes our current understanding of the molecular mechanism of PE. The development of new insights into the pathogenesis of PE in conclusion of a better understanding of the relevant molecular mechanisms will guide further studies.

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